UTILIZATION OF HEALTH CARE SERVICES FOR CHILDREN IN LOW AND MIDDLE INCOME COUNTRIES: ITS DETERMINANTS AND CHILD HEALTH OUTCOMES

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Editorial: Utilization of healthcare services for children in low and middle-income countries: Its determinants and child health outcomes

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Editorial on the Research Topic
Utilization of healthcare services for children in low and middle-income countries: Its determinants and child health outcomes

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Over the past two decades, the children's health systems worldwide have started paying increasing attention to the healthcare infrastructure, especially in low- and middle-income countries, by debating and focusing more on disease prevention rather than curative care approaches. Even though a declining global trend in child morbidity and mortality has been observed, a recent under-5 mortality rate estimate of 64.6 per 1,000 live births from all 137 low- and middle-income countries (excluding China) is still far from sustainable development goals (SDGs) (1). Proper utilization of services in functional healthcare systems that can prevent such events depends on various critical issues, including quality and accessibility of the current healthcare system, timely intervention, geography, cost, insurance, policy, and other social determinants. The unavailability of complete healthcare infrastructure and underutilization of available functional healthcare systems is the foremost cause of poor child health quality and premature death in low and middle-income countries. Further, healthcare expenditure is another potential barrier to health services utilization in low- and middle-income countries.

Contribution to the field

As highlighted under the call for papers for the special topic titled "Utilization of Healthcare Services for Children in Low and Middle-Income Countries: Its

Determinants and Child Health Outcomes" under the Child and Health section, the editorial team welcomed contributions that could encompass numerous study themes including status and trend of child healthcare utilization; social determinants of underutilization; variation in the geographical locations, healthcare infrastructure and accessibility, and their associations with the child health outcomes; critical challenges as well as public and private partnership model for the accessibility of child healthcare services; healthcare cost and insurance; institutional policies; and global health partnerships towards the progress of complete and central healthcare infrastructure to increase child healthcare services utilization. Such an attempt could be essential to identify the barriers to healthcare accessibility in low and middle-income countries, examine its' consequences on child health outcomes, and illuminate the potential solutions. Articles submitted on these issues are critical for health promotion, disease prevention, and developing central healthcare infrastructure. Most of this special topic's contributors are pediatricians or public health researchers. This area considers a comprehensive approach to inclusiveness of acceptance.

The purpose of this research topic was to collect the current evidence on the healthcare services utilization for children in low and middle-income countries. It is worth mentioning and emphasizing the numerous emerged studies under this special edition that significantly contributed to the scientific field and future policy implementation. Some interesting findings were explored in the context of this research topic.

Child mortality remains higher in the developing world compared to the developed world. Pham et al. (2), using the integrated Health and Demographic Surveillance System (iHDSS), estimated child mortality at the sub-national level in Papua New Guinea. The authors concluded that contextual factors such as women's fertility, childhood communicable diseases, and immunization services could have a critical role in explaining the variations in child mortality. Apart from communicable diseases, genetic diseases also lead to disability and death. Bu et al. (3) estimated the overall, demographic, and region-specific burden of down syndrome between 2010 and 2019 among children using 2019 global burden of disease (GBD) data. This study found a higher and heterogeneous burden of down syndrome in selected regions of Asia, Europe, Latin America, and Africa, which certainly indicates the higher burden in the regions with poor health infrastructure.

Two studies focused on identifying the social determinant of healthcare utilization using data from nationally representative health surveys in India and China (4, 5). Specifically, using the fourth round of National Family Health Survey data, Madhumita and Soumitra (4) highlighted the disparities in maternal and child healthcare (MCH) among disadvantaged and advanced social groups in three states of India. They found that the families belonging to the schedule caste/tribe were less likely to receive the antenatal checkup (ANC) and complete immunization for their children. Limited accessibility and poor infrastructure came out as other barriers to the under-utilization of these healthcare services. However, Jing et al. focused on assessing the effect of parental social integration on the physical examination service utilization for young migrant children in China using the 2014 National Internal Migrant Dynamic Monitoring Survey (5). Using four different dimensions of social integration, the authors found that parental social integration was associated with migrant children's physical examination utilization. Concerning structural integration, the authors found that the migrant parents who participated in the society and those who live with registered residents were more likely to use the migrant children's physical examination service. This study provided evidence on the other facets of social integration, such as sense of self-identity, and other parameters such as parents' movement area and duration in the inflow area, children's age, and their link with the utilization of the physical services. More specifically, concerning economic integration, the insured parents were positively associated with the migrant children's physical examination service use.

Discharged against medical advice (DAMA) is common in low-resource countries and causes poor health outcomes among hospitalized patients. An interesting study on the economic burden of hospital costs and the role of medical insurance on families with type 1 diabetes mellitus children in China was carried out by Wang et al. (6). The authors concluded that hospitalization-related costs are a substantial economic burden among the uninsured and low-income insured families. Poverty and lack of affordable healthcare may push parents to get their children DAMA. With a focus on the impact of spiritual/faith-based interventions (FBIs) on DAMA in Nigeria, Alao et al. (7) documented an open-level randomized controlled trial protocol to determine the effectiveness of FBIs on the rate of DAMA in neonates. DAMA is common in low- and middle-income countries and one of the prime reasons for neonatal mortality and other adverse outcomes such as medical complications and readmission. Findings from this study could help establish routine care in Nigeria. Attempting similar investigations in other low-performing countries could be essential to understand lowering the rate of DAMA. Additionally, free healthcare accessibility and health-related educational intervention among the parent may help reduce the incidence of DAMA in low- and middle-income countries.

Lack of health service utilization and self-medication by parents is a significant threat to child health. The high burden of self-medication among children is well-known in developing countries. Using a national survey, Yuan J et al. explored the burden and associated factors of self-medication in the pediatric population in China (8). Authors observed a drastically huge burden (24.2%) of self-medication in children under 12 years. They identified that lower parental educational

attainment is a significant risk factor for self-medication. Target interventions and educational programs among the parent are essential to lower self-medication and improve drug safety.

Low- and middle-income countries also have a high proportion of malnourished children. Considering 106 villages from Tumkur District of Karnataka state in India, Kashyap et al. found a significant decline in the prevalence of severe wasting and stunting with an overall improvement in the nutritional status among the children of 6 months to 6 years of age who consumed the spirulina chikki/granules supplementation for longer duration (9). Implementing such nutritional intervention in the targeted geographical areas with a higher prevalence of malnourishment in low- and middle-income countries is a commendable step to harmonize wellbeing.

Along with proper nutrition and healthcare utilization, it is crucial to have a reference range of parameters for a specific population. A suitable birthweight reference could be helpful for many purposes, such as establishing new treatment models, vaccine intervention, and other public health policy implementations. Wu et al. addressed the new birthweight reference to assess the newborns by gestational age in China by conducting a population-based study (10).

According to the recent report by World Health Organization (WHO), about 100 million people are pushed into extreme poverty every year mainly due to out-of-pocket health-related expenditure (11). "To make health for all a reality" is a prime agenda for SDGs of the WHO, and the healthcare system needs improvement in low- and middle-income countries to reach the universal health coverage target of 3.8 defined by the WHO. A single blueprint cannot be used to straighten out the inadequacies and underutilization of a perfect healthcare system. Strengthening the healthcare systems in low-resource countries is an ongoing developmental process.

Author contributions

BT and MP worked on this special research topic and reviewed the manuscripts to draft this editorial manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The Effect of Parental Social Integration on the Physical Examination Utilization for Young Migrant Children: A National Cross-Sectional Study in China

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Purpose: Physical examination is a key component of child health management. Migrant children are a vulnerable group with lower healthcare service utilization, and this study aims to explore the effect of parental social integration on the physical examination service utilization for young migrant children under 6 years old in China.

Method: This study conducted a secondary data analysis of the 2014 National Internal Migrant Dynamic Monitoring Survey in China. A total of 2,620 participants were included in this study. A total of 22 indicators were selected to measure social integration. Multivariate logistic regression was used to explore the association between parental social integration and physical examination use of young migrant children.

Results: More than half (66.4%) of the migrant children aged 0–6 years had used free physical examination. Parental social integration, especially structural integration, was associated with the physical examination utilization of migrant children. Specifically, those migrant children's parents who had medical insurance ($P < 0.05$; OR = 1.29), who had participated in local activities ($P < 0.001$; OR = 1.98), who had registered local residents as neighbors ($P < 0.05$; OR = 1.34), and who had a deep sense of self-identity ($P < 0.05$; OR = 1.09) were more likely to take children to use physical examination.

Conclusions: This study provided evidence that parental social integration was associated with migrant children's physical examination utilization, and this association was multifaceted, lying in the dimensions of economic, structural, and psychological integration. Improving the social integration of migrant parents would be effective to enhance the migrant children's healthcare service utilization.

Keywords: social integration, social factors, child health services, parent-child relations, transients and migrants

INTRODUCTION

With the rapid development in China, the social-economic disparity across regions has caused a considerable amount of the internal migrant population. The migrant population was approximately 286 million in 2020, accounting for 20.3% of China's total population (1). Recently, more and more migrant parents bring their children together with them to the sites where they work, leading to an increasing new group called "migrant children". In 2015, there were about 34.26 million migrant children aged 0–17 years, accounting for 12.9% of the total number of children in China (2). Correspondingly, the number of migrant children aged 0–5 years has been continually on the rise, from 6.64 million in 2000 to 10.53 million in 2015 (3).

Under the current household registration (Hukou thereafter) system, the migrants have limited access to social welfare, including housing, employment, health care, and public health services (4). Migrant children being a vulnerable group, are more likely to face higher health risks and have limited access to health care services than non-migrant children (5, 6). The New York Declaration of the United Nations General Assembly urged all countries to protect the human rights and freedoms of migrant children and to have access to basic services (7, 8). To improve the accessibility to health care services for migrant children, China launched health management for migrant children aged 0–6 years in 2013 (9). Physical examination is a key component of child health management, which is provided free of charge to children in each period, enabling early detection, diagnosis, and treatment of children's disease, ultimately reducing the occurrence of diseases and improving the quality of life of children.

Nevertheless, migrant children's health service utilization was associated with parental characteristics. A study found that parental birthplace affected access to preventive health services of children and adolescents in the United States (10). A review indicated that the Expanded Program on Immunization's vaccination of migrant children relied on the parental decision (11). However, previous studies mainly focused on the influence of parents' socio-demographic characteristics (such as educational attainment, socioeconomic status) on the healthcare services use among the migrant children (12), few studies have explored whether parental social integration affects health care service utilization of their migrant children. Social integration refers to the process of integrating newcomers into the social structure of the host regions. It is one of the most important factors affecting the health status and health service utilization of migrants, and also can be attributed to the root cause of many related problems in the process of migration (13, 14).

Therefore, this study aims to explore the effect of parental social integration on the physical examination utilization of young migrant children in China. To do so, this study has the following objectives. First, assess the status of the physical examination for young migrant children. Second, study the association between parental social integration and physical examination utilization among young migrant children.

METHODS

Data Source and Sample

This study conducted a secondary data analysis of the 2014 National Internal Migrant Dynamic Monitoring Survey (NIMDMS) (15). The survey has been funded and organized by the Nationally Population and Family Planning Commission of the People's Republic of China since 2009 (NPFPC). The data in 2014 was chosen because it was the most comprehensive thematic survey on the social integration of the migrant population in China. The 2014 NIMDMS collected data from a nationally representative sample of Chinese migrants aged 15–59 years old who did not have local Hukou and had settled in the host cities for more than 1 month, selected using stratified three-stage probability proportionate to size sampling.

For this study, we included data from respondents whose children were born after June 2007 and settled in the local city for more than 1 year. In addition, if the respondents had more than one migrant child who met the inclusion criteria, the youngest one was selected. Finally, a total of 2,620 respondents were included in the analysis.

Measurement

1. Dependent variables

The utilization of physical examination among migrant children was measured by the respondent's self-reported question: "Have your children had received a free health physical examination in the past 12 months?". If the answer was "No", the utilization of physical examination was coded as "no", otherwise it was coded as "yes".

2. Social integration

Based on the existing social integration indicator systems proposed by Zhou and Yang (16, 17), combined with the questionnaire used in the survey, this study measured through four dimensions: economic integration, structural integration, cultural integration, and psychological integration. Among them, economic integration was measured by three indicators: average monthly household income, occupation, and medical insurance; structural integration was measured by two indicators: activity participation and types of neighbors. The indicators of cultural integration and psychological integration were extracted by principal component factor analysis (See **Supplementary Table 1**). Cultural integration was measured by indicators 1–4, with a total score ranging from 5 to 20 points, the higher score indicated the worse integration. Psychological integration was measured by contact intention (indicators 5–9), self-identity (indicators 10–14), and self-perception (indicators 15–17), where the total scores of contact intention and self-identity ranged from 5 to 20 points, with higher scores indicated better integration, and the total scores of self-perception ranging from 3 to 12 points, with higher scores indicated worse integration.

TABLE 1 | Socio-demographic characteristics of migrant children and their parents in China, 2014.

Characteristics	Frequency (%)	Physical examination		*P*-value
		Yes	No	
Total	2,620 (100.0)	1,740 (66.4)	880 (33.6)	
Children's characteristics				
Gender				0.271
Boy	1,527 (58.3)	1,001 (65.5)	526 (34.5)	
Girl	1,093 (41.7)	739 (67.6)	354 (32.4)	
Age (years)				<0.001
≤3	1,366 (52.1)	957 (70.1)	409 (29.9)	
3-6	1,254 (47.9)	783 (62.4)	471 (37.6)	
Duration in inflow areas (years)			0.304	
≤3	1,891 (72.2)	1,267 (67.0)	624 (33.0)	
>3	729 (27.8)	473 (64.9)	256 (35.1)	
One child				0.020
Yes	1,515 (57.8)	1,034 (68.2)	481 (31.8)	
No	1,105 (42.2)	706 (63.9)	399 (36.1)	
Parental characteristics				
Gender				0.187
Male	1,402 (53.5)	947 (67.5)	455 (32.5)	
Female	1,218 (46.5)	793 (65.1)	425 (34.9)	
Age (years)				0.205
<30	1,042 (39.8)	707 (67.9)	335 (32.1)	
≥30	1,578 (60.2)	1,033 (65.5)	545 (34.5)	
Educational attainment				0.038
Primary education or below	143 (5.5)	83 (58.1)	60 (41.9)	
Junior education	1,412 (53.9)	929 (65.8)	483 (34.2)	
Senior education or above	1,065 (40.6)	728 (68.4)	337 (31.6)	
Hukou				0.140
Rural	2,234 (85.3)	1,471 (65.8)	763 (34.2)	
Urban	386 (14.7)	269 (70.0)	117 (30.0)	
Marital status				0.217
Single	53 (2.0)	31 (58.5)	22 (41.5)	
Married	2,567 (98.0)	1,709 (66.6)	858 (33.4)	
Movement area				0.001
Inter-provincial	1,370 (52.3)	871 (63.6)	499 (36.4)	
Intra-provincial	1,250 (47.7)	869 (69.5)	381 (30.5)	
Duration in inflow area (years)			0.006	
1-	1,552 (59.2)	998 (64.3)	554 (35.7)	
5-	1,068 (40.8)	742 (69.5)	326 (30.5)	

3. Statistical analysis

This study used IBM SPSS version 22 (IBM Corporation, Armonk, NY, USA) to conduct the statistical analysis. First, descriptive analyses were performed to describe the social-demographic characteristics of the respondent and their migrant children. Second, the principal component factor analysis was adopted to extract common factors and to compute the scores for dimensions of social integration. Finally, two multivariate logistic regression models were employed to explore the association between parental social integration and the utilization of physical examination of migrant children using odds ratio (OR) and 95% CIs. Sampling weights were used in all the analyses to adjust for the design effect (18, 19).

RESULTS

The Socio-Demographic Characteristics

The characteristics of the respondent and their children were presented in **Table 1**. About 66.4% of migrant children had used free physical examination in the past year. Among the 2,620 respondents, most of them were male (53.5%), were more than 30 years old (60.2%), with the education level of junior school or below (59.4%), were rural origin (85.3%), were married (98%),

TABLE 2 | Social integration of migrant parents in China, 2014.

Characteristics	Frequency (%)	Physical examination		*P*-value
		Yes	No	
Economy integration				
Monthly average household income[a]				0.123
Q1	871 (33.3)	560 (64.3)	311 (35.7)	
Q2	453 (17.3)	297 (65.6)	156 (34.4)	
Q3	601 (22.9)	397 (66.1)	204 (23.9)	
Q4	695 (26.5)	486 (69.9)	209 (30.1)	
Occupation				0.916
Unemployed	333 (12.7)	222 (66.7)	111 (33.3)	
Employed	2,287 (87.3)	1,518 (66.4)	769 (33.6)	
Medical insurance				0.002
Yes	2,293 (87.5)	1,548 (67.5)	745 (32.5)	
No	327 (12.5)	192 (58.7)	135 (41.3)	
Structure integration				
Participate in activities				<0.001
Yes	931 (35.5)	709 (76.2)	222 (23.8)	
No	1,689 (64.5)	1,031 (61.0)	658 (38.9)	
Types of neighbors				0.003
Migrants	1,130 (43.1)	725 (64.2)	405 (35.8)	
Local residents	568 (21.7)	410 (72.2)	158 (27.8)	
Same[b]	922 (35.2)	605 (65.6)	317 (34.4)	
Culture integration[c]	14.67 ± 2.85	14.69 ± 2.89	14.64 ± 2.78	0.689
Psychological integration[c]				
Contact intention	17.71 ± 2.57	17.77 ± 2.59	17.59 ± 2.53	0.091
Self-identity	16.52 ± 2.79	16.65 ± 2.81	16.26 ± 2.75	0.840
Self-perception	5.47 ± 1.87	5.53 ± 1.79	5.44 ± 1.90	0.149

[a] *Quartile 1 (Q1) is the poorest and Quartile 4 (Q4) is the richest.*

[b] *The number of registered residents and non-registered residents is the same.*

[c] *Culture and psychological integration were presented as Mean ± SD and analyzed by using a t-test.*

were intra-provincial migrants (52.3%), and had been migrants <5 years (59.2%).

Social Integration

Social integration was measured by economic, cultural, structural, psychological (**Table 2**). Regarding economic integration, 33.3% were in quartile 1(Q1), about 87.3%were employed, and 87.5% had medical insurance in their host cities. In the aspect of structural integration, 64.5% did not participate in local activities, and 43.1% of neighbors were non-registered residents. As for cultural integration, the average score of the migrant parents was 14.67. Regarding the psychological integration, the average score of contact intention, self-identity, and self-perception was 17.71, 16.52, and 5.47, respectively. The migrant children's physical examination utilization differed significantly by medical insurance ($P = 0.002$), participation in activities ($P < 0.001$) and types of neighbors ($P = 0.003$).

Association Between Parental Social Integration and Migrant Children's Physical Examination Utilization

Table 3 shows the association between parental social integration and migrant children's physical examination utilization. The unadjusted model 1 only included the parental social integration, including dimensions of economic integration, structural integration, and psychological, which were statistically associated with the migrant children's physical examination utilization. After adjusting for the potential confounding factors including children's age, only one child, parents' education degree, movement area, duration in inflow area, model 2 found parental social integration, including dimensions of economic integration, structural integration, psychological, were still statistically associated with the migrant children's physical examination utilization. Those migrant children whose parents had medical insurance ($P = 0.042$; OR = 1.29), had participated in local activities ($P < 0.001$; OR = 1.98), had registered local residents as neighbors ($P = 0.014$; OR = 1.34), and had a deep sense of self-identity ($P = 0.03$; OR = 1.09) were more likely to use physical examination service. Besides, some other factors were also found to be associated with the migrant children's physical examination utilization. Those migrant children who aged over 3 years ($P < 0.001$; OR = 0.64), and were the only child in the family ($P = 0.025$; OR = 0.82) were less likely to use physical examination, and those parents who were inter-provincial migrants ($P = 0.015$; OR = 1.24) and had

TABLE 3 | The relationship between parental social integration and their migrant children's physical examination utilization in China, 2014.

Variables	Model 1 (Unadjusted)			Model 2 (Fully adjusted)		
	***P*-value**	**OR**	**OR 95%CI**	***P*-value**	**OR**	**OR 95%CI**
Economy integration						
Monthly average household income[a]						
Q1		1.0			1.0	
Q2	0.790	1.03	0.81–1.32	0.616	1.06	0.83–1.36
Q3	0.644	1.05	0.84–1.32	0.567	1.07	0.85–1.35
Q4	0.060	1.26	0.99–1.54	0.051	1.26	0.99–1.58
Occupation						
Unemployed		1.0			1.0	
Employed	0.342	0.88	0.69–1.14	0.522	0.92	0.71–1.19
Medical insurance						
No		1.0			1.0	
Yes	**0.024**	1.33	1.04–1.69	**0.042**	1.29	1.00–1.66
Structure integration						
Participate in activities						
No		1.0			1.0	
Yes	**<0.001**	1.97	1.64–2.36	**<0.001**	1.98	1.64–2.38
Type of neighborhood						
Migrants		1.0			1.0	
Local residents	**0.004**	1.39	1.11–1.75	**0.014**	1.34	1.06–1.69
Same[b]	0.675	1.04	0.86–1.25	0.770	1.03	0.85–1.24
Culture integration	0.203	0.95	0.88–1.03	0.123	0.93	0.86–1.01
Psychological integration						
Contact intention	0.936	1.00	0.92–1.09	0.956	0.99	0.92–1.08
Self-identity	**0.012**	1.11	1.02–1.21	**0.030**	1.09	1.00–1.19
Self-perception	0.888	1.00	0.93–1.09	0.657	1.02	0.94–1.11
Children's characteristics						
Age (Years)						
≤3					1.0	
>3				**<0.001**	0.64	0.54–0.76
One child						
Yes					1.0	
No				**0.025**	0.82	0.68–0.97
Parental characteristics						
Educational attainment						
Primary education or below					1.0	
Junior education				0.178	1.29	0.89–1.86
Senior education or above				0.227	1.26	0.86–1.85
Movement area						
Inter-provincial					1.0	
Intra-provincial				**0.015**	1.24	1.04–1.48
Duration in inflow area (Years)						
1-					1.0	
5-				**<0.001**	1.37	1.15–1.64

The P-values in boldface mean statistical significance at 5% level.

[a]*Quartile 1 (Q1) is the poorest and Quartile 4 (Q4) is the richest.*

[b]*The number of registered residents and non-registered residents is the same.*

Adjusted for age, one child, parents' educational attainment, movement area, and duration in the inflow area.

been migrants more than 5 years ($P < 0.001$; OR = 1.37) were more likely to take their children to use physical examination service.

DISCUSSION

This study found that 66.4% of the migrant children aged 0–6 years had used free physical examination services. The utilization rate of physical examination services in this study was lower than the 83.5% among the migrant children aged under 7 years in Zhejiang province in 2013 (20). It was higher than the 41.1% of migrant children under 6 years old in Xinjiang province in 2015 (21). There were some disparities in the utilization rate of physical examination services among migrant children across different provinces in China, which may be related to the level of economic development in different provinces. In addition, even though provided freely, there were still over 30% of the migrant children did not use physical examination services in the inflow areas, which should be studied profoundly in the follow-up research, so as to identify the main determinants of the non-use of this service, and to improve the utilization rate among the migrant children aged 0 to 6 years.

This study provides evidence that parental social integration was associated with migrant children's physical examination utilization, and this association was multifaceted, lying in the dimensions of economic, structural, and psychological integration. Specifically, concerning economic integration, parental medical insurance status was found to be a determinant for migrant children's physical examination service use. Medical insurance is an effective tool to promote access to healthcare services (22). A review found that one of the most important barriers for labor-migrant to access health services was the lack of health insurance (8). One possible explanation for this finding might be that insured parents have strong social security awareness, tend to use physical examination services to find potential health risks for their children so that effective intervention can be developed promptly.

Structural integration, which was measured by activity participation and type of neighbors, was found to be positively associated with migrant children's physical examination utilization. At present, the migrant population was still in a relatively isolated state and trying to integrate into mainstream society. A study conducted in Ethiopia showed that the migrant status of women had a negative impact on child immunization use, and it was largely due to their limited social network and the disconnection of their host community (23). Participation in social activities was one of the crucial ways for migrants to obtain information (such as healthcare information), resources, and opportunities, which could create a beneficial environment for migrants to expand their social network and foster a sense of belonging. In addition, it was beneficial to maintain their physical and mental health (24, 25). As a result, migrant parents who participated in activities were more willing to integrate into the inflow cities, and more likely to use local health services.

Migrant parents with local registered residents as neighbors were more likely to use physical examination services. Hou et al. (26) found that migrants living in the community with a higher composition of local residents had a higher probability of using public health services, which was consistent with the finding of the current study. Localized social interaction could help migrants to be better familiar with the local culture, customers, decrease exclusion of mainstream social settings and have a strong sense of belonging to the inflow areas. On the other hand, migrants could obtain local information from their neighbors, including information on how to use the local health services (16, 27). A study had suggested that mothers who were socially integrated can obtain relevant oral health information from their surroundings individuals, which indirectly improves children's oral health service utilization (28).

In the aspect of psychological integration, only the migrant parents with a deep sense of self-identity were of higher probability to take their migrant children to use physical examination. The migrants are often accompanied by the term "self-identity", which was an important indicator of the integration of the migrants into mainstream society. It refers to mutual recognition and acceptance between the migrant population and the local residents in the process of two-way social interaction. A study found that migrant parents in the middle-acculturation were less likely to take their children to use health services than those in the high-acculturation, largely because they perceived more personal and social discrimination (29). Accumulated evidence has shown that higher identity integration was positively associated with lower levels of stressors, higher social adjustment, and social support (30–33). Migrant parents with a deep sense of self-identity were more likely to have less psychological pressure and a stronger sense of identity and were willing to actively adapt to the environment in inflow areas. Therefore, they tended to regard themselves as local residents and were more willing to take their children to utilize the local health services, including physical examination services.

Furthermore, this study found parents' movement area and duration in the inflow areas, children's age, and whether as an only child in the family were the determinants for physical examination utilization. Regarding the parental characterizes, parents who were from intra-provincial migrant status and have lived in their local area for more than 5 years were more likely to take children to use physical examination. The customs and living habits of the place of origin were more similar to those of the new residence for intra-provincial migrants, and the longer stayed in the new residence, the more familiar they were with that place (34). About the characteristics of migrant children, children aged over 3 years and who were not only one child in the family were less likely to use physical examination services. This finding may be partly because the younger children and only children received more attention and care in the family under the traditional Chinese culture atmosphere, thus their parents were more likely to take them to use physical examination service.

This study had some limitations. First, the cross-sectional survey cannot predict the causal relationship between parental social integration and migrant children's physical examination utilization. Second, although this study used many indicators to measure social integration, due to the limitations of existing

data, it still did not include other potential factors that may affect the utilization of physical examination, such as language, social support. Third, the physical examination utilization was self-reported, which may be over-reported or under-reported due to recall bias. Finally, this study only investigated Chinese migrants, so the main findings of this study should be interpreted with caution, especially for inter-country/continental migrants, as the language, tradition, and culture largely differed across countries.

CONCLUSION

This study provided evidence that parental social integration was associated with migrant children's physical examination utilization. This association was multifaceted, lying in the dimensions of economic, structural, and psychological integration. The government should take measures to improve the social integration of migrant parents, so as to enhance the migrant children's healthcare utilization in the inflow areas.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

CZ and MS contributed to the conception and design of the study. ZJ and SZ performed the statistical analysis and wrote the first draft of the manuscript. NZ, MS, and CZ reviewed and edited the manuscript, were responsible for visualization, supervised the project, and acquired funding. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

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Estimating Child Mortality at the Sub-national Level in Papua New Guinea: Evidence From the Integrated Health and Demographic Surveillance System

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Background: Child mortality is an important indication of an effective public health system. Data sources available for the estimation of child mortality in Papua New Guinea (PNG) are limited.

Objective: The objective of this study was to provide child mortality estimates at the sub-national level in PNG using new data from the integrated Health and Demographic Surveillance System (iHDSS).

Method: Using direct estimation and indirect estimation methods, household vital statistics and maternal birth history data were analysed to estimate three key child health indicators: Under 5 Mortality Rate (U5MR), Infant Mortality Rate (IMR) and Neonatal Mortality Rate (NMR) for the period 2014–2017. Differentials of estimates were evaluated by comparing the mean relative differences between the two methods.

Results: The direct estimations showed U5MR of 93, IMR of 51 and NMR of 34 per 1000 live births for all the sites in the period 2014–2017. The indirect estimations reported an U5MR of 105 and IMR of 67 per 1000 live births for all the sites in 2014. The mean relative differences in U5MR and IMR estimates between the two methods were 3 and 24 percentage points, respectively. U5MR estimates varied across the surveillance sites, with the highest level observed in Hela Province (136), and followed by Eastern Highlands (122), Madang (105), and Central (42).

Discussion: The indirect estimations showed higher estimates for U5MR and IMR than the direct estimations. The differentials between IMR estimates were larger than between U5MR estimates, implying the U5MR estimates are more reliable than IMR estimates. The variations in child mortality estimates between provinces highlight the impact of contextual factors on child mortality. The high U5MR estimates were likely associated with inequality in socioeconomic development, limited access to healthcare services, and a result of the measles outbreaks that occurred in the highlands region from 2014-2017.

Conclusion: The iHDSS has provided reliable data for the direct and indirect estimations of child mortality at the sub-national level. This data source is complementary to the existing national data sources for monitoring and reporting child mortality in PNG.

Keywords: child mortality, surveillance system, Papua New Guinea, direct estimations, indirect estimation

INTRODUCTION

In 1990, approximately 12 million children died globally before they reached their fifth birthday (1). In 2000, the United Nations' Millennium Development Goal 4 (MDG 4) set out a target to reduce child mortality by two-thirds by 2015 (2). Globally, significant progress in the improvement of child health has been made. There has been a 50% decline in child mortality, from 12.7 million in the 1990's to 6.3 million in 2013 (3). However, to date only 31 countries reported having met the MDG targets for child mortality (4, 5). Addressing high child mortality remains a global health priority in the United Nations' Sustainable Development Goals (SDG). SDG 3 target 3.2 to reduce neonatal mortality to 12 per 1,000 live births and under-5 mortality to 25 per 1,000 live births by 2030 (6).

Child mortality is an important indicator of global public health. To monitor progress towards the SDG 3, it is vital to have accurate estimates of under-five mortality rate (U5MR), infant mortality rate (IMR) and neonatal mortality rate (NMR) at the global, national and sub-national levels. National vital and civil registration systems are often referred to as reliable data sources for the estimation of child mortality, based on the complete registration of births and deaths in the population (7, 8). However, these systems may not exist or be fully functioning in many low- and middle income countries (LMICs), where most childhood deaths occur (8). Hence, for these countries, child mortality estimates heavily rely on cross-sectional household survey data. The most common data sources available at the national level are Demographic and Health Surveys (DHS) and National Censuses, in which maternal birth history data are retrospectively recorded either in full or in summary and may be used to estimate child mortality (9).

Estimations of child mortality indicators are widely used by governments and international development partners to monitor and report the progress of international development agendas such as SDGs to inform public policy and national socioeconomic development programs for improving the health and wellbeing of children (10). Thus, lack of data for reliable estimations of child mortality at the national and sub-national levels could lead to ineffective child health policy, affecting childhood communicable diseases preventive measures and child health protection policies (11). Accurate estimation of child mortality largely depends on two main factors: the data quality and the method used for estimation (12).

Although efforts have been made to improve the health of children in the period 2000s-2010s, child mortality is still reportedly high in Papua New Guinea (PNG) and PNG is amongst countries with the highest child mortality rates in the Pacific region (13). Like many LMICs, PNG did not achieve the MDG 4 (14). The lack of updated and reliable data rendered the PNG Government unable to fully report the country's progress and achievement of the MDG 4 to the United Nations in 2015 (14). The PNG Government through its Medium Term Development Plan 2018–2022 (MTDP) has set specific targets to improve child survival in line with the SDG 3. According to this plan, the country aims to reduce the IMR and U5MR to 17 and 20 per 1,000 live births by 2022, respectively (15, 16).

PNG faces challenges in tracking and reporting the country's progress toward achieving the international and national development targets due to lack of reliable data sources and adequate human and financial resources (17). While national vital and civil registration systems are generally known to be reliable data sources for the 'direct estimation' of child mortality, these systems are not fully developed and functioning in PNG in order to provide a complete data series on birth and death statistics (18). The DHS and National Censuses have been used over the last four decades 1990–2020's as the only national data sources available in PNG for estimation of child mortality (19, 20). The most recent data from the DHS 2016 provides U5MR of 49, IMR of 33 and NMR of 20 deaths per 1,000 live births (21). However, the child mortality estimates based on these data sources have never been validated against other data sources in terms of accuracy and reliability.

Bauze et al. (22) assessed the quality of data from the DHS 2006 and they suggested that U5MR estimation should be conducted at the sub-national level by further exploring alternative options of birth and death surveillance data. These measures could include face to face data collection at the village level, particularly in rural and remote regions where child mortality estimates are likely to be higher and under reported.

Given the increasing importance of child mortality data, this study was conducted to estimate child mortality at the sub-national level in PNG, using new data from the integrated Health and Demographic Surveillance System (iHDSS), operated by the Papua New Guinea Institute of Medical Research (PNGIMR). PNGIMR's iHDSS is one of 49 surveillance centres of the International Network for the Demographic Evaluation of Populations and their Health (INDEPTH), a global surveillance network that collects high-quality vital registration information in diverse settings of LMICs by carrying out a series of mortality and morbidity surveillance of the defined populations, in which the fertility and mortality are integrated as part of the household socioeconomic data. These 'ground truth' data series can be used to provide new insights into the child mortality estimates in different demographic and epidemiological settings (23). Little is known about child mortality estimations using data from the iHDSS, especially estimates at the sub-national level.

The objective of this study was to provide child mortality estimates at the sub-national level in PNG using new data from the integrated Health and Demographic Surveillance System (iHDSS). Child mortality direct and indirect estimation methods were used in this study to address four specific research questions: (i) What are the child mortality estimates using the direct estimation method? (ii) What are the child mortality estimates using the indirect estimation method? (iii) How do the child mortality estimates produced by the direct and indirect estimation methods vary? and (iv) How do child mortality estimates vary between provinces?

MATERIALS AND METHODS

Data Source

This study used the PNGIMR's iHDSS data collected in the period 2014–2017, the latest time period when appropriate data for child mortality estimation were collected. The iHDSS was designed as a population-based longitudinal cohort study. The overall purpose of the system was to provide a reliable and up-to-date data series for monitoring the implementation of socioeconomic development programmes and healthcare interventions at the sub-national level in PNG. The iHDSS methodology has been described elsewhere (24, 25).

The geographic coverage of the iHDSS consisted of four rural sites, namely Asaro in Eastern Highlands Province (EHP), Hides in Hela Province, Hiri in Central Province, and Karkar in Madang Province, representing three out of the four geographical regions of PNG: the Highlands, the Southern, the Momase, respectively (no surveillance site in the Islands region in the period of this study) (26). These surveillance sites were selected based on the developmental history and surveillance experience of PNGIMR in consultation with the PNG Government agencies and stakeholders.

As of the end of 2017, the population coverage of the iHDSS was about 54,000 people, equivalent to 1% of the total population of PNG in 2011 when the system was set up. Data collection was conducted by the iHDSS teams via household interviews, using various data collection tools, which were translated from English into *Tok-Pisin*, the most common language spoken by Papua New Guineans. New datasets were released twice a year for data analysis and reporting purposes (26). Data quality assurance and quality control procedures are presented in **Figure 1**.

Settings

Table 1 shows the overall socioeconomic description of the four surveillance sites. Asaro and Hides sites are in the highlands region while Hiri and Karkar sites are both in coastal areas.

Asaro site is located approximately 40–45 km northeast of Goroka. Asaro is primarily a farming and agricultural production area. Coffee and sweet potatoes (*kaukau*) are the main cash crop. Major languages spoken by people living in Asaro are *Tokples, Gahuku, Siane* and *Dano/Tokano*, apart from *Pidgin* that is also regularly spoken. There are three primary health facilities where local people in the site can have access to basic health services.

Geographically, the Hides site is very remote and difficult to access. Tribal cultural norms and practises are an integral part of the local people's lives and have created a complex society. People live in clans and sub-clans, and maintain a traditional tribal lifestyle. Most of the houses are built using bush materials and there are very few semi-permanent buildings. The main

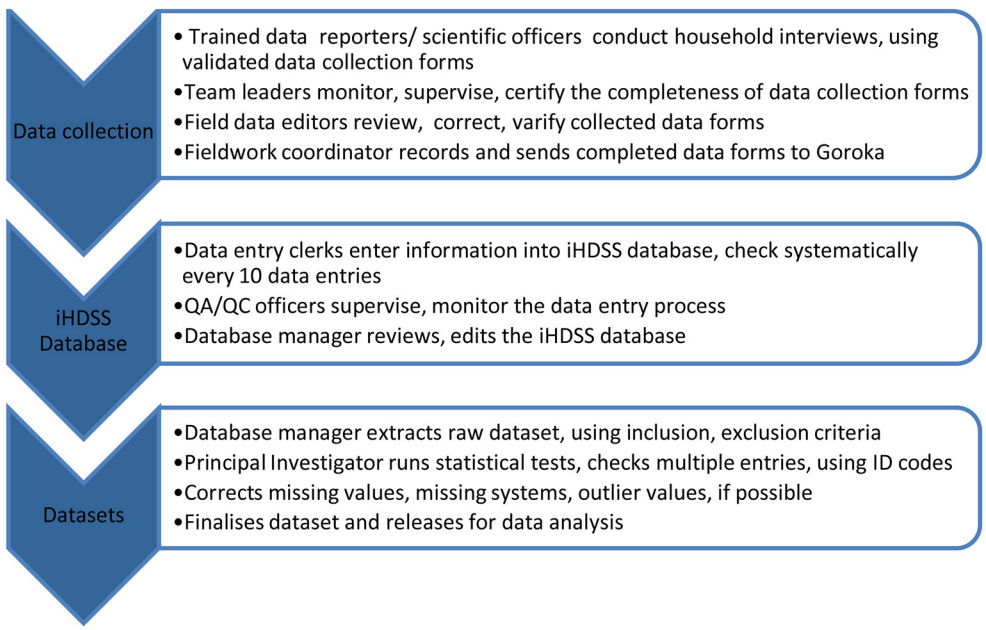

FIGURE 1 | Quality assurance and quality control procedures, PNG IMR's iHDSS, 2011-2017.

TABLE 1 | Overall description of socioeconomic status of surveillance site, PNGIMR's iHDSS, 2016.

Province	EHP	Hela	Central	Madang
Region	Highlands	Highlands	Southern	Momase
Surveillance site	Asaro	Hides	Hiri	Karkar
Location	40 km, northeast of Goroka township	45 km south of Tari township	45 km west of Port Moresby	Island 30 km from Madang township
Main industry	Coffee, sweet potatoes	Coffee, hunting, Liquefied Natural Gas	Fishery, hunting, Liquefied Natural Gas	Fishery, plantation (cocoa, coconut)
Accessibility	Road and airline	Road and airline	Road	Sea
Year of operation	2011-current	2011–2017	2011-current	2011–2015
Surveillance population	10,000	13,000	12,000	19,000
Surveillance household	2,000	2,500	2,000	3,000
Primary public health facility	Asaro health centre, Uritoka health clinic, Tafeto health clinic	Malanda health centre, Para health clinic	Porebada, Papa, and Lealea health clinics	Gaubin hospital, Miak, Wadau, and Kuburne health clinics
Laboratory service	N/A	Goroka Lab	N/A	Madang Lab

Tokples language spoken is *Huli*. Hides site is also home to the Komo Airfield.

Hiri site is located in Central Province, approximately 30–40 km west of Port Moresby, the National Capital of PNG. The iHDSS covers four coastal villages i.e., *Porebada, Boera, Papa* and *Lealea*. Each village has its own health clinic. Most inhabitants are either *Motu* or *Koitabu* speakers. Hiri site can be reached by road in < 1 h from Port Moresby.

Karkar district is a volcanic island located 30 km off the PNG coast in the Bismarck Sea. The island's soil is known for its fertility and the large plantations produce the island's main exports of cocoa and coconut and provide a large amount of the local employment opportunities. Inhabitants of the island come from one of two language groups: *Waskia* in the North half of the island and *Takia* in the South. Karkar site was closed at the end of 2015 due to staff safety issues.

Estimating Child Mortality

The iHDSS adopted a life-circle approach to capture key demographic events such as births, deaths and migration at the household level, as well as individual health data of the defined populations including women of reproductive age 15–49 years, and children under 5 years of age. Hence, these data from the iHDSS can be used for estimations of child mortality indicators. Two estimation methods were used in this study: (i) the direct estimation method is based on household demographic change data including birth and death records; and (ii) the indirect estimation method uses maternal birth history data. A summary of these two estimation methods are presented in **Table 2**. Comparing and contrasting of child mortality estimates between the two methods could also evaluate the reliability and accuracy of the estimates.

This study reports on three key child mortality indicators: (i) NMR is the proportion of children dying within the first month of life (age at death is between 0 and 27 days); (ii) IMR is the proportion of children dying before their first birthday (age at death is between 0 and 11 months; (iii) U5MR is the proportion of children dying before their fifth birthday (age at death is between 0 and 4 years). These child mortality rates are expressed per 1,000 live births. Stillbirth rates are not included in these analyses.

Direct Estimation

In the direct estimation, child mortality rates were calculated by dividing the total number of child deaths by the total number live births recorded in a given period of time i.e., one year. This method involves birth and death data, extracted from the iHDSS household socioeconomic data component. Household Update Book (HUB) was used to record household identification information, list of all household members, and their identification information such as name, sex, date of birth, date of death, and date of migration in and out of the villages. Data used in this study were mostly from the data module on household demographic changes, including birth and death data. Main variables were used including the number of children born in the household, the child's date of birth (day, month and year), the age of the child at the time of the visit (in days, months or years), and sex of the child. Death statistics included the number of deaths in the household, the date of their death (date, month, and year) and their age at death (in years, months and days).

This information was collected by village-based data collectors. With the social network, local background and knowledge, data collectors had an advantage when collecting these data from households in their localities. Data collectors were trained to use the HUB and basic interview skills prior to their visits to the households. They asked household members, mostly household heads to provide information about the births and deaths that occurred in the household since the last visit. Two rounds of HUB data collection were conducted in July-December 2014 (in all four provinces), and in July-December 2017 (for three provinces, except Madang).

The HUB dataset was extracted from the iHDSS database for direct estimation of child mortality rates. The information on "date of birth" and "date of death" were used to calculate "age at death" of deceased children in the households, which allowed checking for internal consistency across information provided by the respondents. The "age at death" data were used to

TABLE 2 | Summary of direct and indirect estimation methods used for estimation of child mortality in Papua New Guinea, PNGIMR's iHDSS 2014–2017.

	Direct estimation method	Indirect estimation method
Estimation/calculation method	(Total child deaths)/(Total live births) × 1,000	Brass W method (model life tables)
Data component	Household socioeconomic	Women of aged 15–49 years
Data collection tool	Household Update Book	Women of reproductive age Questionnaire
Data module	Household demographic change: births, deaths, migration	Child mortality
Variables used	Date of birth, date of death, age at death, total numbers of live births, CU5, infant and neonatal deaths in a given period of time	Women' birth history: Numbers of child ever born, child survived, child dead, maternal age
Data collector	Village-based data collectors	National scientific officers
Data collection period	July-December 2014 July-December 2017	July-December 2015
Child mortality indicators reported	NMR, IMR, and U5MR	IMR and U5MR
Year of estimate	Each year in the period 2014–2017	2014 only

classify child deaths into three groups: neonatal mortality (0–27 days), infant mortality (0–11 months) and under 5 mortality (0–4 years). Three child mortality indicators: NMR, IMR and U5MR were estimated for each surveillance site and for all sites for 2014, 2015, 2016, and 2017, and for the entire period 2014–2017. Findings are presented in **Table 3**.

Indirect Estimation

The indirect estimation method for child mortality was first introduced by Brass William (27). This method summarises birth history data using a model life table (mathematical models of the variation of mortality with age) to estimate proportions of child death in specific maternal age groups for the years prior to the interview time. This is achieved by taking into account the approximate length of exposure of children to the risk of dying, and assuming a particular model age pattern of mortality (28, 29).

The dataset used for indirect estimation of child mortality was extracted primarily from the women of reproductive age 15–49 years data component of the iHDSS database. These data were collected by the PNGIMR's iHDSS national scientific officers using the individual questionnaire on Women of Reproductive Age, 15–49 years in the period from July-December 2015. This questionnaire was designed by the iHDSS team in 2014, based on various existing data collection tools in use across international organisations such as the INDEPTH, the United Nations' Multi-indicator Cluster Survey (MICS), and the Measure Evaluation's DHS. The questionnaire comprises eight data modules: Household identification information, Women's background, Marriage and family, Sexual behaviour, Domestic violence, Child mortality, Unmet need for contraception, and Maternal and newborn health.

Data from the child mortality component of the iHDSS database were used in the current study. In this data module, women were asked questions about their birth history, including maternal age, numbers of son/daughter living at home, and numbers of sons/daughters living elsewhere, and numbers of boys/girls born alive but died later. Based on this information, new variables on total numbers of live births, children surviving, and children deceased were created. These new variables were used to calculate a mean of total live births and a mean of total children surviving per woman, in order to estimate total live births, total children surviving, and total children deceased for each woman who participated in the study. Based on these estimates, the proportion of children, who had died was calculated for 5-years maternal age groups i.e., 15–19, 20–24, 25–29, 30–34, 35–39, 40–44, and 45–49 years, in each province and for all provinces.

This estimation process and data on U5MR and IMR estimates are shown in **Table 4**. U5MR and IMR estimates are obtained by converting the proportions of children dead, which was obtained from the step (vii) into probabilities of children dying for 2014, the year prior to the data collection. Descriptive statistical data analyses were conducted using Statistics Package of Social Science (SPSS version 20.0).

Comparison of Child Mortality Estimates Produced by Direct and Indirect Estimations

To show the differences of child mortality estimates, mean relative differences between U5MR estimates and IMR estimates derived from the direct and indirect estimation methods were calculated for each province (except for Madang) and for all provinces. The relative difference d between these two estimation methods was calculated using the formula below:

$$d_i = \frac{x_{i,indirect} - x_{i,\ direct}}{\frac{1}{2} \times \left(x_{i,indirect} + x_{i,direct}\right)}$$

Where, $x\ I,\ indirect$ and $x\ I,\ direct$ are the estimated child mortality rates derived from the indirect method and the direct method, respectively, for year i in a population. This method has been discussed elsewhere (23).

U5MR and IMR estimates for the calendar year 2014 obtained from the direct estimations were included in the calculation of paired means of relative differences between indirect and direct estimates to ensure the estimated referencing periods between the two methods corresponded. The paired means of relative differences indicate whether the indirect estimates are

TABLE 3 | Direct estimation of under 5 mortality rate, infant mortality rate and neonatal mortality rate using birth and death data from household update book, PNGIMR's iHDSS, 2014–2017.

Year of estimate	Child morality estimates	Central	EHP	Madang	Hela	All provinces
2014	Total live births	254	204	153	243	854
	Number of children under 5 deaths	10	30	16	31	87
	Number of infant deaths	4	16	8	17	45
	Number of neonatal deaths	3	10	7	12	32
	U5MR estimate (per 1,000 live birth)	39.37	147.06	104.58	127.57	101.87
	IMR estimate (per 1,000 live births)	15.75	78.43	52.29	69.96	52.69
	NMR estimate (per 1,000 live birth)	11.81	49.02	45.75	49.38	37.47
2015	Total live births	302	220	NA	217	739
	Number of children under 5 deaths	11	26	NA	32	69
	Number of infant deaths	5	18	NA	16	39
	Number of neonatal deaths	5	9	NA	11	25
	U5MR estimate (per 1,000 live birth)	36.42	118.18	NA	147.47	93.37
	IMR estimate (per 1,000 live births)	16.56	81.82	NA	73.73	52.77
	NMR estimate (per 1,000 live birth)	16.56	40.91	NA	50.69	33.83
2016	Total live births	328	296	NA	98	722
	Number of children under 5 deaths	15	33	NA	14	62
	Number of infant deaths	6	21	NA	8	35
	Number of neonatal deaths	6	12	NA	5	23
	U5MR estimate (per 1,000 live birth)	45.73	111.49	NA	142.86	85.87
	IMR estimate (per 1,000 live births)	18.29	70.95	NA	81.63	48.48
	NMR estimate (per 1,000 live birth)	18.29	40.54	NA	51.02	31.86
2017	Total live births	152	128	NA	57	337
	Number of children under 5 deaths	7	15	NA	7	29
	Number of infant deaths	3	9	NA	4	16
	Number of neonatal deaths	3	5	NA	3	11
	U5MR estimate (per 1,000 live birth)	46.05	117.19	NA	122.81	86.05
	IMR estimate (per 1,000 live births)	19.74	70.31	NA	70.18	47.48
	NMR estimate (per 1,000 live birth)	19.74	39.06	NA	52.63	32.64
2014-2017	Total live births	1,036	848	153	615	2,652
	Number of children under 5 deaths	43	104	16	84	247
	Number of infant deaths	18	64	8	45	135
	Number of neonatal deaths	17	36	7	31	91
	U5MR estimate (per 1,000 live birth)	41.51	122.64	104.58	136.59	93.14
	IMR estimate (per 1,000 live births)	17.37	75.47	52.29	73.17	50.90
	NMR estimate (per 1,000 live birth)	16.41	42.45	45.75	50.41	34.31

measurably different from the corresponding direct estimates. Data are presented in **Table 5**.

RESULTS

Table 3 shows the direct estimates of U5MR, IMR and NMR in the period 2014-2017, based on the numbers of total live births and child deaths recorded in the iHDSS database. U5MR estimates in EHP declined in this period, from the level of 147 per 1,000 live births in 2014 to 111 in 2016. A similar trend was also observed in Hela, where U5MR estimates declined from 147 per 1,000 live births in 2015 to 123 in 2017. In contrast, U5MR in Central remained low with 42 per 1,000 live births during the period 2014–2017. Unlike the varied U5MR estimates, IMR estimates were relatively stable with 50 deaths per 1,000 live births for all sites from 2014∼2017, with highest estimates observed in EHP and Hela (∼70–80 per 1,000 live births), and lowest in Central (∼15∼20 per 1,000 live births). Similarly, NMR estimates were ∼30–35 per 1,000 live births for all sites from 2014 to 2017, but the highest level was estimated for Hela (30), followed by EHP and Madang (31–36), and lowest in Central (10–20).

Table 4 illustrates the process of indirect estimation of U5MR and IMR using Brass indirect estimation method. Birth history data of 5,554 women aged 15–49, including 22,216 live births, 17,615 children surviving, and 4,601 children dead were included in the estimation. The proportions of child deaths in two maternal age groups: 15–19 and 30–34 years were 0.067 and 0.105, respectively. Hence, the IMR estimate was approximately 67 deaths per 1,000 live births and the U5MR estimate was

TABLE 4 | Estimation of under 5 mortality and infant mortality rates in 2014, Brass indirect estimation method, women aged 15–49 birth history data, PNGIMR's iHDSS, 2015.

Province	Woman age group	No. of women (i)	Mean of total live births (ii)	Mean of total children surviving (iii)	Estimated total live birth (iv)= (i)*(ii)	Estimated total children surviving (v)= (i)*(iii)	Estimated total children dead (vi) = (iv)−(v)	Proportion of children dead (vii) = (vi)/(iv)
Central	15–19	455	1.52	1.49	692	678	14	0.020
	20–24	407	1.58	1.50	642	611	31	0.049
	25–29	387	2.84	2.70	1,101	1,045	56	0.051
	30–34	307	3.69	3.54	1,134	1,087	47	0.042
	35–39	287	4.25	3.67	1,220	1,053	166	0.136
	40–44	246	4.68	3.84	1,151	944	207	0.180
	44–49	174	4.90	4.02	853	699	153	0.180
EHP	15–19	343	2.00	1.80	686	617	69	0.100
	20–24	262	2.35	1.93	615	507	108	0.176
	25–29	266	2.96	2.62	789	696	92	0.117
	30–34	289	4.64	3.90	1,340	1,127	213	0.159
	35–39	194	4.79	3.90	928	757	171	0.184
	40–44	285	5.63	4.47	1,606	1,274	331	0.206
	44–49	167	5.82	4.93	973	824	149	0.153
Madang	15–19	313	1.60	1.50	501	470	31	0.063
	20–24	235	1.81	1.60	426	376	50	0.117
	25–29	193	2.57	2.28	496	441	56	0.112
	30–34	177	3.49	3.11	617	551	66	0.108
	35–39	169	4.35	4.07	735	687	48	0.065
	40–44	139	5.42	4.94	754	687	67	0.089
	44–49	82	5.80	5.03	476	412	63	0.133
Hela	15–19	66	1.00	1.00	66	66	0	N/A
	20–24	25	2.00	1.47	50	37	13	0.265
	25–29	32	2.33	2.24	75	72	3	0.041
	30–34	23	2.25	2.20	52	51	1	N/A
	35–39	9	4.67	3.89	42	35	7	0.167
	40–44	15	4.20	3.54	63	53	10	0.158
	44–49	7	5.80	3.29	41	23	18	0.433
All provinces	15–19	1,177	1.50	1.40	1,766	1,648	118	0.067
	20–24	929	1.93	1.62	1,791	1,507	283	0.158
	25–29	878	2.84	2.37	2,494	2,083	411	0.165
	30–34	796	3.98	3.56	3,166	2,834	332	0.105
	35–39	659	4.42	3.83	2,915	2,526	389	0.133
	40–44	685	5.30	4.30	3,632	2,946	686	0.189
	44–49	430	5.27	4.48	2,264	1,927	337	0.149
	Total	5,554	4.00	3.17	22,216	17,615	4,601	0.207

approximately 105 child deaths per 1000 live births for all provinces. The IMR estimate was lowest in Central Province (20), followed by Madang (63), and the highest estimate in Eastern Highlands (100). The U5MR estimates were highest in EHP (159), followed by Madang (108), and lowest in Central (42) (data of Hela were ineligible for estimation since small numbers were reported). These estimates were referred to mid-2014, the year prior to the data collection.

Table 5 shows the mean relative differences of IMR and U5MR estimates calculated from the indirect and direct estimations. NMR rates were not included in this analysis as the data were only available from the direct estimation. The indirect estimation provided higher IMR estimates than the direct estimation by 24 percentage points for the IMR estimate for all provinces. However, the U5MR direct and indirect estimates were relatively consistent, varying by 3 percentage points for all provinces. Further examining the mean relative differences of IMR and U5MR estimates at the provincial level, the data showed that the IMR and U5MR estimates were most reliable in Madang, where the mean relative differences of IMR and U5MR estimates were minimum among provinces, at 18 and 3 percentage points, respectively.

TABLE 5 | Mean relative differences (reported as percent points) between indirect and direct estimations for IMR and U5MR estimates in 2014, PNGIMR's iHDSS, 2015.

Province	Child mortality	Indirect estimate	Direct estimate	Indirect − Direct	Indirect + Direct	Mean (indirect + direct)	Mean relative difference
		(1)	(2)	(3) = (2) – (1)	(4) = (2) + (1)	(5) = [(1) + (2)]/2	(6) = (3)/(5)
Central	IMR	19.74	15.75	3.99	35.49	17.74	0.225
	U5MR	41.80	39.37	2.43	81.17	40.59	0.060
EHP	IMR	100.00	78.43	21.57	178.43	89.22	0.242
	U5MR	158.82	147.06	11.76	305.88	152.94	0.077
Madang	IMR	63.00	52.29	10.71	115.29	57.65	0.186
	U5MR	108.00	104.58	3.42	212.58	106.29	0.032
Hela	IMR	N/A	69.96	N/A	N/A	N/A	N/A
	U5MR	N/A	127.57	N/A	N/A	N/A	N/A
All provinces	IMR	67.00	52.69	14.31	119.69	59.85	0.239
	U5MR	104.99	101.87	3.12	206.86	103.43	0.030

DISCUSSION

To our knowledge this is the first study to provide an update on child mortality estimates in PNG at the sub-national level using the data from the iHDSS. National data sources available for child mortality estimations were reviewed to highlight gaps in analysing and monitoring child mortality at the sub-national levels.

Comparison Between Direct and Indirect Child Mortality Estimates

The use of direct and indirect estimation methods strengthened the rigour of the research method of this study. Comparison between these methods highlighted the consistency and the differences between the methods. This comparison sheds light on the reliability of the child mortality estimates based on the vital statistics of households for direct estimation and maternal birth history data for indirect estimation. This approach is a methodological strength of our study, allowing assessment of the reliability of the surveillance data by comparing the two data sets to determine the accuracy of child mortality estimates, based on the direct and indirect estimation methods (27, 37).

Maternal retrospective birth history data are most commonly used for child mortality indirect estimation in situations where complete vital registration data are unavailable (9). Previous empirical investigations into child mortality in LMICs relied heavily on maternal birth history data (in the forms of full or summary birth histories) to generate child mortality estimates (8), meaning that the birth-history based indirect estimation approach lacks "ground truth" data that could be use to validate the estimates. However, it is not easy, especially for male data collectors to talk with women about child birth issues in the PNG local context, where asking women about their sexual reproductive behaviours is considered as insulting (38). This challenges population-based studies and surveys conducted in PNG using face-to-face interview data collection strategies. In this study, the large vital statistics data from households were therefore used for the first time for the direct estimation of child mortality indicators at the sub-national level in PNG.

Comparing the results of the direct and indirect estimations, we see that similar IMR estimates for 2014 were produced, 53 and 67 child deaths per 1,000 live births, respectively. Similarly, the U5MR estimates for 2014 were 102 and 105 per 1,000 live births for the direct and indirect estimates, respectively. These findings suggest that the indirect estimates are generally consistent with direct estimates. The differentials in child mortality estimates of the two methods were reconfirmed by the analysis of the means of relative differences between the direct and indirect U5MR and IMR estimates. The consistency between IMR and U5MR estimates produced by the two methods indicates indirect estimation may be useful in instances were direct estimation is not possible. The research methods used in this study have provided insights into the quality of the data produced by the PNGIMR's iHDSS.

Both direct and indirect estimations can suffer from data errors. Life table used in indirect estimation provides probabilities of deaths, based on the mortality experience among a real cohort of children (39). Indirect child mortality estimates are often biassed when women do not know their age or the ages of their children. This issue is commonly observed in the surveillance sites, where the proportion of the population having a birth or death certificate is low, particularly among children who live in rural areas (11). The biases could be even greater when the indirect estimates are drawn out from the self-reported number of children ever born and the number of children born alive but who later died. In our study, the questionnaire for women aged 15–49 contained a module on child mortality, which was specifically designed to collect data for mortality estimation. However, in some cases stillbirths and live births could have been included in women's responses to the question of how many children were ever born, leading to overestimates of child mortality. Indirect estimations could also be biassed due to high child mortality from HIV/AIDS (40), which might have led to different mortality patterns among PNG children. Data for indirect estimation of child mortality in PNG could be obtained from the national census and demographic and health surveys, which are conducted around every 10 years. Although data from these sources are not always up-to-date and

are sometimes inadequate for child mortality estimation (22), they are still an option in a low resource setting like PNG, where the civil registration and vital statistics systems are often deficient (41).

The direct estimation method requires birth data from specifically designed data collection tools such as the household update book used in the iHDSS. The reliability of direct estimation of child morality depends on the correct reporting of age at death, and especially the information on date of birth and date of death, including day, month and year because this information is used to calculate the age at death of the deceased child. Missing information or misreporting of these data could have resulted in biases in direct estimations, either underestimated or overestimated. From our field observations, underreporting of child mortality is more likely to happen than over-reporting in the surveillance population.

By defining the child mortality estimations in relation to the PNG context and the availability of data, the current study contributes to the existing literature on child mortality estimation. The comparison of child mortality direct and indirect estimation methods in the local context of PNG has highlighted possible avenues to further improve the accuracy of child mortality estimates in LMICs. Both direct and indirect estimation methods work well in the PNG context, suggesting both can be replicated in low resourced settings.

The question remains as to which estimation method is a better choice to provide optimal output in low resource settings, where it is not possible to carry out both estimation methods. Comparison of mean relative differences is a common method which is used to demonstrate the differentials in estimates produced by different estimation approaches. In our study, we analysed the mean relative difference between IMR estimates provided by the direct and indirect estimations. We also used this method to examine the difference between direct and indirect U5MR estimates. Measuring mean relative differences is an approach to assessing consistency between direct and indirect estimations of a child mortality rate. For IMR estimates, the mean relative differences were 22.5% for Central, 24.2% for Eastern Highlands, 18.6% for Madang, and 23.9% for all provinces. By contrast, the mean relative differences between direct and indirect U5MR estimates were 6% for Central, 7% for Eastern Highlands, 3% for Madang, and 3% for all provinces. As shown in **Table 5**, compared with U5MR estimates, larger differentials were consistently observed for all IMR estimates, suggesting that the IMR estimation is more susceptible to biases than the U5MR estimation. As such, the U5MR estimates are, to some extent, more reliable than the IMR estimates. For U5MR, the difference between the direct and indirect estimates was low (3%), meaning the both direct and indirection estimations can be used depends on the availability of data and technical expertise, but cheaper method could be preferred. By contrast, the difference between IMR estimates was relatively high (24%). We cannot conclude which estimation method is more reliable than the other by comparing the mean relative differences only. Hence the IMR estimates based the iHDSS data should be triangulated with other data sources available in the country.

These data observations are important for improvement in child mortality estimation in LMICs. First for collecting birth and death records, and household socioeconomic data, the network of village-based data reporters, including both males and females is crucial. By having their own social networks including families, relatives, neighbours and friends who live in the communities, data reporters can visit households on a regular basis and they have insightful knowledge of changes in their communities. With the local background and knowledge of the surveillance sites, data collectors can provide reliable and up-to-date information on births and deaths that have occurred in their villages. This village-based data collection approach makes the iHDSS a unique data source for the monitoring and reporting of child mortality at the sub-national level, where surveillance data is likely more complete and up-to-date than the cross-sectional survey data (9, 17). However, to sustain the village-based surveillance system is expensive as it requires continuous training and supervision of the data collectors as the data collection is on-going over a long period of time.

Second, the accurate and complete birth and death data such as date of birth and date of death (including the day, month, and year) among children are crucial in providing quality data for the direct estimation of child mortality. On the other hand, women's birth history retrospective data particularly among women aged 15–19 and 30–34 years are essential for the indirect estimation of child mortality. To produce reliable estimates, recall biases and record errors could be minimised during household interviews by recruiting interviewers, who are familiar with the local contexts.

Understanding the Variation of Child Mortality Estimates

Globally, two main factors increasing child mortality include high total fertility rates (TFR) and high incidences of preventable childhood communicable diseases (13). Noticeably, there has been little variation in TFRamong woman of reproductive age in PNG over the period 2006–2016. Furthermore, the proportion of vaccination coverage among children aged 12–23 months in PNG dropped by half, from 52 to 20% in the same period. As they are the key factors influencing child mortality, one can expect little improvement in child mortality indicators at the national level in the period 2000–2020's.

The surveillance data used in this study focused only on rural areas, where child mortality is higher than urban areas due to its lower socioeconomic development status. Children living in rural areas often experience higher mortality risks than their urban counterparts due to limited access to health services and lower education of parents (42). Central Province appears to be exceptional among the four provinces with consistently lowest estimates across all three child mortality indicators over the period 2014–2017. It is possibly because this province has higher socioeconomic development than other provinces. Hiri surveillance site in Central Province is located surrounding the PNG Liquefied Natural Gas (LNG) Project, where urbanisation is occurring at a rapid pace, resulting in a marked improvement in the transportation infrastructure in the

province. The population in Central Province have better access to public services such as electricity, water supply, and education and healthcare services (43).

The declining trend in child mortality was observed across the surveillance sites in the period 2014-2017 (see **Table 3**). For example, U5MR for all provinces declined from 100 child deaths in 2014 to 90 in 2015, 86 in 2016 and 2017. The data also highlighted the variation in the child mortality estimates across provinces. Hence, understanding local settings and contextual factors underlying the variations in child mortality estimates at the sub-national levels is important knowledge that would be helpful for the development of effective interventions, and monitoring and evaluation of the implementation of public health programs at the local level.

The declining trend in child mortality in EHP was shown as the U5MR estimate declined from 150 in 2014 to 120 in 2015, 110 in 2016. This trend was even more obvious in Hela Province, with U5MR declining from 150 in 2015 to 140 in 2016 and 120 in 2017. However, such high U5MR in the highlands region is of great concern. Previous studies showed that the highlands region was well known for high child mortality in the past, and Eastern Highlands and Hela provinces had historically higher mortalities than the national level in the 1990's (31, 44). The possible factors underlying the high level of U5MR observed in these provinces need to be further investigated. From our field observation, the high U5MR in these provinces might be associated with a measles outbreak in the highlands region between 2014 and 2017. Measles is a highly infectious disease and one of the leading causes of deaths among CU5 in developing countries and globally (32, 33). A study of the global causes of child mortality showed that preventive measures for childhood infectious diseases have halved the 3.6 million child deaths recorded in the period 2000–2013 (13). In PNG, the measles outbreak was first reported in Eastern Highlands and Hela in the 1990's (34). Since then a series of measles outbreaks have been reported in PNG among other South Pacific countries (35). The most recent measles outbreak in PNG was reported by the iHDSS in 2014 and it was most severe in the highlands (36).

To better understand the impact of the measles outbreak on child mortality in the highlands region, we conducted further analysis of morbidity data and immunisation data available from the iHDSS in the period 2014–2017. The morbidity surveillance data from primary health facilities suggest that the outbreak possibly started in Eastern Highlands with the first measles suspected child patient recorded in 2013 (45). The outbreak scaled up and reached its peak in 2014, and declined in the following years. In Hela, the measles outbreak likely started later in 2014, reached its peak in 2015 and 2016, before it declined toward the end of 2017 (45, 46). The total caseload of under-five-years old patients presenting at the primary healthcare facilities in EHP and Hela provinces increased eight and four times in the period 2014–2015, respectively (46).

Measles vaccination coverage in the iHDSS surveillance sites was as low as 50% among children under 5 years of age (45), 70% among child patients seeking healthcare services (46), and $<$ 50% among children aged 12–23 months. Measles vaccination coverage was even lower in EHP and Hela Province, only 45 and 44%, respectively (47). These data evidence suggests that the high U5MR estimates in the highlands region i.e. Eastern Highlands (147 per 1000 live births) and Hela (127 per 1,000 live births) are likely associated with limited access to immunisation service. It is noted that measles had little impact on U5MR in Central Province (41 per 1,000 live births), with no measles cases reported in the period 2014–2015.

Epidemiologically, the measles death rate has a greater impact on U5MR, and less on IMR and NMR because children aged 0–11 months are often highly protected from measles because of immunity gained through breastfeeding (48). This paper has provided evidence of how the measles outbreaks could have contributed to an increased U5MR at the sub-national level, which was hidden in the national data. Lessons learned from vaccination programmes in LMICs suggest that inequity in socioeconomic development are the root causes of the ineffective delivery of the immunisation service (30). The reduction of U5MR will depend on addressing the most common causes of death such as childhood communicable diseases (49). More efforts including supplementary and regular immunisation programmes are needed to improve the vaccination coverage among CU5 (50).

National Censuses and DHS are the main data sources of child mortality estimation in PNG. These cross-sectional data are collected every ten years, with the most recent National Census conducted in 2010 and the DHS in 2016. Key population health indicators derived from these data sources are presented in **Table 6**. According to these data sources, U5MR estimates halved over the past three decades, from 90 deaths per 1,000 live births in the 1990's to 80 per 1,000 live births in the 2000's and 50 per 1,000 live births in the 2020s (51). The IMR estimates were also halved from 70 child deaths per 1,000 live births in the 1990's to 30 in the 2020's. These data sources provided U5MR estimates at the national level, but not on the variations of U5MR across geographical regions or between provinces. These data sources failed to provide estimates of IMR and NMR in the period 1990–2010. The 2020 National Census was launched on 17 August 2019, but no data has been released. The estimation of U5MR from this data source needs to be closely followed up.

Compared to the national data, the sub-national child mortality estimates presented in this study are higher. This could be because the iHDSS data had captured local contextual factors such as women fertility, childhood communicable diseases and immunisation service. As shown in **Figure 2**, our data suggests an overall trend of declining child mortality at the sub-national level in PNG in the period 2014–2017. This trend is likely to be sustained in the coming years. However, it is unlikely to meet the national targets for child mortality as set out in the MTDP 2018–2022. The above findings show the gaps in data for child mortality analysis, strongly suggesting a pressing need for closely monitoring and reporting child mortality at the national and sub-national levels. More concerted efforts are required to further examine child mortality at the sub-national level. Data sources other than DHS and National

TABLE 6 | Key population health indicators of PNG, national statistics office's national censuses and demographic health surveys, 1990–2020's.

	Census 1990	DHS 1996	Census 2000	DHS 2006	Census 2010	DHS 2016
Under 5 mortality rate (per 1,000 live births)	91.6	92.8	80.5	74 0.7	63.9	49.0
Infant mortality rate (per 1,000 live births)	N/A	69.3	N/A	56.7	N/A	33.0
Neonatal mortality rate (per 1,000 live births)	N/A	31.6	N/A	29.1	N/A	20.0
Total Fertility Rate (number of children per women)	N/A	4.8	N/A	4.4	N/A	4.2
Vaccination coverage (children aged < 12 months)	N/A	38.7%	55%	52.1%	61%	20%

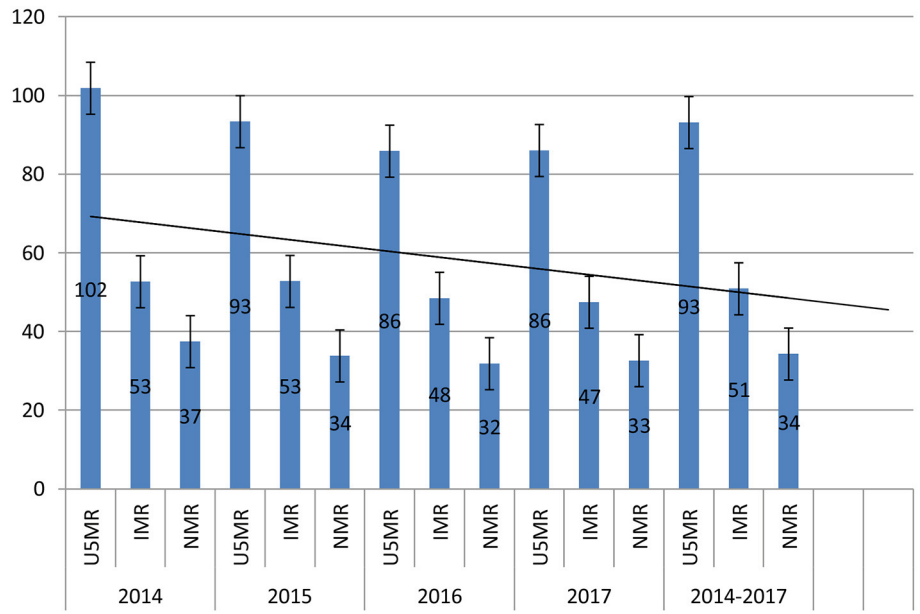

FIGURE 2 | Under 5 mortality rate, infant mortality rate and neonatal mortality rate, with error bars and overall forecast linear trend line, PNGIMR's iHDSS, 2014-2017.

Censuses available in the locality such as the iHDSS should be used for the estimation of child morality at the sub-national level, thus strengthening reliability of child mortality estimates in PNG.

Limitations

There are a number of limitations in the surveillance data used for estimations of child mortality in PNG. The PNGIMR's iHDSS provides a data series for the estimation of U5MR, IMR and NMR only at the sub-national level. The iHDSS is an important additional data source for monitoring and reporting child mortality in the rural areas of PNG, it did not offer disaggregated data for rural and urban sectors as of 2017, which is now a requirement for the PNG Government in the implementation of the SDG and reporting child mortality indicators (52). This limitation has been fixed since early 2018, when the iHDSS was upgraded to a comprehensive health and epidemiological surveillance system (CHESS) (53).

The selection of the four iHDSS sites was purposively based on the consultations and consensus with stakeholders at the national and provincial level. These sites were not representative for the provinces where they are located, in terms of socioeconomic development. Hiri and Hides were two sites experiencing considerable socioeconomic and demographic changes associated with the implementation of the PNG Liquefied Natural Gas Project in early 2010's. By contrast, Asaro and Karkar sites were selected as a continuity of PNGIMR's surveillance activities in the previous phase.

Child mortality data were collected from the populations living within the catchment areas of the iHDSS over the reporting periods. Consequently, the estimated IMR and U5MR did not necessarily represent for the mortality profile of entire child population of each province. Although child deaths in the surveillance sites were identified by data reporters, who were based in their villages and as such, were able to conduct regular household visits as part of the study on population census and demographic change, there was no guarantee that all the child deaths had been adequately reported within the time frames. For these reasons, interpretations of the IMR and U5MR estimates in this study should be made with caution.

Reducing child mortality holds the key for PNG. As a member of the United Nations, in 2020 the PNG Government should be able to submit a report for the first 5 years of

the implementation of SDGs. More effort, national resources and international assistance are therefore, needed to further accelerate the country's progress towards achieving SDG targets on child mortality by 2030. The integrated approach to collecting and reporting data in the iHDSS has made it an important data source for estimations of child mortality at the sub-national level (24). The iHDSS can provide longitudinal data series which can be used for the projection of child mortality trends in the long term. This is important infrastructure for conducting population-based epidemiological studies, clinical trials and delivery of healthcare services to the population, which are needed for the development of evidence-based and informed policy for the target populations, and to measure changes over long periods of time (54). This approach is particularly important in the global and local contexts of COVID-19 outbreaks because the local network of the iHDSS would be used to effectively roll out contact chasing, public awareness, and vaccine delivery.

Data used in this study were based on self-reported information on children's date of birth and dates of deaths. Without supporting documents such as birth certificate and death certificate, it could have led to errors in the calculation of the children's age at death (in year, month and day), which could be a bias in estimating child mortality rates. The retrospective birth history data could also have errors associated with recall biases, particularly among the older women. The Brass indirect estimation method has also limitations. A key assumption of the Brass method is the constant fertility in the recent past years, resulting from the simplified life table model (29). Although the fertility of PNG was reportedly declined in the period 2006–2016, and the decline is relatively small at the national level, but this could have varied substantially at the sub-national level. Hence, this fixed fertility assumption may result in systematic bias, potentially increasing indirect estimates of child mortality.

CONCLUSION

This study has provided a systematic assessment of child morality estimates in PNG. For the first time, both the direct and indirect estimation methods were conducted using vital statistics and maternal birth history data available from the PNGIMR's surveillance system. The differential of child mortality estimates produced by the two methods was evaluated. Variation of child mortality estimates across the provinces was assessed. PNGIMR's surveillance systems are a powerful public health tool for the PNG Government agencies to monitor the child mortality at the sub-national level. These data are essential for the health sector to respond to emerging child health issues in a timely manner. The surveillance system is more important than ever in the context of COVID-19 pandemic in PNG and globally. More consultation among PNG Government and stakeholders are needed to develop a suitable and sustainable mechanism and process for integrating recent improvements in surveillance data collection such as CHESS into the routine monitoring and evaluation systems in PNG. Benefits of the system are not limited to the provision of data for health and development, but more importantly it would be a reliable referral data source, complimentary to the existing national data sources for monitoring the implementation of the international and national development agendas, including the United Nation's SDGs 2030 and the PNG's Vision 2050.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The iHDSS was granted ethics approvals from Institutional Review Board of PNG Institute of Medical Research (IRB Approval No. 11.13) and the Medical Research Advisory Committee of Papua New Guinea (MRAC Approval No. 11.20). These approvals covered all the data components under the iHDSS, including data of women of reproductive health (15-49 years) and household demographic changes, which were used in this manuscript. Informed consent was sought from self-identified household heads and female participants. Women were informed about their right to withdraw from the study at any stage. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

BP designed and oversight the iHDSS, conceptualised the manuscript, analysed the data, drafted, revised, and finalised the manuscript. RE supervised the fieldwork, collected and analysed the data, and drafted the manuscript. TH, A-MP, and AO reviewed, provided comments, and inputs and edited the manuscript. All authors contributed to the article and approved the submitted version.

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Effectiveness of Faith-Based Interventions on the Rate of Discharged Against Medical Advice in Tertiary Newborn Units in Nigeria: A Protocol for an Open Label Randomized Control Trial

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Background: Discharged against medical advice (DAMA) is a risk factor that often leads to adverse outcomes and hospital readmissions in neonatal units. A few studies have shown that spiritual/faith-based interventions (FBIs) tend to have a lower incidence of DAMA compared with public hospitals. Perhaps, a holistic approach to patient care that addresses the spiritual needs, the soul and the body component of a being in this setting may account for the observed lower incidence of DAMA. Limited randomized control trials (RCTs) exist on FBIs with regard to DAMA in the published literature. This study seeks to compare the effectiveness of FBI, social support, religiosity, and types of FBI on neonatal DAMA against standard of care in tertiary hospitals in Nigeria.

Methods: This RCT will be conducted in two public tertiary teaching hospitals in two of the six geopolitical zones in Nigeria. The sociodemographic and clinical details of all patients admitted to the neonatal wards during the study period will be documented. Study participants will be selected through a multistage sampling technique. Subjects will be randomized and allocated to treatment and control arms having the established baseline measure of social support and religiosity. Ethical approval was obtained from the State Research Ethics Review Committee. A written informed consent will be obtained from the parents/caregivers prior to patient enrolment. The study will be conducted in line with the Declaration of Hesinki 2000. Appropriate statistical tools will be used for data collection and analysis.

Discussion: The outcome of this analysis will give insights into the effectiveness of FBI on DAMA. It will also predict the effect of the mediators of parents/caregivers' religiosity, spirituality, forms of FBI, the religious sect of parents/caregivers, and social support on the rate of DAMA on neonatal admission in tertiary hospitals in Nigeria. This could help Public Health Institutions and Governments make decisions about the determinants of neonatal DAMA and how to mitigate such outcomes. It is hoped that the evidence from this

study may guide policy formulation and guidelines on enhancing hospital retention of sick neonates until they are fit for discharge.

Trial Registration: This study was registered at the Pan Africa Clinical Trial Registry (PACTR202102670906630).

Keywords: discharged against medical advice, religion, faith-based interventions, Nigeria, neonates, newborn, randomized control trial

BACKGROUND AND RATIONALE

Approximately 130 million babies are born annually, about 4 million of these newborns in low- and middle-income countries (LMICs) do not survive beyond the neonatal period (1). More worrisome is the increasing contribution of childhood mortality from the neonatal death. This narrative is not different in Nigeria where neonatal mortality represents one of the highest in the world, only behind India (2).

The reasons for this trend are multifactorial. They vary from ignorance, harsh healthcare workers altitude to caregivers/parents, poverty, the lack of access to good healthcare, the need for spiritual support at a very trying time, and discharged against medical advice (DAMA) (3–7). It is, therefore, important that those who get to a health service be treated holistically, providing physical, psychological, and spiritual support to enable them complete treatment until when discharge is recommended by the treating clinicians (3–5).

Discharged against medical advice occurs when an in-patient decides to leave the hospital before discharge is recommended by the treating clinicians or physicians. DAMA poses serious clinical, ethical, and legal challenges to the individual physician as well as to the hospital (1, 6–9). The DAMA prevalence has been shown to vary depending on geographical areas and the study population. The rate of DAMA compares inversely with the socioeconomic status: a relatively lower rate was observed at a hospital serving primarily middle- and upper-class populations, whereas a higher rate was observed at a hospital serving disadvantaged urban areas (9–13). The pediatric age group, and especially the newborns are at a greatest risk for DAMA in Nigeria from the published literature (9–11).

Discharged against medical advice has been shown to increase the risk of adverse outcomes ranging from medical complications requiring readmission to death (6, 8). Associated outcomes also include higher morbidity, increased mortality, longer hospital stays, and higher costs of treatment when readmitted (10, 11).

More challenging with DAMA is the ethical issues in neonates as they have the least autonomy to participate in their health decision. The parents/caregivers entrusted with the right of decision-making often fail this vulnerable population. The very sick babies with a risk for residual long-term outcomes, higher risk for mortality, and foreseeable future of being a burden are often thought of dispensing with by the parents/caregivers, and hence there is a request for DAMA. This poses a great challenge to the managing physician on maintaining a balance between the parents/caregivers autonomy against the fiduciary role of the physician (4, 6, 8).

A few observational studies have shown lower incidences of DAMA in faith-based hospitals where spiritual leaders actively participate in patient care (14–20). A holistic approach to patients' care that addresses the spiritual needs, the soul, and the body component of a being in this setting may account for the observed lower incidence of DAMA. However, it may not be sufficient to explain the lower incidence of DAMA with just the involvement of the spiritual leader in care, the literature has suggested that a number of variables can interact to influence decision-making. In this instance, perceived social support of parents/caregivers of newborns as well as their levels of religiosity may significantly influence the decision to engage in DAMA (20–22). Limited randomized control trial (RCT) studies on the effectiveness of faith-based intervention (FBI) are available in the published literature.

This protocol provides a workflow for an open label randomized clinical trial to evaluate the effectiveness of spiritual/FBI intervention on hospital retention of neonates compared with standard of care in tertiary hospitals. It also includes secondary outcomes such as patients' clinical outcome, parents/caregivers' satisfaction with intervention, and their desire to see the intervention established as routine care for newborns in a public tertiary hospital.

OBJECTIVES

General Objective

The general objective is to determine the effectiveness of religion intervention rates of DAMA in neonates.

Specific Objectives

To determine:

1. a comparison of the effectiveness of religion intervention with standard of care on newborn rates of DAMA.
2. the association in case of between clinical and sociodemographic characteristic of patients on the rates of DAMA.
3. the delineation of the reasons for DAMA among neonates in Nigeria.
4. a model for a prediction of the rates of DAMA in neonates using explanatory variables (reasons) for DAMA.
5. the effect of parents/caregivers religiosity, spirituality, types of FBI, the religious sect of parents/caregivers, and social support on the outcomes of DAMA or hospital retention till discharge.

Abbreviations: RCT, Randomized clinical trial; PACTR, Pan Africa Clinical Trial Registry; FBI, Faith-based intervention; LMIC, Low- and middle-income countries.

TABLE 1 | Participant timeline (25).

	STUDY PERIOD				
	Enrolment	**Allocation**	**Post-allocation**		**Close-out**
Timepoint	$-t_1$	**0**	***12hs***	***72hrs***	t_x
Enrolment:					
Eligibility screen	X				
Informed consent	X				
Administration of research screening tools	X				
Clinical history and examination	X			X	
Allocation		X			
Interventions:					
[Intervention A]			X	X	
[Intervention B]					
Assessments:					
[List outcome variables]					X

Trial Design

Intervention Assignment

This will be an open label, parallel RCT.

Simple randomization using a randomization table created by a computer software program would be used for randomization.

Allocation sequence would be concealed in sealed opaque envelopes.

METHODS: PARTICIPANTS, INTERVENTIONS, AND OUTCOMES

Study Setting

This study is a multicenter study involving two public tertiary hospitals located in two of the six geopolitical zones/regions in Nigeria (23, 24). The selected tertiary hospital includes University College Hospital Ibadan and The Federal Medical Center Katsina, Katsina state as shown in **Figure 2**.

Eligibility Criteria

Inclusion Criteria

1. All newborns admitted into selected public hospitals whose parents/caregivers gave their consent to participate in this study.

Exclusion Criteria

1. Babies whose parents/caregivers fail to give consent for this study.
2. Babies were taken into custody by institutions such as motherless home or by government agencies for legal reasons.

Who Will Take Informed Consent?

Prior to recruitment, the research would be explained to parents/caregivers by the investigator who will obtain a written informed consent. Parents/caregivers will be informed of their freedom to refuse to take part in this study without any negative consequences to them or their wards in the course of treatment.

Additional Consent Provisions for the Collection and Use of Participant Data and Biological Specimens

Additional consent would be obtained for data availability for secondary analysis and for ancillary studies in the future.

Interventions

Explanation for the Choice of Comparators

The comparator will provide standard of care for all babies admitted to a newborn unit. The active treatment of control arm is in line with basic principles of medical ethics for RCT.

Intervention Description

There will be two arms of this study; one arm (the experimental arm) will receive a FBI. The FBI will involve religious counseling encouraging the caregivers/parents to stay in the hospital until their baby is medically discharged. This will also involve offering prayers and reading of holy books for the babies recovery. Each participants will have two to three sessions of the FBI with each session lasting 20–30 min.

The control arm will be exposed to standard of care observed for all babies admitted to a newborn unit.

Criteria for Discontinuing or Modifying Allocated Interventions

Participant who also wishes to exit study after due counseling.

Strategies to Improve Adherence to Interventions

Prior to recruitment, parents/caregivers of study participants will be educated on the study in order to gain their cooperation.

Relevant Concomitant Care Permitted or Prohibited During the Trial

Both the experimental and control group will have access to the same treatment except for the intervention in the experimental arm.

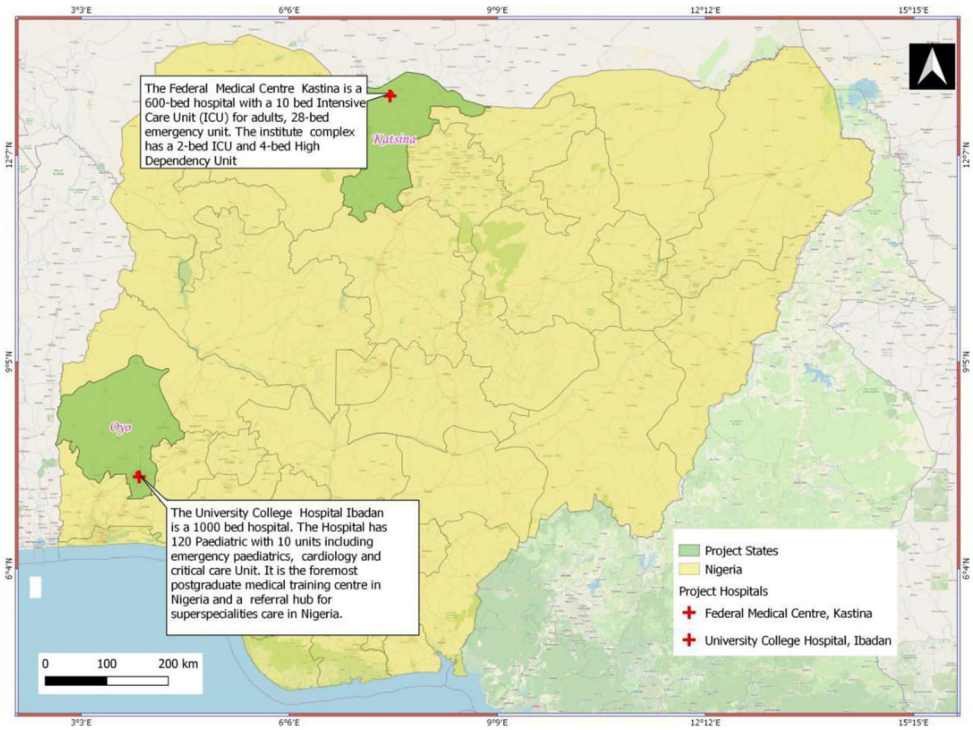

FIGURE 1 | Study participant flow chart.

Provisions for Post-trial Care

The outcome of measure is a one-time off measure and would not require a follow-up.

Outcomes

The Primary Outcome

1. The primary outcome of this study is the retention rate of sick newborns with the FBI in public tertiary hospitals in Nigeria compared with the standard of care.

Secondary Outcomes

1. The secondary outcomes are the reasons and determinants of DAMA among neonates in tertiary hospitals in Nigeria.

The effect of parents/caregivers religiosity, spirituality, types of FBI, the sect of parents/caregivers, and social support on the outcomes of DAMA or hospital retention in neonatal admission.

2. Patients' clinical outcome.
3. Parents/caregivers' satisfaction with intervention and their desire to see the intervention established as routine care for newborns in a public tertiary hospital.

Participant Timeline

Sample Size

The details of participant timeline is shown in **Table 1**. The sample size required for this study was determined using the Raosoft sample size calculator (http://www.raosoft.com/samplesize.html) for single proportion with estimated 50% prevalence of DAMA. A sample size of 359 has 80% power to detect the prevalence of cerebral malaria at an alpha level of probability 0.05.

Recruitment

The details of patients' recruitment are shown in the study participant flow chart in **Figure 1**.

Invitation: the caregivers/parents of eligible patients will be verbally invited during their hospital admission.

Eligibility: subjects will be assessed based on the eligibility criteria enumerated earlier.

Enrolment: eligible subjects will be enrolled into this study after giving a written informed consent.

Informed consent: parents and caregivers will give a written informed consent during enrolment. This will be signed by Principal Investigator, the parent/caregiver, and a witness. A copy of informed consent will be retained by the parent, while a copy will be kept in the patient's file.

Sampling Technique

In stage I, the list of tertiary hospitals in Nigeria will form the sample frame for this study. A random number will be allocated to each center. Two institutions will be randomly selected from this list.

In Stage II, an allocation sequence for the two arms will be generated using simple randomization from GraphPad Prism version 9. In the selected hospitals, consecutive neonates whose

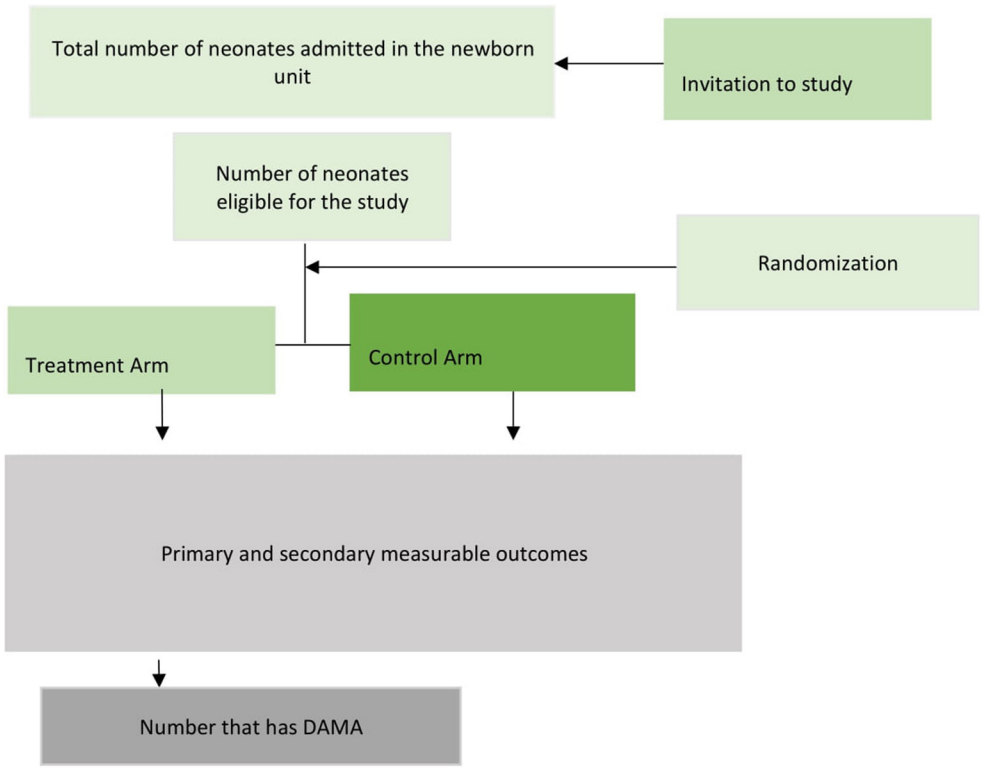

FIGURE 2 | Map of the study centers in Nigeria.

parents/caregivers give an informed consent would be allocated to one of the two arms based on the allocation sequence.

Allocation

Allocation will be done by simple randomization using the random numbers generated from GraphPad Prism (version 9) for this study.

1. Arm A: The intervention for FBI.
2. Arm B: The standard of care for neonates admitted into the unit born units of selected hospital.

Subjects will be allocated to two arms of this study in parallel (concurrent): FBI (Arm A) and standard of care (Arm B) based on the randomization process.

Assignment of Interventions: Allocation

Sequence Generation

A random number will be generated using simple randomization from GraphPad Prism version 9 for consecutive patients being enrolled for this study.

Concealment Mechanism

This study will be an open label (masking not used).

Implementation

A record officer will be responsible for generating a random number and its allocation using GraphPad Prism version 9.

Assignment of Interventions: Blinding

Who Will Be Blinded

This is an open label trial. The intervention and comparator will not be concealed. Both the investigator and the subject will be aware of what intervention they would receive.

Procedure for Unblinding if Needed

This study will be an open label (masking not used).

Data Collection and Management

Plans for Assessment and Collection of Outcomes

Training will be held for the researcher prior to the commencement of the trial *via* online zoom meeting. The validated questionnaire, the trial protocol, religiosity, spirituality, and social scales would be tested. Experience on understanding the tools and the ease of administration of the tools would be assessed. The observation from the training will be incorporated into the study instruments to improve the data entry and address other observed limitations.

Plans to Promote Participant Retention and Complete Follow-Up

This study's outcome would be measured at a single time point, with no follow up.

Data Management

The data obtained from this study will be entered into a password and encrypted institutional Red Cap database. Only specific

individuals from the collaborating centers will be given access to the database. The data from all the centers will be de-identified and managed through a secured code.

Confidentiality

All information collected in this study will be given code numbers, and no name will be recorded. This cannot be linked to the patients, parents, or a care provider in any way. Identifier will not be used in any publication or reports from this study.

Plans for Collection, Laboratory Evaluation, and Storage of Biological Specimens for Genetic or Molecular Analysis in This Trial/Future Use

This trial has no intention to collect the biological samples for a genetic study.

Statistical Methods for Primary and Secondary Outcomes

Data from this study will be analyzed in GraphPad Prism 9 (GraphPad Software, San Diego, CA, USA). The appropriate descriptive statistics will be used to present the sociodemographic characteristics of study participants. The comparison of categorical outcomes between the arms will be analyzed using the Chi-squared or Fisher's exact tests, as appropriate, and presented as risk differences, risk ratios, or odds ratios and 95% CIs. The values of $p < 0.05$ will be considered statistically significant for all analyses.

Interim Analyses

Data will be analyzed at the end of this study.

Methods for Additional Analyses (e.g., Subgroup Analyses)

Subgroup analysis will be performed using variables such as geopolitical region, gender, socioeconomic status of parents and care providers, and the levels of education and occupation.

Methods in Analysis to Handle Protocol Nonadherence and Any Statistical Methods to Handle Missing Data

The result of this study will be analyzed per protocol. Missing data will be accounted and the proportion with a desirable outcome will be presented.

Plans to Give Access to the Full Protocol, Participant Level-Data, and Statistical Code

The protocol shall be published in a peered review journal and made publicly accessible to interested individuals or body.

Individual patient data will be de-identified and stored to be encrypted in a passworded computer. De-identified data will also be stored in highly secured cloud computing. The participant level-data set and statistical code shall be made available after following due process adhering to good ethical standard.

Sharing Time Frame

The de-identified data will be publicly available for 2 years on the trial website.

Key Access Criteria

Open access to de-identified data set, which can be used for any analysis related to DAMA.

Oversight and Monitoring

Composition of the Coordinating Center and Trial Steering Committee

A trial steering committee consists of the Principal Investigator, two scientific enquirers, the public enquirer, and a biostatistician. They will meet frequently to provide an oversight function for the trial conduct over the two centers in the country.

Each center will have a hospital trial group headed by a consultant pediatrician, who will be saddled with running daily events in the hospital, providing organizational support, and reporting on a weekly basis to the steering committee.

Composition of the Data Monitoring Committee and Its Role and Reporting Structure

The data monitoring committee consists of the Head of the Information Technology at the University College Hospital Ibadan. He will centrally manage the database. He will be supported by two assistants if he is unable to perform his duties. They will be responsible for entering the data from the UCH center to the database. The head will give access to focal persons (information technologist) at the collaborating centers in Nigeria. These individuals will be responsible for entering the data into the central database in UCH. Regular zoom meeting will be held among the group members to address pressing issue. The data monitoring committee shall be independent of the core trial committee.

Adverse Event Reporting and Harms

The trial is asocial intervention. If any instance of abuse is reported by the participant, they will be handled on case by case bases by the steering committee.

Frequency and Plans for Auditing Trial Conduct

The local ethics board will monitor the progress of this trial, and all medications and update will be relayed to the body as events unfold.

Plans for Communicating Important Protocol Amendments to Relevant Parties (e.g., Trial Participants and Ethical Committees)

Any modification to the protocol or trial update will be communicated to the Ethical Approval bodies, Trial Registry, and any other relevant parties.

Dissemination Plans

The outcome of this study will be communicated to participants, ethics board, and healthcare professionals. It will be published in peer-reviewed scientific journals for public access. Data will be made available to the public maintaining ethic guidance.

DISCUSSION

The outcome of this analysis will give insights into the effectiveness of FBI on DAMA. It will also predict

the effect of the mediators of parents/caregivers religiosity, spirituality, forms of FBI, the religious sect of parents/caregivers, and social support on the rate of DAMA on neonatal admission in tertiary hospitals in Nigeria. This could help Public Health Institutions and Governments make decisions about the determinants of neonatal DAMA and how to mitigate such outcomes. It is hoped that the evidence from this study may guide policy formulation and guidelines on enhancing hospital retention of sick neonates until they are fit for discharge.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by ethical approval was obtained from the State Research Ethics Review Committee (Ref:AD13/479/3047A) and the trial was also registered (PACTR202102670906630). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

MA conceived the study, led the proposal and protocol development, critically revised the protocol for important intellectual content, gave final approval, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. OI, BO, EN, and PO contributed to the design and development of the proposal and protocol, critically revised protocol, gave final approval, and agreed to be accountable for all aspects of work ensuring integrity and accuracy. All authors read and approved the final manuscript.

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frontiers in Public Health

BRIEF RESEARCH REPORT
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Prevalence and Risk Factors of Self-Medication Among the Pediatric Population in China: A National Survey

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Background: Self-medication of antibiotics is common in China, whereas the self-medication of other medicines is still unknown, especially for the younger children who are vulnerable to adverse drug events. The aim of this study was to estimate the prevalence of self-medication reported by parents among children under age 12 in China.

Methods: A national cross-sectional survey was conducted among parents of children under age 12 in China by using a self-administered online questionnaire. Parents were asked whether they have self-medicated their children in the past 12 months. Logistic regression analysis was performed to access the risk factors of self-medication.

Results: Eligible questionnaires were obtained from 4,608 parents. The majority of respondents were mothers aged between 30 and 39 years old who held a college degree. A total of 1,116 (or 24.21%) respondents reported self-medication in the previous year. In the logistic regression model, parents with graduate degrees were less likely to self-medicate their children [Adjusted OR (AOR) = 0.436; 95% CI = 0.296–0.641]. The odds of self-medication were associated with being a father, living in Northern China, having a child at age 6–11, even though these did not reach statistical significance.

Conclusions: Our findings indicate that self-medication are common in children under age 12, highlighting the drug safety issue in China. It seems that the educational level is the risk factors of self-medication. More targeted intervention and educational program should be implemented to improve drug safety.

Keywords: self-medication, self-prescription, survey, pediatric, drug safety

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INTRODUCTION

Drug safety remains a serious public health issue. The WHO estimates that about 50% of patients fail to take their medicines correctly (1). Every year, nearly nine million children aged under five die worldwide (2), a large part of which is caused by irrational drug use (2). Self-medication or self-prescription by parents is considered as one of the biggest risk factors of drug safety (3). Parental self-medication is common globally, ranging from 7 to 70% (4–8). According to a recent study, one-third of children's population in China had parental self-medication of antibiotics without consultation of physicians or healthcare providers (9). To our best knowledge, however, there is

limited data on self-medication of other commonly used medications, such as cold and cough medicines, corticosteroids, and traditional Chinese medicine.

Children are still in the developmental stage, with different pharmacokinetic (PK) and pharmacodynamic (PD) characteristics. Hence, they are more vulnerable to adverse drug events compared to their adult counterparts (10). Due to limited pediatric formula available in the market (11), off-label use of medication is prevalent, ranging from 40 to 90% (12). In China, among 6,020 medicines commonly used in pediatrics, only 238 or 3.95% drugs are approved for pediatric use (13), and most of them are adult formulations with an extended use in children. In addition, the limited availability of pediatric formulations further exaggerates the issue of parental self-medication in China. Considering the adverse outcomes associated with parental self-medication (3, 14), the aim of this study was to estimate the prevalence and the associated risk factors of self-medication among children under age 12 in China.

MATERIALS AND METHODS

Study Design

We employed a cross-sectional design. Parents of children under age 12 were invited to an anonymous online survey, which was available in 34 provinces, autonomous regions, and municipalities which are directly under the central government in China. The study participants were the parents of the children aged under 12 years old. The survey period was from March 2018 to November 2019. This study was approved by the Institutional Review Boards of the Children's Hospital of Fudan University. This study followed the Checklist for Reporting Results of Internet E-Surveys (CHERRIES).

Survey Questionnaire

The questionnaire, which assessed the prevalence of self-medication use and drug related problems (DRPs), was created based on previous surveys conducted by China Population Communication Center (15). This questionnaire has been developed by an expert panel that consisted of pediatricians, pharmacists, outcomes researchers, and parents. The questionnaire included three sections. The first section asked the demographic and the socioeconomic characteristics of parents, including age, gender, education, and provinces. The second section was to access the prevalence of self-medication for their children. Parents were asked whether their children had been in self-medication in the past 12 months. For those who reported a self-medication for their children, we collected information on the drug classes they commonly used for the self-medication.

Participant Recruitment

To reach a representative sample of parents, following the previous research (16), we first selected 34 research coordinators to be the original deliverers who invited the parents in their communities to participate. Parents with children aged under 12 were invited to participate. Then, we sent out requests *via* WeChat private messages, including a link to the web-based questionnaire through an internet survey portal (https://www.wjx.cn/). As one of the largest social media platforms in China, WeChat has been used previously to distribute online surveys (17–19). To avoid multiple responses from the same individuals, each WeChat account was only allowed to answer the questionnaire once. A total of 5,189 parents were invited and 4,608 of them completed the survey. The response rate was 88.80%.

The accomplished questionnaire was considered as eligible if (1) all the questions were answered, (2) self-reported age of children was <12, and (3) they were parents who take care of their children. We also excluded questionnaire with the same answers to different questions to ensure the quality of survey.

Data Analysis

For descriptive analysis, frequency distributions (e.g., percentage) were estimated for categorical variables. Fisher's exact test was used to compare the difference between categorical variables. We also constructed a logistic regression model to examine the potential predictors of self-medication. Both crude and adjusted OR were estimated. Statistical significance was determined at a-level of 0.05. All statistical analyses were performed using SAS 9.4.

RESULTS

Characteristics of Respondents

A total of 4,608 (or 88.80%) of 5,189 questionnaires were included in the analysis, after discarding 581 questionnaires that were considered ineligible based on the predefined selection criteria. As shown in **Table 1**, the majority (n = 2,982; 64.71%) of respondents were aged between 30 and 39 years old, 3,563 (77.32%) were mothers, and 2,437 (52.89%) held a college degree. The majority of parents had a child aged between 6 and 11 (n = 2,799; 60.74%).

Prevalence of Self-Medication

As shown in **Table 1**, a total of 1,116 (or 24.21%) respondents reported self-medication in the previous year. Respondents who reported self-medication for their children were more likely to be aged between 30 and 39 (66.67 vs. 64.09%), live in Northern China (54.03 vs. 34.11%), and have a child aged 6–11 (65.95 vs. 59.08%). Respondents with graduate degrees were less likely to self-medicate their children (3.41 vs. 8.48%).

Among those reported parental self-medication, a total of 842 (75.45%) parents reported the use of cold and cough medicine (**Figure 1**). More than half of respondents reported self-use of respiratory medications (n = 605; 54.21%) and gastrointestinal medicine (n = 519; 46.51%). A total of 330 (or 29.57%) parents reported self-medication of antibiotics.

Risk Factors of Self-Medication

In the logistic regression model, the risk factors of self-medication were fathers (**Table 2**; Crude OR = 1.269; 95% CI = 1.075–1.502), living in Northeastern China (OR = 2.278; 95% CI = 1.001–6.131), and children aged 3–5 (OR = 1.823; 95% CI

TABLE 1 | Characteristics of respondents.

Characteristics	Overall (n = 4,608)		Self-medication (n = 1,116)		No self-medication (n = 3,492)		*P*-value
	n	%	*n*	%	*n*	%	
Parent's age							0.292
LT30	921	19.99	211	18.91	710	20.33	
30–39	2,982	64.71	744	66.67	2,238	64.09	
GT40	705	15.30	161	14.43	544	15.58	
Relationship							0.005
Father	1,045	22.68	219	19.62	826	23.65	
Mother	3,563	77.32	897	80.38	2,666	76.35	
Parent's education							<0.0001
Middle school	847	18.38	233	20.88	614	17.58	
High school	990	21.48	270	24.19	720	20.62	
College	2,437	52.89	575	51.52	1,862	53.32	
Graduate	334	7.25	38	3.41	296	8.48	
Regions							<0.0001
Northeast China	33	0.72	6	0.54	27	0.77	
Northern China	1,794	38.93	603	54.03	1,191	34.11	
Eastern China	1,472	31.94	243	21.77	1,229	35.19	
Southern China	87	1.89	11	0.99	76	2.18	
Central China	302	6.55	66	5.91	236	6.76	
Northwest China	477	10.35	118	10.57	359	10.28	
Southwest China	443	9.61	69	6.18	374	10.71	
Children's age							<0.0001
LT1	150	3.26	21	1.88	129	3.69	
1–3	309	6.71	50	4.48	259	7.42	
3–5	1,350	29.30	309	27.69	1,041	29.81	
6–11	2,799	60.74	736	65.95	2,063	59.08	

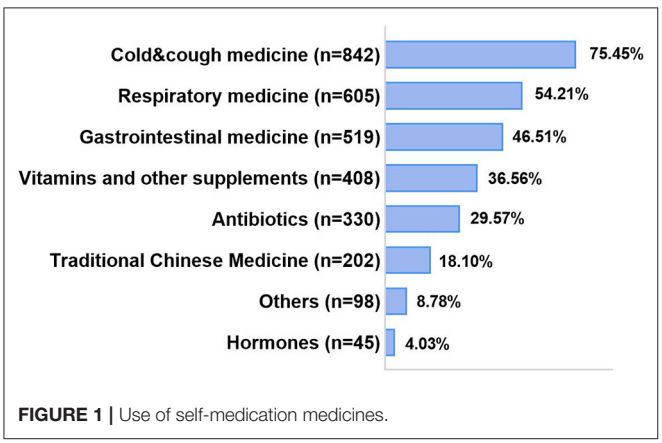

FIGURE 1 | Use of self-medication medicines.

= 1.155–3.020), and aged 6–11 (OR = 2.192; 95% CI = 1.402–3.599). Parents with college (OR = 0.814; 95% CI = 0.682–0.973) or graduate education (OR = 0.338; 95% CI = 0.231–0.484) were less likely to self-medicate their children.

After adjusting for other risking factors, parents with graduate degrees were less likely to self-medicate their children [**Table 2**; Adjusted OR (AOR) = 0.436; 95% CI = 0.296–0.641]. The odds of performing self-medication were higher among fathers (OR = 1.125; 95% CI = 0.946–1.339), living in Northern China (OR = 1.792; 95% CI = 0.726–4.426), and having a child at age 6–11 (OR = 1.489; 95% CI = 0.903–2.455), even these did not score statistical significance.

Nearly half of respondents reported misuse of antibiotics (n = 1,976; 42.88%), a total of 1,654 (or 35.89%) respondents reported abuse or misuse of cold and cough medicines. The abuse or misuse of traditional Chinese medicine (TCM) was also reported among 24.48% of respondents (n = 1,128).

DISCUSSION

In this large national survey, nearly one-fourth of parents reported self-medication in the previous year, indicating that self-medication is common in children under age 12. Our findings highlight the drug safety issue in China. The risk of self-medication reported by our study is similar to those observed in other countries. The prevalence of parental self-medication was 16.1% in Brazil (5) and 32.8% in France (6), suggesting that parental self-medication is a global issue in both developed and developing countries.

TABLE 2 | Crude and adjusted Odd Ratios (ORs) of having self-medication in the previous year.

Variables	Crude				Adjusted			
	Estimate	OR	95% CI	*P*-value	Estimates	OR	95% CI	*P*-value
Parent's age								
LT30	Ref	Ref	—	—	Ref	Ref	—	—
30–39	0.112	1.119	(0.941–1.334)	0.208	−0.059	0.943	(0.777–1.145)	0.554
GT40	−0.004	0.996	(0.788–1.257)	0.972	−0.225	0.798	(0.618–1.032)	0.085
Relationship								
Father	0.238	1.269	(1.075–1.502)	**0.005**	0.118	1.125	(0.946–1.339)	0.183
Mother	Ref	Ref	—	—	Ref	Ref	—	—
Parent's education								
Middle school	Ref	Ref	—	—	Ref	Ref	—	—
High school	−0.012	0.988	(0.805–1.214)	0.910	0.102	1.108	(0.896–1.369)	0.346
College	−0.206	0.814	(0.682–0.973)	**0.023**	−0.086	0.917	(0.756–1.113)	0.382
Graduate	−1.084	0.338	(0.231–0.484)	**<0.001**	−0.831	0.436	(0.296–0.641)	**<0.001**
Regions								
Northeast China	Ref	Ref	—	—	Ref	Ref	—	—
Northern China	0.823	2.278	(1.001–6.131)	**0.040**	0.583	1.792	(0.726–4.426)	0.206
Eastern China	−0.117	0.890	(0.388–2.404)	0.798	−0.324	0.723	(0.292–1.790)	0.484
Southern China	−0.429	0.651	(0.224–2.046)	0.440	−0.594	0.552	(0.185–1.651)	0.288
Central China	0.230	1.258	(0.530–3.485)	0.626	−0.003	0.997	(0.391–2.543)	0.995
Northwest China	0.391	1.479	(0.636–4.04)	0.399	0.158	1.172	(0.466–2.947)	0.737
Southwest China	−0.186	0.830	(0.352–2.29)	0.692	−0.401	0.670	(0.264–1.701)	0.399
Children's age								
<1 year	Ref	Ref	—	—	Ref	Ref	—	—
1–3 years	0.171	1.186	(0.692–2.095)	0.545	0.256	1.292	(0.737–2.263)	0.371
3–5 years	0.601	1.823	(1.155–3.020)	**0.014**	0.428	1.534	(0.933–2.520)	0.092
6–11 years	0.785	2.192	(1.402–3.599)	**0.001**	0.398	1.489	(0.903–2.455)	0.119

The bold font indicates these variables reached statistical significance.

Parents are usually the main caregivers for their children, and are mainly responsible for managing the medication therapy of their children. Their knowledge level and attitude toward drug safety greatly affects whether their children use medications rationally. In this analysis, parents with higher education were less likely to perform self-medication for their children, which was different from other countries. In both Germany and Italy, educated parents were more likely to practice self-medication compared to those with lower education level (20, 21). This discrepancy may be explained by how Chinese parents with higher education are more aware of the importance of drug safety. In addition, our findings also indicate that children living in Northern China had a higher risk of self-medication than those living in other regions, which could be potentially explained by the geographic disparities in the economic development level. It seems that the risk of self-medication increases with the age of children. Particularly, our analysis suggested that children aged 6 to 11 were more likely to be self-medicated by their parents, which was consistent with findings from other countries (7, 22).

In China, antibiotics have been pervasively used for children at home or in the clinical settings. In other developing countries, the prevalence of self-medication with antibiotics was as high as 80% (23, 24), leading to the growing concern of the antimicrobial resistance (AMR). Parental self-medication of antibiotics further increases the risk of developing antimicrobial resistance. The self-medication of antibiotics was more prevalent in rural or less economically developed areas. Since parents play a key role in medication management of their children, targeted intervention should be developed for those with lower socioeconomic status to improve their knowledge on the rational drug use. For parents living in the rural or less developed areas, targeted educational campaign should be offered to improve awareness of rational use of medication.

There are several limitations in this study. First, even though this is a national survey, our findings may not reflect the risk of self-medication among the general population because only a small proportion of parents in China participated in the survey. Second, we cannot exclude the possibility of selection bias because parents with higher literacy level were more likely to participate in the survey. As such, it will be difficult to access the knowledge level of those physicians who failed to respond. Lastly, we only included a couple of predictors for self-medication in the survey. Parental self-medication may be influenced by other factors, such as level of income, non-availability of health care centers, and the number of children.

In conclusion, in this large, national survey in China, parental self-medication is prevalent in children under age 12, highlighting the drug safety issue in China. It seems that educational level is the risk factors of self-medication. More targeted intervention and educational program should be implemented to improve drug safety.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Children's Hospital of Fudan University. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

JY and GM: concept and design. GM: acquisition, analysis, or interpretation of data. JY: drafting of the manuscript and statistical analysis. JY, WD, and GM: critical revision of the manuscript for important intellectual content. GM, WD, and QD: administrative, technical, or material support. GM and ZL: supervision. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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A New Birthweight Reference by Gestational Age: A Population Study Based on the Generalized Additive Model for Location, Scale, and Shape Method

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Background: It is important to choose a suitable birthweight reference to assess newborns, especially those that are small for gestational age (SGA). Currently, there is no regional standard reference for the north of China or for Shandong province.

Methods: A total of 130,911 data records of singleton, live neonates born at 24–42 weeks of gestation were collected from 2016 to 2018 in Shandong province. A new birthweight-for-gestational age percentile reference was constructed based on the Generalized Additive Model for Location, Scale and Shape (GAMLSS) package in R version 3.5. The established gestational age weight curve was compared separately with the Fenton curve, INTERGROWTH−21st curve, and the Chinese Neonatal Network Standard curve of 2015.

Results: We established the reference values of birthweight by gestational age at the 3rd, 10th, 25th, 50th, 75th, 90th, and 97th percentiles. Newborns had much heavier birthweights than those in the INTERGROWTH-21st and Fenton curves at most gestational ages. Although the newborns' birthweight references were closer to the Chinese Neonatal Network Standard except a few for gestational age, this study and INTERGROWTH-21st had similar birthweight curve shapes.

Conclusions: There are obvious differences among the criteria for newborn birthweights. Therefore, it is more accurate to assess newborns using the local birthweight reference.

Keywords: child public health, growth chart, birthweight, early growth, gestational age

INTRODUCTION

As a traditional index, birthweight has been used to evaluate intrauterine fetal growth and nutritional status (1). Small for gestational age (SGA), which are newborns whose birthweight falls below the 10th percentile of the reference population, has been identified as the strongest predictor of neonatal morbidity and mortality by pediatricians (2). Many countries have built their

own birthweight standard. Current studies on birthweight standards have focused primarily on developed countries (1, 3–11) with limited research from developing and less developed countries (12–15). In 2008, the International Fetal and Newborn Growth Consortium for the Twenty-first Century (INTERGROWTH-21st) (16) developed guidelines for fetal growth and newborn size. The Fenton growth chart for preterm newborns, a meta-analysis based on six related studies, was updated in 2013 and has been widely used in the United States, Britain, Australia, and many other countries to evaluate the intrauterine growth of newborns (17, 18).

In 1986, the birthweight of newborns with gestational ages from 28 to 44 weeks from 15 cities of China was collected and analyzed. Then, the first Chinese newborns' birthweight percentile reference curve was drawn (19). However, the curve did not distinguish between genders and the method used to analyze the data was relatively simple. In 2015, the Chinese Neonatal Network established the newest nationwide neonatal birthweight reference curve with Generalized Additive Model for Location, Scale, and Shape (GAMLSS) method, which has been used in China (20). Subsequently, other provinces in China also successively carried out relevant research (21, 22).

Birthweight can be affected by factors such as ethnicity (23), socioeconomic status, living conditions and natural environment (24, 25), the level of maternal nutrition, and many other factors (26–28). However, limited by sample choice and study design, there is yet to be a consensus on which reference should be adopted for clinical work. Large differences in socioeconomic status, living conditions, and natural environment between the north and south of China make it inappropriate to use the same birthweight reference. It is necessary to establish different birthweight references for different areas. Shandong Province is in the north of China, with a population of 100 million and annual births more than 1.3 million. Therefore, it is essential to establish a local standard for Shandong province. In our study, we aimed to produce a standard growth curve of gestational-age-specific birthweight based on data from the Shandong province and compare the reference from Shandong with international standards.

METHODS

Study Design and Participants

From each city in the Shandong province of China one hospital was randomly selected from the secondary and tertiary public hospitals to participate in this research. For cities with a resident population of more than eight million, two hospitals were randomly selected. A total of 12 cities and 17 hospitals were included in the study. The data on live-born newborns admitted to the selected hospitals were collected from September 1, 2016, to August 31, 2018, and newborns born at 24–42 weeks of gestation were chosen for the study.

The inclusion criteria for newborns in this study were gestational age $\geq$24 weeks and $\leq$42 weeks based on the last menstrual period (LMP) or early pregnancy ultrasound examination (e.g., 40 weeks + 0 day −40 weeks + 6 days) and singleton birth. Exclusion criteria were any congenital malformations or syndromes. The flowchart for sampling of study participants grouped by gestational age is shown in **Supplementary Figure 1**. Eventually, a total of 130,212 newborns with gestational age of 24–42 weeks were included in the birth data and remained in the data analysis.

Ethical approval was obtained from the Medical Ethics Committee of the First Affiliated Hospital of Shandong First Medical University. Informed consent was obtained from the parents of study participants.

Weight Measurements and Data Collection

The birthweight (kg) was measured by an electronic weighing scale, accurate to 10 g, after the umbilical cord was cut. The newborns were weighed twice before the weight was recorded. The data collected were gestational age, sex, birthweight, parity, and mode of delivery.

Data Analysis and Construction of Growth Charts

After removing outliers from the data, we constructed the birthweight curves with the Generalized Additive Models for Location, Scale and Shape (GAMLSS) model proposed by Rigby and Stasinopoulos (29). The box-plot (30) method was used in this study to eliminate the interference with the extreme values of curve fitting. We described six parameters and arranged them in order of size by box-plot, followed by calculation of the upper and lower limits, quartiles, median, and outliers. The critical value was set at two.

The upper and lower limits of birthweight at each gestational age were exported and data outside that scope was deleted. Growth curves for the 3rd, 10th, 25th, 50th, 75th, 90th, and 97th percentiles of birthweight were constructed and stratified by sex, with the variables gestational age, birthweight, and gender by using the R software (R version 3.5) GAMLSS package (29, 31). The selection of the GAMLSS model for newborn birthweight stratified by sex can be based on the Akaike information criterion (AIC) (32), the Bayesian information criterion (BIC), or Schwarz Bayesian criterion (SBC) (33). Because of the sample size, we chose the SBC, since it can draw smoother curves with more accurate predictions (**Supplementary Table 1**). The worm plot (34) and Q–Q plot (35) were selected to detect and fit the residual map of the model.

Comparisons

The established gestational age birthweight curve was compared separately with the Fenton curve (a meta-analysis based on intrauterine growth curves from several developed countries), INTERGROWTH-21st curve (growth curves based on a multi-ethnic prospective study), and the Chinese Neonatal Network Standard (CNNS) curves of 2015 (growth curves based on Chinese native population prospective study).

RESULTS

The study participants included 68,962 male (53%) and 61,250 female (47%) newborns (male-to female-ratio 1.13:1).

TABLE 1 | Birthweight (kg) percentiles by gestational age.

Gestational age, weeks	Male							Female						
	P3	P10	P25	P50	P75	P90	P97	P3	P10	P25	P50	P75	P90	P97
24	0.542	0.632	0.709	0.780	0.851	0.930	1.023	0.553	0.631	0.695	0.745	0.798	0.873	0.977
25	0.601	0.700	0.789	0.871	0.955	1.046	1.149	0.606	0.695	0.768	0.829	0.893	0.978	1.094
26	0.665	0.776	0.876	0.974	1.072	1.175	1.292	0.665	0.765	0.850	0.923	0.999	1.097	1.224
27	0.737	0.859	0.974	1.087	1.202	1.321	1.452	0.728	0.841	0.940	1.028	1.119	1.230	1.370
28	0.816	0.952	1.082	1.214	1.348	1.484	1.631	0.798	0.926	1.040	1.145	1.253	1.379	1.532
29	0.905	1.056	1.202	1.355	1.511	1.665	1.831	0.874	1.019	1.151	1.275	1.403	1.546	1.714
30	1.006	1.172	1.336	1.511	1.69	1.865	2.051	0.958	1.122	1.274	1.421	1.572	1.733	1.917
31	1.120	1.304	1.487	1.684	1.886	2.083	2.291	1.055	1.240	1.412	1.585	1.760	1.942	2.143
32	1.251	1.455	1.658	1.875	2.098	2.315	2.544	1.170	1.375	1.569	1.768	1.969	2.173	2.393
33	1.404	1.628	1.849	2.084	2.324	2.559	2.807	1.308	1.533	1.748	1.972	2.198	2.425	2.667
34	1.580	1.825	2.063	2.313	2.567	2.815	3.079	1.477	1.717	1.951	2.196	2.446	2.694	2.960
35	1.786	2.046	2.297	2.560	2.824	3.083	3.357	1.680	1.931	2.178	2.439	2.706	2.973	3.261
36	2.027	2.291	2.548	2.819	3.093	3.359	3.639	1.918	2.173	2.425	2.694	2.973	3.255	3.560
37	2.292	2.551	2.806	3.079	3.356	3.626	3.911	2.182	2.432	2.683	2.952	3.235	3.523	3.839
38	2.550	2.797	3.044	3.311	3.586	3.855	4.138	2.443	2.681	2.921	3.185	3.463	3.745	4.054
39	2.743	2.978	3.217	3.480	3.752	4.015	4.291	2.642	2.865	3.096	3.356	3.630	3.899	4.188
40	2.862	3.091	3.328	3.594	3.869	4.128	4.395	2.771	2.989	3.216	3.477	3.750	4.012	4.286
41	2.967	3.192	3.427	3.697	3.974	4.229	4.486	2.885	3.099	3.323	3.580	3.848	4.103	4.367
42	3.061	3.285	3.521	3.795	4.075	4.327	4.576	2.987	3.198	3.420	3.675	3.941	4.189	4.443

P, percentile.

Table 1 shows the birthweight percentiles (3rd, 10th, 25th, 50th, 75th, 90th, 97th) for newborns by gestational age. All the male newborns were heavier than female newborns at birth except some in the 3rd percentile.

Figures 1, **2** shows newborn birthweight at the 10th, 50th, and 90th percentiles by gestational age based on CNNS and INTERGROWTH-21st. The birthweight curves show similar shapes, although some differences exist for both sexes. As shown, birthweight increased faster in CNNS before 37 weeks of gestation, then flattened out. In the 10th and 50th percentiles, newborns with gestational age from 28–37 weeks had similar birthweights compared to the CNNS curve, but after 37 weeks birthweights gradually increased in our study. In the 10th and 50th percentiles, before 28 weeks of gestation, newborn birthweights in CNNS gradually decreased with decreasing gestational age. In contrast to CNNS, the present study and INTERGROWTH-21st have similar birthweight curve shapes, with slow weight gain before 28 weeks of gestation and a good rate or weight gain after 37 weeks of gestation. However, in the present study, boys were much heavier than in INTERGROWTH-21st.

Figure 3 shows that the male newborns' birthweight curves in present study are higher than Fenton curves before 39 weeks gestational age and gradually be exceeded after that.

Figure 4 shows that the 90th and 97th birthweight curves of female newborns were consistent from 31 to 38 weeks gestational age compared to the Fenton curves. The 50th curve was higher than Fenton curves before 40 weeks gestational age. The 3rd and 10th curves were much heavier than Fenton curves.

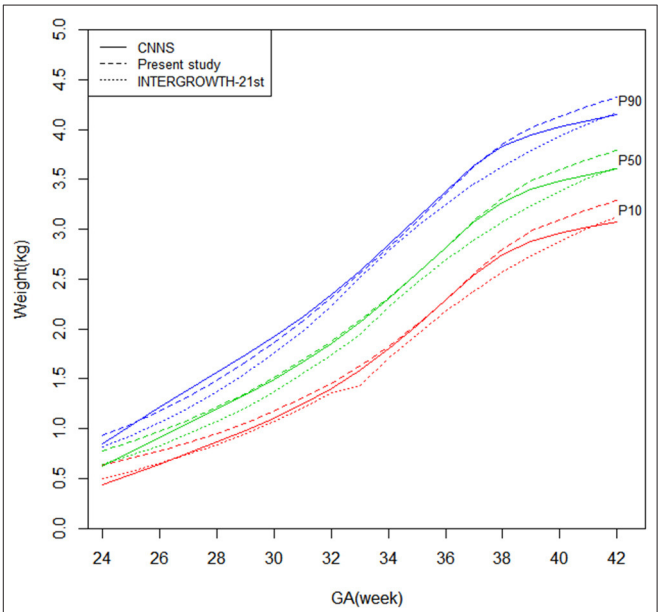

FIGURE 1 | Comparison of birthweight (kg) curves by gestational age among the present study, CNNS and INTERGROWTH-21st Newborns Size Standards/ References (male).

DISCUSSION

It is essential to choose an effective birthweight reference curve to estimate birth outcomes in clinical practice (36–38). Using

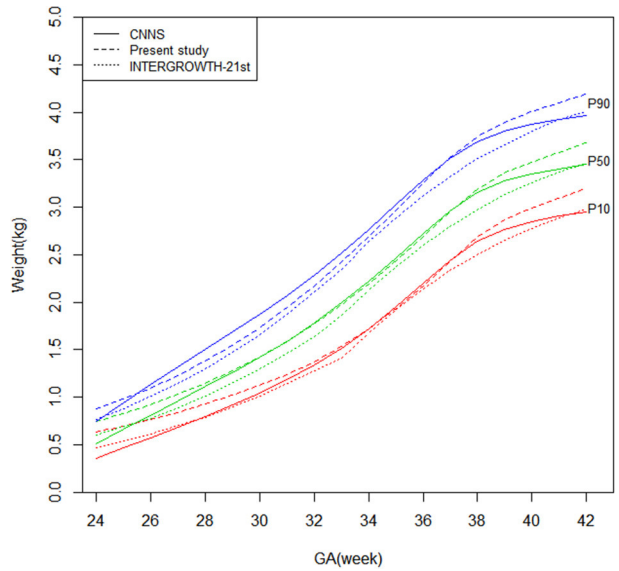

FIGURE 2 | Comparison of birthweight (kg) curves by gestational age among the present study, CNNS and INTERGROWTH-21st Newborns Size Standards/ References (female).

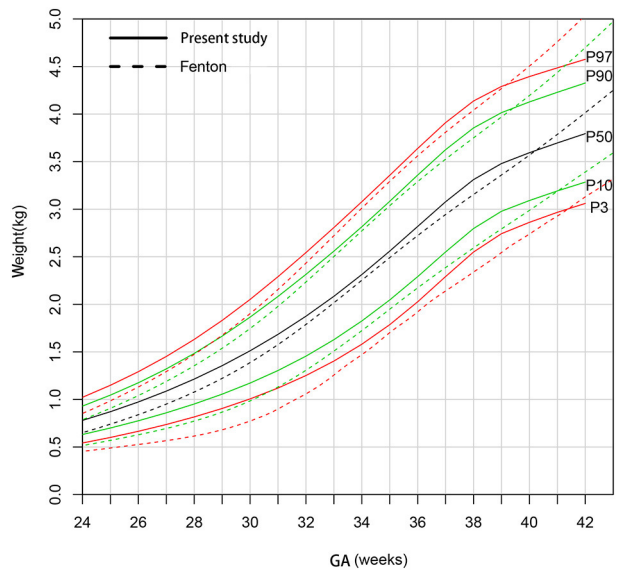

FIGURE 3 | Comparison of birthweight (kg) curves by gestational age between the present study and Fenton curve (male).

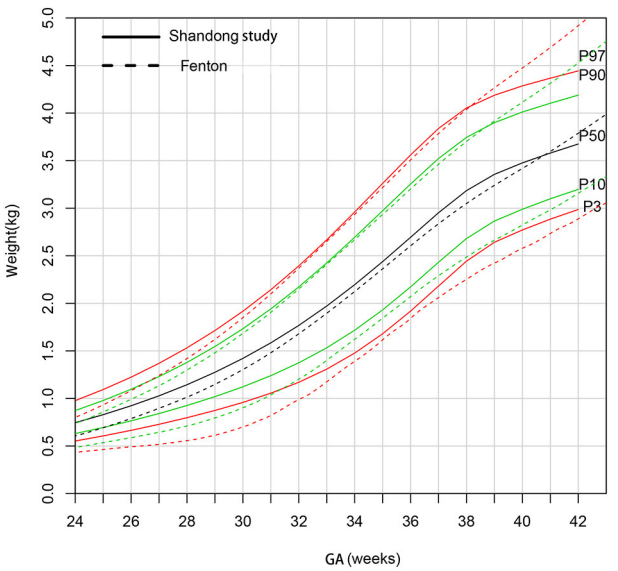

FIGURE 4 | Comparison of birthweight (kg) curves by gestational age between the present study and Fenton curve (female).

an outdated standard to screen high-risk neonates may lead to a classification error and thereby mislead the doctors who must decide on clinical diagnosis, treatment, and health resource allocation. Shandong and the other provinces in north China have not yet formulated their local standards. Although the population sample of this study is from 12 cities in Shandong Province, most of the northern China provinces, specifically Liaoning, Jilin, Hebei, and Henan, are mainly Han population and have similar local economic conditions and population migration background. Therefore, in addition to representing Shandong, these data can also represent northern China.

After the Two-Child Policy was implemented in China, many couples tried to have a second baby later in life. This was associated with a greater number of older mothers and assisted fertility methods, both of which increase the risk of low birthweight premature babies (39–41). Premature infants generally have a different pattern of early growth than term infants (42). Assessing these babies properly will improve their prognosis. In China, newborns with gestational age of $\leq$37 weeks are defined as premature infants.

There are three methods commonly used to construct child growth reference curves: cubic splint function (43); locally-weighted regression and smoothing scatterplots; and coefficient of skewness-median-coefficient of variation, LMS (44). In recent years, LMS, a relatively established method, was widely used in calculating age-related growth references for children and adolescents, such as height, weight, head circumference, and sex development. GAMLSS is an emerging method to construct reference curves for child development. When modeling the variables like gestational age and sex, GAMLSS can use all data in the model; therefore, the distribution curve tends to be stable, even if the sample size is small. In this study, the percentile reference standard of birthweight for Shandong province at a gestational age of 24–42 weeks was created by using the GAMLSS method. The reasons that we chose GAMLSS were the more accurate prediction, smoother curve, and successful use in China and overseas (45, 46). Verified by Q–Q plot, worm plot, and residual plot, our reference standard shows that the data distribution is well-fitted.

Our study corroborates those of the CNNS, showing that newborns in north China are much heavier than those in the Fenton curve and INTERGROWTH-21st. This difference has also been shown in other studies, where Chinese newborns were

found to be heavier than those in Europe and the United States (42, 47). There are economic and hereditary reasons to be considered concerning this phenomenon. Comparing recent research data on Chinese birthweights and back to 1986 (19), we found that with improvement in economic levels, the birthweights of term infants were significantly higher than 30 years ago. In addition, pregnant women in China have improved their nutrition during pregnancy, which results in increased weight gain during pregnancy and a heavier baby. On the other hand, gaining too much weight during pregnancy has an adverse effect on blood glucose, which will severely affect birthweight (48–51). The newborns in our study >40 weeks of gestation become much lighter than those in the Fenton reference because our curves were based on intrauterine growth data, while the Fenton reference was based on extrauterine growth data.

In the 10th percentile, most of the gestational ages show much heavier birthweights in our study than those in the CNNS, which might result from genetic, economic, and geographic factors. Most importantly, there will be a more accurate assessment for SGA newborns in north China if we use the birthweight reference from Shandong.

Our research has several limitations. First, because of the different medical treatment levels in different regions, higher birthweights are associated with higher chances of survival. Our data comes from level II or level III public hospitals and the medical treatment level at these hospitals is relatively high. Although we can collect more data on SGA newborns, this can cause sampling error, so that birthweight in our study is slightly high, especially for newborns with gestational age <28 weeks. Second, our study is a cross-sectional study, and more follow-up is needed to observe weight fluctuations. In future studies, we can establish an array of research including local newborns with larger sample size, complete sets of growth measurements like birth height and birth head circumference, and long-term follow-up, and construct a more reliable growth curve for newborns especially for newborns with gestational age <28 weeks.

CONCLUSIONS

It is important to choose suitable criteria to assess newborn birthweight. We established the first birthweight references from Shandong Province. Our birthweight references are higher than those of Fenton and INTERGROWTH-21st and are somewhat higher than those of the CNNS. Although the reason for this needs to be further clarified, it might indicate possible economic and hereditary differences and creates concern over the appropriateness of Fenton, INTERGROWTH−21st, and the CNNS in assessing the local newborn population. Therefore, it is necessary to construct and use regional birthweight standards for newborns from northern China.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

YL and QW designed the study. YL and LZ revised the manuscript. QW and H-YZ constructed growth charts and wrote the manuscript. LZ, Y-QX, and JS data collection and organization. N-NG and X-YQ data analyses. YL had primary responsibility for final content. All the authors guided and give many useful suggestion for this research, they both read and approved the final manuscript.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fped.2022.810203/full#supplementary-material

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Impact of Spirulina Chikki Supplementation on Nutritional Status of Children: An Intervention Study in Tumkur District of Karnataka, India

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Objective: To assess the impact of Spirulina Chikki supplementation on the nutritional status of children (6 months−6 years).

Design: A cross-sectional study design was adopted to assess the changes in nutritional status among the children (after 12 months of intervention period). The bassline and endline assessment were carried out from September 2020 to August 2021, respectively.

Setting: Total 106 villages (108 Anganwadi Centers in nine circles) from Tumkur District were covered.

Methods: Children aged 6 months−6 years were the study subjects. Anthropometric measurements viz., height, weight, and mid-arm circumference were collected from total 971 and 838 children during baseline and endline assessments correspondingly. The information on children's health and nutrition status was gathered from the mothers of sampled children. WHO's Anthro and AnthroPlus software were utilized to estimate the anthropometric measurements (Stunting, wasting, and underweight) of study participants.

Results: The study found apparent disparities in the prevalence of stunting, wasting and underweight among the male and female children. There was a significant decline viz., 4% (28.6%-baseline to 24.5%-end line) in the prevalence of severe wasting. Also, severe stunting dropped by 6% at end line (30%-end-line to 24%-baseline). Improvement in nutritional status was evident among both female male children in all three indicators stunting, wasting, and underweight. Mid-upper arm circumference (MUAC) measurement shows substantial improvements from baseline to end line: SAM (5.3–0.6%), MAM (23–9%), and normal (72–91%). The study discloses significant improvements in the nutritional status among those children who consumed spirulina chikkis/granules for a longer duration viz., 9–10 months as compared to those who consumed for lesser duration.

Conclusions: Findings reveal improvement in nutritional status among the beneficiaries who consumed spirulina chikki/granules as per the recommended quantity (amount) during the intervention period. Post intervention, spirulina chikki supplementation for nutritional intervention is implied to address large scale malnutrition among young children.

Keywords: nutritional status, anthropometric measurements, MUAC, spirulina, Tumkur, India

INTRODUCTION

Health and nutrition are the critical for the growth and human development. Since birth, better nutrition is of utmost importance for a child to have a robust immune system. It is essential to lower the chances of acquiring communicable and non-communicable diseases (1). Any form of malnutrition has significant threats to human health. At present, globally, especially in low- and middle-income countries double burden of malnutrition viz., both undernutrition (wasting, stunting, and underweight) and overnutrition are rising immensely (2). It is estimated that by 2020 globally, among the under five children, stunted, wasted, and overweight or obese children would be 149, 45, and 38.9 million, respectively (3).

India is the home to a sizable number of malnourished children across the world. According to NFHS-5 India, more than one-third of the under-five children (35.5%) were reported stunted, 19.3% were wasted (7.7% were severely wasted), and a little less of one-third (32.1%) were underweight. Further, it is evident that, the burden of malnutrition is high among the rural population in Tumkur. The most recent estimate exhibits that prevalence of stunting is high in Tumkur district (40.3%) as compared to it's the state (35.4%). This is an alarming situation since the prevalence of stunting is also higher than the national average (35.5%). Substantial change was observed in wasting in Tumkur District (10.9%) and Karnataka State (19.5%). Also, there is considerable improvement in severe wasting in Tumkur district (3.1%), and in the State (8.4%) (4–6).

Since independence through various national programmes including ICDS program, a considerable improvement in nutrition and well-being of children have been evident in India (7). Despite these improvements, malnutrition remains a critical issue of concern where India confers one-third of the global burden for undernutrition. To improve the nutritional status of the children and mothers, the National Nutritional Strategy provides a comprehensive platform for stakeholders to converge together and drive the agenda of "Mission Malnutrition Free India-2022" (8). Also, nutritional issue is a focused concern of Sustainable Development Goals (SDGs) no 12. Notably, the UN has acted on nutrition, offering a robust, joint country-driven program for all nutrition stakeholders to increase visibility, coordination, efficiency, and effectiveness of policy processes and activities across sectors at the national level to achieve the existing global nutrition targets by 2025 and the nutrition-related targets in the Agenda for Sustainable Development by 2030 (9).

Thus, aligning with the national goal to address the malnutrition in the country, Spirulina Foundation has trained and empowered local SHG women groups to cultivate spirulina and make Spirulina Fortified Chikkis (SFCs)/Granules in Kolar district of Karnataka. Spirulina Foundation has obtained approval from Central Food Technological Research Institute (CFTRI) Mysore for the processing of Spirulina chikkis/granules. Spirulina has superior macronutrient and micronutrient contents, and rich in amino acids, unsaturated fatty acids, B12, Provitamin A (β carotene), Vitamin E and Minerals, especially iron. It is also rich in gamma linolenic acid (GLA), an omega 3 fatty acid (10). Spirulina consists of 55–70% protein content, 15–25% polysaccharide, 5–6% total lipid, 6–13% nucleic acids, and 2.2–4.8% minerals (11). The Food and Drug Administration (FDA) has permitted GRAS certification (Generally Recognized as Safe) for Spirulina consumption and allowed to consume it as a food or food supplement (12). Consumption of Spirulina has potential health effects such as immunomodulation, antioxidant, anticancer, antiviral, and antibacterial activities and positive effects against malnutrition and anemia (13, 14). The addition of Spirulina in food has been seen as an emerging trend in several studies in the past decade (15–17).

Considering the higher prevalence of malnutrition in Tumkur district of Karnataka, Spirulina Foundation launched its program and distributed the spirulina chikki/granules to the children from 6 months to 6 years in Pavagada Taluk of Tumkur district. Before the launch of the program, baseline assessment was carried out, followed by intervention viz., distribution of spirulina chikkis/granules and endline assessment. It is hypothesized that nutritional supplementation in the form of spirulina chikki/granules could improve the nutritional status of malnourished children. With this background, the objective of the study is to evaluate the impact of Spirulina Chikki intervention on the nutritional status of children (6 months−6 years) in the Tumkur district, Karnataka, India.

MATERIALS AND METHODS

Study Design and Participants

The study assessed nutritional status of the children (6 months−6 years) who consumed spirulina chikki/granules during the intervention period (September 2020–August 2021). Total 106 villages viz., 108 AWCs in nine circles was covered in Pavagada Taluk, Tumkur District. A cross-sectional study design was adopted to assess the changes in nutritional status among the children (after 12 months of intervention). The baseline and end-line assessment were carried out from September 2020 to August 2021, respectively. Children aged 6 months−6 years were the sample respondents. In the sample, all the Moderately

TABLE 1 | Quantity of chikki bars/granules distributed to beneficiaries during intervention.

Age 2–6 years		
SAM children	4 Chikkis/day	1 Chikki = 10 g
MAM children	2 Chikkis/day	
06–23 months		
SAM children	2 Spoon granules/day	1 Spoon =5 g
MAM children	1 Spoon granules/day	

Chikki *is ready to eat a traditional sweet snack (bars) that can be consumed by school children or pre-schoolers, or any other specific target group.* ***Granules*** *are small balls that can be consumed by children aged <2 years; basically, those who cannot chew the food items.*

Acute Malnourished (MAM) and Severely Acute Malnourished (SAM) children selected by the Spirulina Foundation for the intervention were covered. A pretested study tool was utilized to collect the information from the parents of the program beneficiaries. Informed written consent was obtained from the beneficiaries/subjects' parents/guardians for participation in the interview. Anthropometric measurements viz., Height, Weight, and Mid-Arm Circumference have been collected from 971 children and 838 children in baseline and endline assessment, respectively. The dropout rate of subjects was around 14 percent from baseline to end line. The information on children's health and nutrition status was collected from the mothers of beneficiaries/children.

Sampling Design

A multi-stage sampling design was adopted for the study. Firstly, the Tumkur district was selected for the study. Secondly, Pavagada taluk was selected out of 10 taluks purposively due to the high prevalence of SAM/MAM children. Thirdly, all 106 AWCs from 106 villages (nine circles) from the taluk was chosen for the study. Fourthly, information from all the mothers/caretakers of program beneficiaries (6 months−6 years children) at the Anganwadi centers was collected for the study.

Ingredients and Nutritional Values of Spirulina Chikki

Spirulina chikki consists of the following ingredients per KG: Ground Nut 500 g, Jaggery 245 g, Millet 200 g, Spirulina 50 g, and Cardamom 5 g. Approximate Nutritional value (per 100 g): Energy 425 Kcal, Protein 9.22 g, Fat 6.58, Carbohydrate 82.14 g, and Total sugar 49.5 g.

Approximate Nutritional value (per chikki.): Energy 42.5 Kcal, Protein 0.922 g, Fat 0.658, Carbohydrate 8.214 g, and Total sugar 4.95 g.

Recommended quantity of chikki bars/granules distributed to the various sample population is presented in **Table 1**. Chikki bars/granules was provided for a period of 1 year from September 2020–August 2021.

Anthropometric Measurements and Variable Description

The study has considered the four forms of malnutrition for children 6 months−6 years. We have considered four indicators Wasting (WHZ < −2SD), Stunting (HAZ < −2SD), and Underweight (WAZ < −2SD). Mid-Upper Arm Circumferences (MUAC) were categorized as per the WHO and UNICEF; normal (>12.5 cm), yellow (11.5–12.5 cm), and red (<11.5 cm) for malnutrition for children aged between 6 months and 6 years.

Each child was measured for height, weight and MUAC in the metric system, using the standardized technique recommended. Using a stadiometer (measuring rod), measured the height to an accuracy of 0.1 cm. Children were made to stand without footwear with the feet parallel and with heels, buttocks, shoulders and avoid touching the measuring rod, hand hanging by the sides. The head was at ease upright, with the top of the head making firm contact with the horizontal headpiece. The height of infants was measured using the infantometer. A convenient balance with a precision of 100 g was used to record the weight of the children. Children were directed to stand on the balance out with light clothing and without footwear and with feet apart and seeing straight. Mid-upper arm circumferences of children aged 6 months−6 years were measured using the MUAC tape endorsed by UNICEF.

A study has considered program-related variables along with anthropometric variables. The program-associated variables are heard about the spirulina foundation program, beneficiary of the program, frequency, and quantity of receiving Chikki/Granules, knowledge about the consumption patterns of Chikki/Granules and changes observed in terms of growth and feeding practice among the children.

Statistical Analysis

Univariate and bivariate analysis was used to understand the frequency distribution of the variables. For the continuous variables, the mean and standard deviation was estimated. For the anthropometric measurements, WHO-recommended Anthro, AnthroPlus software and SPSS Version 25 Software was used.

RESULTS

Table 2 presents the awareness about the program among the beneficiaries. Most of respondents (97%) reported that they had heard about the program launched by the Spirulina foundation. Among them, 92% of the respondent said that they are the program beneficiaries.

TABLE 2 | Awareness about the program among the beneficiaries.

	Frequency (*N*)	Percent (%)
Heard about Spirulina foundation's program		
Yes	810	96.7
No	28	3.3
Total	**838**	**100.0**
Beneficiaries of the program		
Yes	744	91.7
No	68	8.3
Total	**812**	**100.0**

TABLE 3 | Spirulina chikkis/granules received and consumed by the beneficiaries.

Indicators	Frequency (*N*)	Percent (%)
Child offered chikki/granules		
Chikki bar	582	78.2
Granules	162	21.8
Frequency of receiving chikkis/granules		
Monthly	720	96.8
Weekly	24	3.2
Duration of receiving chikkis/granules		
Average months	9.4 ± 1.54	740
1–8 months	63	8.6
9 months	174	23.5
10 months	480	64.7
11–12 months	23	3.2
Received chikki packets/granules bottles in 1 month		
4 packets chikkis	578	77.8
One bottle granules	136	18.6
Two bottles granules	26	3.6
Number of chikkis/granules spoon consumed by the child in a day		
2 Chikkies/day	578	77.9
One spoon granule	127	17.3
Two spoon granules	35	4.8
Chikki bars/granules consumed by the child		
Average months	9.4 ± 1.54	739
1–8 months	61	8.3
9 months	168	22.6
10 months	490	66.3
11–12 months	21	2.8
Proportion of chikkis/granules consumed by the child		
All the chikki/granules	690	93.2
75% of the chikki/granules	27	3.6
50% of the chikki/granules	15	2.0
25% of the chikki/granules	06	0.8
None	02	0.3
Chikkis shared with their siblings or other members		
Yes	44	5.9
No	696	94.1

TABLE 4 | Mothers perception about the changes in child's diet, and growth after consumption of chikkis/granules (*N* = 740).

Variables	Frequency (*N*)	Percent (%)
Any change observed in child after consumption of chikki/granules		
Yes	657	88.8
No	80	10.8
Don't know/can't say	03	0.4
Changes observed in diet and growth		
Increase in appetite	366	49.3
Increase in food intake	101	13.6
Increase in height	59	7.9
Increase in weight	131	17.7
No response	83	11.4
Change in feeding pattern		
Feeding more	601	81.3
Feeding less	11	1.5
No change	128	17.2
Child liked the taste of the chikki/granules		
Yes	703	95.1
No	32	4.3
Don't know/can't say	04	0.5
Child demanded for more chikki/granules		
Yes	673	90.9
No	65	8.8
Don't know/can't say	02	0.3
Child ate the chikki/granules eagerly		
Yes	700	94.6
No	36	4.9
Don't know/can't say	04	0.5

Knowledge and consumption patterns of spirulina chikki/granules are described in **Table 3**. More than three-fourths of the children (78%) received Spirulina chikki, and 22% received granules. Almost all the beneficiaries (97%) had received spirulina chikkis/granules every month and the rest 3 percent every week. Furthermore, around two-thirds of the children received spirulina chikki/granules for 10 months and 24 percent for 9 months. In terms of the quantity received, 78% stated that they had collected four packets of spirulina chikki, and 19% said that they received one bottle of granule, and the rest 3.6% received two bottles of granules in the month.

Regarding the mother's knowledge about the number of chikkis and amount of granules to feed the children, 78% of mothers informed two chikkis per day, 17% mothers reported one spoon granules, and around 5% mothers told two spoon granules in a day. And almost the same amount of chikkis and granules was consumed by the children. On average child consumes chikki/granules for 9.4 months. However, 66% of children consumed for 11–12 months. Majority of the children (93%) consumed all the chikki and granules. In contrast, 6% of the children shared chikkis/granules with their siblings.

Perception of the mothers on changes in the child's growth indicated that; a large majority (89%) of them reported that they had observed the change/growth in their child due to consumption of spirulina chikkis/granules. Approximately 50% of the mothers observed an increase in appetite, and 11% stated an increase in the child's weight. Mothers also reported that their children started eating increased quantity of food. It was evident that a majority (95%) of the children liked the taste of the chikki and asked for more chikkis/granules. A large proportion of the mothers reported (95%) their child eagerly ate the chikkis/granules (**Table 4**).

Anthropometric indicators show positive change over 1 year from baseline to end line assessment. The mean weight of the children improved from 9.76 to 11.1 Kg and height from 83.07 to 89.11 cm. Mid-Upper Arm Circumferences also exhibit an improvement from 13.19 to 13.8 cm in a 1-year intervention period. Further, results pointed out decline in Severely Wasted (WHZ < -3 SD) children from 9.5 to 13.1%, 3% decline in

Wasted children (29.2–32.2%) at endline. In terms of Stunting, the result shows an improvement viz., with 4% (28.6–24.5%) decline in Severely Stunted (HAZ < −3SD) at endline. For the indicator Underweight, the result found a positive change in terms of reduction (6% at endline) in Severely Underweight children (WAZ < −3 SD) (30–23.9%) in the study (**Table 5**).

The differentials in prevalence of anthropometric measurement among gender presented in **Table 6**. Incline in Severely Wasted (WHZ < −3 SD) children was observed among male (3%; 13.5–16.5%) and female (4%; 5.9–10.2%) children at endline. However, incline in the prevalence of Wasted (WHZ < −2 SD) was higher among female children (7%) as compared to their male counterparts (1.5%). Further, the prevalence of Severely Stunting (HAZ < −3 SD) showed a positive change viz., decline was higher among male children's (8%) than their female counterparts (0.7%) at endline. A substantial proportion of the male children (9%) shifted from severely underweight to moderately underweight; however, this shift was lower (3%) among the female children at endline.

The Mid-Upper Arm Circumferences of the children showed constructive improvements. At endline, the overall proportion of Severe Acute Malnutrition (SAM) declined from 5.3 to 0.6% and Moderately Acute Malnutrition (MAM) from 23 to 9%. Due to these improvements, the proportion of normal children incline from baseline (72%) to end line (91%). These improvements were observed among both male and female children; percentage of male SAM children declined to 0.8 from 3.8% and female MAM children to 0.4 from 6.6% at endline from baseline, respectively (**Table 7**).

The nutritional status viz., Stunting, Wasting, and Underweight across duration of the consumption of chikkis and granules is presented in **Table 8**. The children who consumed chikkis/granules for at least 9 months regularly had the lowest prevalence (11.7%) of Severely Wasted (WHZ < −3 SD), and the prevalence was the highest (18.3%) among those children who consumed for 1–8 months. The proportion of Severely Stunted children (21.9%) and Severely Underweight children (21.7%) were the lowest among those children who consumed chikkis/granules for 10 months.

TABLE 5 | Nutritional status of the children.

Anthropometric indicator	Baseline		End line	
	Mean ± SD	Number	Mean ± SD	Number
Weight	9.76 ± 2.2	930	11.1 ± 2.0	735
Height	83.07 ± 10.99	930	89.6 ± 11.0	735
MUAC	13.19 ± 0.94	930	13.8 ± 1.1	735
Wasted				
Severely wasted	9.5	88	13.1	96
Moderately wasted	29.2	272	32.2	236
Normal	61.3	570	54.8	402
Stunted				
Severely stunted	28.6	267	24.5	180
Moderately stunted	34.7	324	34.4	253
Normal	36.8	344	41.1	302
Underweight				
Severely underweight	30.0	281	23.9	152
Moderate underweight	46.2	433	50.2	319
Normal	23.9	224	25.9	165
Total	**100.0**	**930**	**100.0**	**735**

TABLE 7 | Mid-arm circumferences of children aged 6 months−6 years.

MUAC	Male (%)	Female (%)	Overall	Color coding as based on measuring tape
Baseline				
SAM	3.8	6.6	5.3 (51)	Red (<11.5 cm)
MAM	24.9	21.2	23.0 (223)	Yellow (11.5–12.5 cm)
Normal	71.3	72.2	71.8 (697)	Normal (>12.5 cm)
End line				
SAM	0.8	0.4	0.6 (0.6)	Red (<11.5 cm)
MAM	8.4	9.4	8.9 (8.9)	Yellow (11.5–12.5 cm)
Normal	90.9	90.1	90.5 (758)	Normal (>12.5 cm)

TABLE 6 | Nutritional status of the children.

Anthropometric measurements	Baseline			End line		
	Boy (%)	Girl (%)	Overall	Boy (%)	Girl (%)	Overall
Wasted						
Severely wasted	13.5	5.9	9.5	16.5	10.2	13.1
Wasted	32.0	26.8	29.2	30.6	33.5	32.2
Normal	54.6	67.2	61.3	52.9	56.3	54.8
Stunted						
Severely stunted	34.8	23.0	28.6	27.1	22.3	24.5
Stunted	32.0	37.0	34.7	32.1	36.5	34.4
Normal	33.2	40.0	36.8	40.9	41.3	41.1
Underweight						
Severely underweight	34.5	25.9	30.0	25.4	22.5	23.9
Moderately underweight	46.8	45.6	46.2	49.2	51.1	50.2
Normal	18.7	28.5	23.9	25.4	26.4	25.9

TABLE 8 | Nutritional status across duration of the consumption of chikkis and granules.

Anthropometric measurements	1–8 months	Up to 9 months	Up to 10 months	11–12 months	Overall
Wasted					
Severely wasted	18.3	11.7	13.0	14.3	13.2
Wasted	26.7	37.4	31.1	23.8	32.0
Normal	55.0	50.9	55.9	61.9	54.9
Stunted					
Severely stunted	32.8	27.6	21.9	33.3	24.4
Stunted	31.1	34.4	35.5	28.6	34.7
Normal	36.1	38.0	42.7	38.1	41.0
Underweight					
Severely underweight	27.1	28.4	21.7	31.6	23.9
Moderately underweight	50.0	50.4	50.7	47.4	50.5
Normal	22.9	21.3	27.6	21.1	25.6

DISCUSSION

The high prevalence of child malnutrition in India has been considered a significant challenge as the proportion of stunted and underweight children are considerably higher in India. To address the issue of malnutrition among children, the Spirulina Foundation launched the program under which they had trained and empowered local self-help group (SHG) women to cultivate spirulina and make Spirulina Fortified Chikkis (SFCs)/granules. The program's overall aim is to improve the nutrition level/status of young children's overall health by providing the Spirulina Chikkis consistently in the study area. Institute of Health Management Research (IIHMR), Bangalore, is a nodal agency/technical partner for conducting the impact assessment to identify the changes in nutrition status of the children. The present study measured the impact of Spirulina Chikki intervention on the nutritional status of the children (6 months−6 years) in Pavagada Taluk, Tumkur district of Karnataka, India.

The result reveals that a majority of the mothers reported that they had observed the change/growth in their child after consumption of spirulina chikkis/granules. Approximately 50% of the mothers observed an increase in appetite, and eleven percent stated an increase in the child's weight. A study conducted in Burkina Faso reveals that the treatment with Spiruline plus Misola have synergically favor the nutrition recovery better than the simple addition of protein and energy intake (18). The spirulina is beneficial and essential for the growth of infants and suitable for children, especially in the growth phase. It helps in case of general weakness and anemia. Due to its nutritional value, WHO considered spirulina as a superfood for the future (14). The mean weight of the children improved from 9.76 to 11.1 Kg and height from 83.07 to 89.11 cm. Another critical indicator mid-upper arm circumferences also exhibit an improvement from 13.19 to 13.8 cm at endline. Evidence from the study conducted in Bellary district of Karnataka observed that 47 and 68% reduction in malnutrition among children who received 1 and 2 g of Spirulina, respectively, as compared to little change in two control groups ($p < 0.05$). In 2 g Spirulina arm, an increase in mean weight of 1.25 g/kg/day ($p < 0.01$); and maximum weight gain of 7.3 g/kg/day (19).

The present study showed a slight upsurge in Severely Wasted (WHZ < -3 SD) and Wasted (WHZ < -2 SD) children. However, results of Stunting showed the improvement viz., decline of 4% (from 28.6% baseline to 24.5% endline) in Severely Stunting (HAZ < -3 SD) at endline. And study observed a positive change viz., 6% reduction in Severely Underweight children (WAZ < -3 SD) (from 30% baseline to 23.9% endline) at endline. A study also documented that the Spirulina is found to be the best alternative dietary supplement to the malnutrition. Spirulina is a safe food with absolutely no side effects, and it is a comprehensive bundle of macro and micronutrient (20–23).

In 1992 WHO has declared Spirulina as "Best food for future" to redress malnutrition especially in children (24). A study based on 50 samples confirmed that the weight-for-age *Z*-scores and weight-for-height *Z*-scores increased significantly in the intervention group (16). Weight for age *z*-score data a significant 44% reduction in malnutrition in mission data was validated by study conducted in Bellary district of Karnataka (19). Upsurge in Severely Wasted (WHZ < -3 SD) children observed more among male than female children over the intervention period. An incline in the prevalence of Wasted children were higher among the girl children than male children. The prevalence of Severely Stunted showed positive change, eight percent among male and around one percent among female children. A substantial proportion of the male children shifted from Severely Underweight to Moderately Underweight category. A Zambian study that examined the efficacy of spirulina on malnourished children found that 10 g of spirulina daily intake leads to improvement by producing 0.29 elevated points in the height-for-age *z*-score (HAZ). Also, the weight-for-age z-score (WAZ) and the Mid-Upper Arm Circumference *z*-score (MUACZ) did not show a significant difference. However, treated children showed a more extensive improvement by 0.09 and 0.38 points, respectively (17).

A substantial decrease in proportion of Severe Acute Malnutrition (SAM) and Moderate Acute Malnutrition (MAM) children was observed at endline. Due to these improvements, the proportion of normal children inclined from 72 to 91%.

The improvements were observed among both male and female children. The children who consumed chikkis/granules for at least 9 months regularly had the lowest prevalence (11.7%) of Severely Wasted (WHZ < -3 SD), and the prevalence was the highest (18.3%) among those children who consumed for 1–8 months. The proportion of Severely Stunted children (21.9%) and Severely Underweight children (21.7%) were the lowest among those children who consumed chikkis/granules for 10 months. A study by Ramesh et al. (25) too revelated a significant increase in anthropometric measurements and Hemoglobin, serum ferrtin, serum zinc, serum protein and serum albumin levels in the study sample after 6 months of intervention (25).

CONCLUSIONS

The supplementation with spirulina into a snack bar (known as chikki) and granules was well-accepted by the caretakers/mothers in the study sites. Consumption of spirulina chikki/granules for more than 9 months had impacted the nutritional status of the children positively. Strengthening the health literacy among the beneficiaries' families about the importance of spirulina chikki is critical for acceptance and successful of the program. The approach of utilizing algae as a source of alternative food supplements in the form of spirulina into a snack bar (known as chikki) and granules can represent one of the most promising approaches in the long term to address malnutrition in the developing country like India. The intervention shall be considered for incorporation into the government existing nutritional program for its sustainability along with local ownership/local production units and microeconomics. The world challenged by severe economic crises, which make the resources for development more uncertain, such endeavors seem more crucial than ever.

Limitations of the Study

Only one Taluk (area) of Tumkur district was covered in this study. Therefore, we cannot generalize the findings for the entire district. Also, the present study had included the children (6 months−6 years) who were enrolled in the Anganwadi centers and program beneficiaries of the Spirulina Foundation program.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Women and Child Development, Tumkur. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

GK and RS developed the questionnaire. GK collected the data, contributed to acquisition of data, statistical analysis of data, and wrote the manuscript. RS and UM enhanced the questionnaire, contributed to the concept and design of the article, literature searches, and critically revised the manuscript. All authors read and approved the final manuscript.

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Analysis of the Global Disease Burden of Down Syndrome Using YLDs, YLLs, and DALYs Based on the Global Burden of Disease 2019 Data

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Purpose: This study aimed to determine Down syndrome (DS) burden using years lived with disability (YLDs), years of life lost (YLLs), disability-adjusted life years (DALYs), and the trends in these parameters.

Methods: We obtained the annual YLDs, YLLs, DALYs, and age-standardized rates (ASRs) of DS from 2010 to 2019 using the Global Health Data Exchange tool. The estimated annual percentage changes (EAPCs) in ASR were used to quantify and evaluate DS burden trends. Gaussian-process regression and Pearson's correlation coefficient were used to assess the relationship between DS burden and socio-demographic index (SDI).

Results: Global DALYs decreased by 2.68% from 2010 to 2019 but the ASR was stable, which was mostly explained by the stability in the ASR for YLLs. The ASR of YLDs showed an increasing trend (EAPC = 1.07, 95% CI = 0.45 to 1.69). There was notable regional imbalance, with most of the DALYs or ASRs in areas with relatively low SDI. The DALY rates of DS were mostly from the YLLs of children younger than 1 year. Lower SDI areas tended to have higher DS burdens ($\rho = -0.3$, $p < 0.001$).

Conclusion: This systematic analysis of the global disease burden of DS from 2010 to 2019 revealed that although the global DS DALY and YLL rate is stable, the YLD rate is increasing. And the DS burden varies significantly differences among regions or countries. The present results suggest that future strategies should focus on DS-related deaths in children younger than 1 year and the DS burden in low-SDI regions or countries, since this may be effective in further reducing DS burden.

Keywords: Down syndrome, global disease burden, trend, YLD, YLL, DALY

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INTRODUCTION

Down syndrome (DS) is a chromosomal abnormality consisting of the presence of a third copy of chromosome 21 in somatic cells due to nondisjunction (1). DS is the most-common chromosomal condition associated with intellectual disability and is characterized by various additional clinical manifestations. It occurs in ∼1 of 800 births worldwide (2). In the United States, DS occurs

in approximately 5,000 live births annually, and more than 200,000 people are currently living with this condition (3). Children with DS have multiple malformations, medical conditions, and cognitive impairment (4, 5).

The DS phenotype varies, but multiple features typically enable the experienced clinician to consider a diagnosis. The more-common physical findings include hypotonia, small brachycephalic head, epicanthal folds, flat nasal bridge, upward-slanting palpebral fissures, Brushfield spots, small mouth, small ears, excessive skin at the nape of the neck, a single transverse palmar crease, and a short fifth finger with clinodactyly and wide spacing, often also with a deep plantar groove between the first and second toes. The degree of cognitive impairment typically varies from mild (IQ = 50–70) to moderate (IQ = 35–50), but is occasionally severe (IQ = 20–35). There are significant risks of hearing loss (75%), obstructive sleep apnea (50–79%), otitis media (50–70%), eye disease (60%) including cataracts (15%) and severe refractive errors (50%), and congenital heart defects (50%), while other comorbidities include neurological dysfunction (1–13%), gastrointestinal atresia (12%), hip dislocation (6%), thyroid disease (4–18%), transient myeloproliferative disorder (4–10%), leukemia (1%), and Hirschsprung's disease (1%) (6). Among fetuses with DS, 27% of pregnancies are reportedly terminated, 4% are spontaneous late abortions or stillbirths, and 12% die within 1 year of birth (7). There are reports from various countries that the number of fetuses conceived with DS has increased concomitantly with the mean age of pregnant females (8–12). DS represents a significant burden on affected patients and their families, as well as society as a whole. However, no previous study has systematically assessed the global disease burden of DS.

The present study therefore aimed to determine the global disease burden of DS using years lived with disability (YLDs), years of life lost (YLLs), and disability-adjusted life years (DALYs) from different periods, regions, and populations based on the Global Burden of Disease (GBD) 2019 data. The findings of this study can be useful when designing more-effective region-specific policies and methods for improving the disease burden of DS.

METHODS

Data Source

Data sources from the GBD 2019 data can be explored using the online Global Health Data Exchange (GHDx) data source tool (http://ghdx.healthdata.org/gbd-results-tool). The GHDx is a data catalog created and supported by the Institute for Health Metrics and Evaluation, an independent global health research center at the University of Washington. The GBD 2019 is the most comprehensive multi-institutional and multi-individual global collaborative epidemiological database for estimating the annual burden of 369 diseases and injuries (e.g., incidence, prevalence, mortality, YLDs, YLLs, and DALYs) for 204 countries and territories according to sex and age group from 1990 to 2019 (13–15). YLDs refer to the number of years lived with any short-term or long-term health loss weighted by the severity of the disability, YLLs refer to how many years of life were lost due to premature mortality, and DALYs were calculated by summing YLLs and YLDs. The GBD case definition of DS includes the International Classification of Diseases codes Q90.0–Q90.2, and Q90.9. In this study, we obtained data from the GBD 2019 including YLDs, YLLs and DALYs of DS, their rates, their age-standardized rates (ASRs) from 2010 to 2019, the change between 2010 and 2019 and 95% uncertainty interval (UI) of the estimates according to sex, age, region, and country. In GBD, every estimate is calculated 1,000 times, sampled from the distribution each time, and sorted from the minimum value to the maximum value. The 95% UI is determined by the 25th and 975th values of 1,000 values. Many types of data sources are used in the estimation of DS, including literature prevalence, with-condition mortality and excess mortality data, birth prevalence and neonatal with-condition mortality data from a number of international birth defects registries and surveillance systems, etc. The estimates of DS are mostly based on modeling when the good data sources are lacking, which may cause some biases. More detailed information on the GBD 2019 data, standardization methods and its limitations is available elsewhere (15). The socio-demographic index (SDI) has been used to comprehensively evaluate the social development levels within countries and regions. This metric is a geometric average ranging from 0 to 1 in each country or region calculated by combining the total fertility rate of females younger than 25 years, the education level of people aged at least 15 years, and the logarithm of the per-capita income distribution. Lower SDI values indicate lower social development levels, and the countries and regions included in the GBD 2019 were divided into five SDI levels: high, middle-high, middle, low-middle, and low (16). The SDI of each country or territory was determined using the GHDx (http://ghdx.healthdata.org/record/ihme-data/gbd-2019-socio-demographic-index-sdi-1950-2019). In addition, the world is geographically divided into 21 regions based on GBD 2019 (**Table 1**).

Statistical Analysis

The ASRs and estimated annual percentage changes (EAPCs) of YLDs, YLLs, and DALYs were used to evaluate their trends from 2010 to 2019, and the DS burden. EAPC was introduced as a concept to describe ASR trends within a specified time interval. The natural logarithm of ASR is assumed to vary linearly with time; in the formula $Y = \alpha + \beta X + \varepsilon$, where Y is ln(ASR), X is the calendar year, and ε is an error term. From this formula, β determines whether there is a positive or negative trend in ASR. EAPC is calculated as $100 \times (\exp(\beta) - 1)$. From the linear model, 95% confidence intervals (CIs) are obtained. A positive EAPC and lower bound of the CI indicated that the ASR is exhibiting an upward trend, while negative EAPC and upper bound indicate a decreasing trend; otherwise ASR is considered stable. However, ASR is still considered stable regardless of EAPC when the change between 2010 and 2019 is not significant. We also evaluated the relationship between ASR and SDI using locally weighted regression (Loess) and Pearson's correlation coefficient. In Loess, when estimating the value of a response variable, a linear regression is performed based on the points near the response variable. The regression adopts the weighted least square method (the closer the value is

TABLE 1 | The age-standardized rates for YLDs, YLLs, and DALYs of Down syndrome in 2019 and their temporal trends from 2010 to 2019.

Characteristics	YLDs			YLLs			DALYs		
	ASR per 100,000 No. (95% UI)	Change between 2010 and 2019 No. (95% UI)	EAPC No. (95% CI)	ASR per 100,000 No. (95% UI)	Change between 2010 and 2019 No. (95% UI)	EAPC No. (95% CI)	ASR per 100,000 No. (95% UI)	Change between 2010 and 2019 No. (95% UI)	EAPC No. (95% CI)
Overall	1.87 (1.2 to 2.79)	0.08 (0.03 to 0.13)	1.07 (0.45 to 1.69)	24.15 (18.09 to 38.87)	−0.06 (−0.22 to 0.12)	−0.71 (−0.85 to −0.57)	26.02 (19.83 to 40.75)	−0.05 (−0.21 to 0.11)	−0.59 (−0.69 to −0.49)
Sex									
Male	2.03 (1.3 to 3.02)	0.07 (0.02 to 0.13)	1.06 (0.45 to 1.68)	23.71 (18.41 to 43.11)	−0.03 (−0.23 to 0.15)	−0.42 (−0.55 to −0.28)	25.74 (20.22 to 45.11)	−0.03 (−0.21 to 0.15)	−0.31 (−0.41 to −0.21)
Female	1.71 (1.09 to 2.56)	0.08 (0.03 to 0.13)	1.07 (0.44 to 1.7)	24.62 (16.4 to 42.53)	−0.09 (−0.26 to 0.12)	−1 (-1.17 to −0.83)	26.33 (18.11 to 44.13)	−0.08 (−0.25 to 0.11)	−0.88 (−1 to −0.76)
Socio-demographic index									
Low	1.17 (0.73 to 1.79)	0.14 (0.08 to 0.2)	1.74 (1.16 to 2.32)	34.26 (17.65 to 77.48)	0 (−0.22 to 0.34)	0.08 (−0.22 to 0.37)	35.43 (18.96 to 78.49)	0 (-0.22 to 0.33)	0.13 (−0.15 to 0.41)
Low-middle	1.28 (0.81 to 1.94)	0.15 (0.1 to 0.2)	1.81 (1.17 to 2.46)	22.51 (16.3 to 33.58)	−0.07 (−0.3 to 0.19)	−0.9 (−1.1 to −0.7)	23.79 (17.59 to 34.96)	−0.06 (-0.29 to 0.18)	−0.77 (−0.93 to −0.61)
Middle	1.71 (1.1 to 2.59)	0.12 (0.07 to 0.18)	1.6 (0.79 to 2.41)	19.24 (15.93 to 23.26)	−0.15 (−0.33 to 0.02)	−1.94 (−2.24 to −1.63)	20.96 (17.75 to 24.94)	−0.13 (−0.31 to 0.03)	−1.69 (−1.95 to −1.43)
Middle-high	2.25 (1.45 to 3.39)	0.04 (-0.02 to 0.11)	0.79 (0.35 to 1.24)	20.09 (17.07 to 24.14)	−0.16 (−0.28 to −0.03)	−2.04 (−2.62 to −1.46)	22.34 (19.33 to 26.28)	−0.14 (−0.26 to −0.02)	−1.78 (−2.3 to −1.25)
High	4.28 (2.77 to 6.24)	0.08 (0 to 0.15)	1.01 (0.4 to 1.63)	16.6 (13.27 to 18.95)	0.03 (−0.05 to 0.11)	0.51 (0.36 to 0.67)	20.88 (17.27 to 23.75)	0.04 (-0.03 to 0.11)	0.61 (0.4 to 0.83)
Region									
Asia Pacific to high income	5.15 (3.23 to 7.58)	−0.01 (−0.08 to 0.06)	0.53 (−0.36 to 1.42)	6.59 (4.92 to 7.91)	−0.02 (−0.16 to 0.11)	−0.09 (−0.33 to 0.15)	11.75 (9.22 to 14.52)	−0.01 (−0.1 to 0.07)	0.18 (−0.3 to 0.67)
Central Asia	1.66 (1.03 to 2.52)	0.06 (−0.03 to 0.15)	1.02 (0.09 to 1.96)	7.72 (5.49 to 10.2)	−0.12 (−0.34 to 0.12)	−1.48 (−1.66 to −1.3)	9.39 (7.01 to 11.87)	−0.09 (−0.29 to 0.11)	−1.07 (−1.26 to −0.88)
East Asia	1.24 (0.77 to 1.89)	0.07 (−0.01 to 0.15)	0.85 (0.27 to 1.44)	14.82 (11.34 to 19.56)	−0.35 (−0.51 to −0.18)	−4.95 (−6.06 to −3.82)	16.05 (12.53 to 20.77)	−0.33 (−0.48 to −0.17)	−4.59 (−5.66 to −3.52)
South Asia	1 (0.62 to 1.5)	0.17 (0.12 to 0.23)	2.1 (1.41 to 2.79)	13.47 (8.08 to 19.93)	−0.07 (−0.32 to 0.22)	−0.85 (−1.06 to −0.65)	14.47 (8.99 to 20.91)	−0.06 (−0.3 to 0.22)	−0.67 (−0.83 to −0.51)
Southeast Asia	1.9 (1.2 to 2.86)	0.2 (0.13 to 0.29)	2.26 (1.46 to 3.07)	13.64 (10.84 to 17.06)	−0.02 (−0.28 to 0.26)	−0.18 (−0.39 to 0.04)	15.54 (12.67 to 18.94)	0 (−0.25 to 0.26)	0.09 (−0.04 to 0.22)
Australasia	4.41 (2.8 to 6.54)	0.06 (−0.12 to 0.25)	0.79 (0.49 to 1.09)	20.35 (14.41 to 25.49)	−0.05 (−0.23 to 0.15)	−0.61 (−0.92 to −0.3)	24.76 (18.38 to 29.78)	−0.03 (−0.18 to 0.13)	−0.37 (−0.62 to −0.13)
Caribbean	3.15 (2.02 to 4.76)	0.08 (−0.01 to 0.17)	1.12 (0.57 to 1.67)	46.39 (23.32 to 79.53)	0 (−0.29 to 0.35)	−0.14 (−0.4 to 0.12)	49.55 (26.07 to 82.6)	0.01 (−0.26 to 0.34)	−0.07 (−0.29 to 0.16)
Central Europe	2.09 (1.35 to 3.08)	0.28 (0.18 to 0.42)	2.92 (2.62 to 3.22)	10.45 (8.07 to 13.51)	−0.08 (−0.26 to 0.13)	−0.78 (−0.99 to −0.57)	12.55 (10.05 to 15.5)	−0.03 (−0.2 to 0.15)	−0.25 (−0.45 to −0.05)
Eastern Europe	2.29 (1.47 to 3.48)	−0.05 (−0.16 to 0.01)	0.02 (−0.79 to 0.83)	12.53 (9.21 to 17.03)	0.01 (−0.15 to 0.23)	−0.01 (−1.07 to 1.07)	14.82 (11.21 to 19.13)	0 (−0.13 to 0.18)	0 (−0.89 to 0.9)
Western Europe	5.78 (3.83 to 8.42)	0.11 (0.03 to 0.2)	1.28 (0.8 to 1.77)	19.16 (14.43 to 22.25)	0.02 (−0.08 to 0.12)	0.39 (0.17 to 0.61)	24.94 (19.99 to 28.64)	0.04 (−0.04 to 0.12)	0.59 (0.44 to 0.74)
Andean Latin America	1.59 (1 to 2.4)	0.1 (0 to 0.19)	1.2 (0.67 to 1.73)	28.95 (19.22 to 39.77)	−0.22 (−0.45 to 0.11)	−2.8 (−3.53 to −2.06)	30.55 (21.02 to 41.86)	−0.21 (−0.44 to 0.11)	−2.62 (−3.35 to −1.89)
Central Latin America	2.25 (1.44 to 3.38)	0.04 (−0.03 to 0.13)	0.96 (0.2 to 1.71)	25.92 (18.01 to 34.21)	−0.02 (−0.25 to 0.26)	−0.31 (−0.82 to 0.19)	28.17 (20.16 to 36.52)	−0.01 (−0.23 to 0.24)	−0.22 (−0.65 to 0.22)
Southern Latin America	5.59 (3.54 to 8.53)	−0.09 (−0.26 to 0.1)	−0.49 (−1.19 to 0.22)	40.69 (29.39 to 51.5)	−0.08 (−0.27 to 0.15)	−1.05 (−1.24 to −0.86)	46.29 (34.27 to 57.67)	−0.08 (−0.24 to 0.12)	−0.98 (−1.14 to −0.82)
Tropical Latin America	2.63 (1.69 to 4.05)	0.21 (0.13 to 0.31)	2.31 (1.61 to 3.03)	57.51 (43.75 to 82.75)	−0.06 (−0.24 to 0.18)	−0.9(−1.32 to −0.48)	60.14 (46.55 to 85.79)	−0.05 (−0.23 to 0.19)	−0.78 (−1.2 to −0.36)
North Africa and Middle East	2.93 (1.82 to 4.45)	0.11 (0.05 to 0.19)	1.56 (0.76 to 2.36)	40.57 (30.98 to 56.63)	−0.12 (−0.31 to 0.11)	−1.55 (−1.71 to −1.38)	43.5 (34 to 58.89)	−0.11 (−0.3 to 0.11)	−1.36 (−1.54 to −1.19)
North America to high income	3.44 (2.23 to 4.96)	0.17 (0.04 to 0.3)	1.57 (0.65 to 2.5)	15.68 (12.8 to 17.64)	0.04 (−0.04 to 0.11)	0.62 (0.34 to 0.9)	19.12 (15.97 to 21.43)	0.06 (−0.01 to 0.12)	0.78 (0.47 to 1.09)
Oceania	1.29 (0.79 to 1.97)	0.14 (0.04 to 0.24)	1.69 (1.07 to 2.3)	26.66 (11.1 to 68.75)	0 (−0.32 to 0.55)	−0.01 (−0.18 to 0.16)	27.95 (12.46 to 69.94)	0.01 (−0.3 to 0.52)	0.06 (−0.12 to 0.25)
Central Sub-Saharan Africa	1.06 (0.66 to 1.59)	0.09 (−0.01 to 0.2)	1.11 (0.67 to 1.56)	30.15 (16.04 to 60.79)	−0.15 (−0.51 to 0.52)	−1.94 (−2.4 to −1.47)	31.2 (17.04 to 61.73)	−0.15 (−0.5 to 0.51)	−1.85 (−2.29 to −1.41)
Eastern Sub-Saharan Africa	0.9 (0.57 to 1.36)	0.13 (0.07 to 0.2)	1.65 (1.1 to 2.2)	30.89 (16.19 to 63.77)	−0.01 (−0.26 to 0.41)	−0.13 (−0.5 to 0.24)	31.79 (17.16 to 64.79)	0 (−0.25 to 0.4)	−0.09 (−0.43 to 0.26)
Southern Sub-Saharan Africa	1.68 (1.07 to 2.55)	0.1 (0.02 to 0.2)	1.59 (0.6 to 2.58)	32.85 (24.55 to 42.8)	0.18 (−0.09 to 0.52)	1.81 (1.18 to 2.44)	34.53 (26.36 to 44.44)	0.18 (−0.08 to 0.5)	1.79 (1.23 to 2.36)
Western Sub-Saharan Africa	0.98 (0.62 to 1.48)	0.09 (0.05 to 0.14)	1.15 (0.72 to 1.58)	43.03 (16.09 to 114.51)	−0.01 (−0.24 to 0.44)	0.15 (−0.38 to 0.69)	44.01 (17.28 to 115.77)	−0.01 (−0.23 to 0.42)	0.17 (−0.35 to 0.7)

YLDs, years Lived with Disability; YLLs, years of Life Lost; DALYs, disability-Adjusted Life Years; ASR, age-standardized rate; CI, confidence interval; EAPC, estimated annual percentage change; UI, uncertainty interval.

to the estimation point, the greater the weight is). Finally, the obtained local regression model is used to estimate the value of the response variable. The distribution of weight is Gaussian distribution. Statistical analyses were performed using R software (version 3.4.3), and the criterion for statistical significance was $p < 0.05$.

RESULTS

Global DS Burden

The total global DALYs due to DS decreased by 1.78 million (2.68%) from 2010 to 2019 (95 % UI = 1.37 to 2.75 million) (**Figure 1A**). The ASR of DALYs was stable (EAPC = −0.59, 95% CI = −0.69 to −0.49), mostly due to the stability of ASR for YLLs (EAPC = −0.71, 95% CI = −0.85 to −0.57), whereas the ASR of YLDs exhibited an increasing trend (EAPC = 1.07, 95% CI = 0.45 to 1.69) (**Table 1**).

In the five SDI regions, DALYs increased in the low- and high-SDI regions from 2010 to 2019, but decreased in the other three SDI regions (**Figures 1B–F**). DALYs were mostly attributable to YLLs in all SDI regions (**Figures 1B–F**). The ASR of YLLs and DALYs decreased only from 2010 to 2019 (YLLs, EAPC = −2.04, 95% CI = −2.62 to −1.46; DALYs, EAPC = 0.61, 95% CI = 0.40 to 0.83) in the middle-high-SDI regions (**Table 1**). The ASR of YLDs in the middle-high-SDI regions was stable from 2010 to 2019, and increased in the remaining four SDI regions (**Table 1**).

The DALYs and ASRs differed among the 21 regions (**Figure 2**; **Table 1**). In addition to Asia Pacific–high income, DALYs in other regions were mostly attributable to YLLs (**Figure 2**). DALYs were lower in 2019 than in 2010 in most of 21 regions (**Figure 2**). The ASR of DALYs in 2019 was the highest in Tropical Latin America (60.14, 95% UI = 46.55 to 85.79) and lowest in Central Asia (9.39, 95% UI = 7.01 to 11.87) (**Table 1**). The ASR of DALYs or YLLs in most (20 of 21) regions exhibited a stable trend from 2010 to 2019. This trend was decreasing only in East Asia. However, The ASR of YLDs is increasing in 12 regions including South Asia, Southeast Asia, Central Europe, Western Europe, Andean Latin America, Tropical Latin America, North Africa and Middle East, North America–high income, Oceania, Eastern Sub-Saharan Africa, Southern Sub-Saharan Africa, and Western Sub-Saharan Africa. The remaining 9 regions exhibited stable trends in their ASRs of YLDs (**Table 1**).

The DS burden varied between countries and territories (**Supplementary Table S1**). The trend of ASRs of DALYs was stable in most countries (192 of 204), decreased in 4, and increased in the remaining 8 (**Supplementary Table S1**).

DS Burden Distribution by Age

As shown in **Figure 3**, the DS DALY rate was mostly attributable to the YLLs of children younger than 1 year, followed by those aged 1–4 years, and there was no significant difference in DS burden between males and females.

Relationship Between ASR and SDI

Figure 4 shows the relationship between ASR and SDI for the 204 countries and territories. There was a significant positive association ($\rho = 0.62$, $p < 0.001$) between the ASR of YLDs and SDI, a significant negative association ($\rho = -0.37$, $p < 0.001$) between the ASR of YLLs and SDI, and a significant negative association ($\rho = -0.3$, $p < 0.001$) between the ASR of DALYs and SDI. From **Figure 4** it can been seen that the ASR of YLDs increased more when SDI exceeded 0.75, which led to the stability of the ASR of DALYs after this point.

DISCUSSION

DS is the most-common chromosomal disease in children, with a reported prevalence in live births of 0.07–0.2%. DS exerts many adverse effects on affected patients (17, 18). DS is the most frequent cause of intellectual disability due to chromosomal disorders and, unlike other neurodevelopmental disorders, it lasts throughout life. Thus, DS is a severe social burden. However, the disease burden of DS in different regions or countries is different and unclear. This study examined the global disease burden of DS using three types of distribution (time, geographical, and population), and analyzed the relationship between the disease burden of DS and SDI based on the DS data in the GBD database.

This study found that DALYs decreased worldwide by 2.68% from 2010 to 2019. After age standardization, the DALY rate decreased by an average of 0.71% annually over this period. However, there was notable regional imbalance. Most of DALYs or their ASRs were attributable to areas with relatively low SDI. This may be due to the lack of good medical conditions and policies in low-SDI regions and countries. DALYs are calculated as the sum of YLDs and YLLs, which are attributable to death and disability, respectively. The main method used to reduce the disease burden of DS is prenatal neonatal disease screening and DS-related disease screening, prevention and treatment, which require a series of medical policies, technology, and condition support that can be very difficult to provide in low-SDI regions and countries. Our analysis of the relationship between SDI and DALY rates indicated that DALY rates decrease as SDI increases. Take China as an example. Although its fertility rate is declining (19), the education level and per capita income of the population have increased significantly (20, 21). Accordingly, in the GBD database, its SDI increased from 0.621 in 2010 to 0.686 in 2019. In this study, its DALY rate decreased by 34% with an EAPC of −4.67 in 10 years. It was particularly interesting that the YLD and YLL rates exhibited the opposite trend. That is, the YLL rate decreased as SDI increased and YLD rates increased alongside SDI. For example, the high-SDI regions had the lowest YLL rates but the highest YLD rates among the five SDI regions. This phenomenon can also be observed at the geographical and national levels. This may be due to high levels of medical conditions reducing the mortality of DS and thus reducing YLL rates, but the risk of disability increases due to the increased survival duration for children with DS, which increases YLD rates. According to the current results, the main method used to reduce DALYs in areas with low SDI should still be reducing deaths from DS. Prenatal neonatal disease screening is a more-suitable and realistic method since patients with DS have many

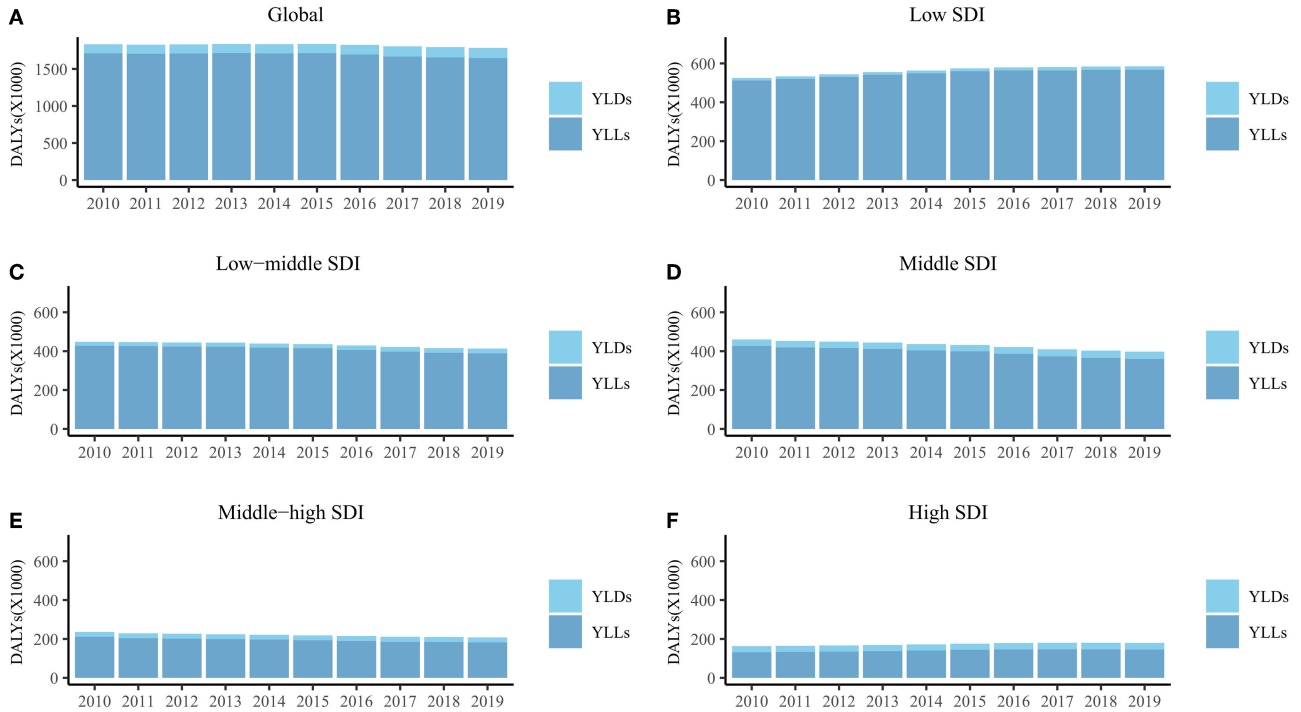

FIGURE 1 | The DALYs, YLDs, and YLLs of Down syndrome for global **(A)**, low SDI region **(B)**, low-middle SDI region **(C)**, middle SDI region **(D)**, middle-high SDI region **(E)** and high SDI region **(F)** from 2010 to 2019. DALYs, disability-adjusted life years; YLDs, years lived with disability; YLLs, years of life lost; SDI, socio-demographic index.

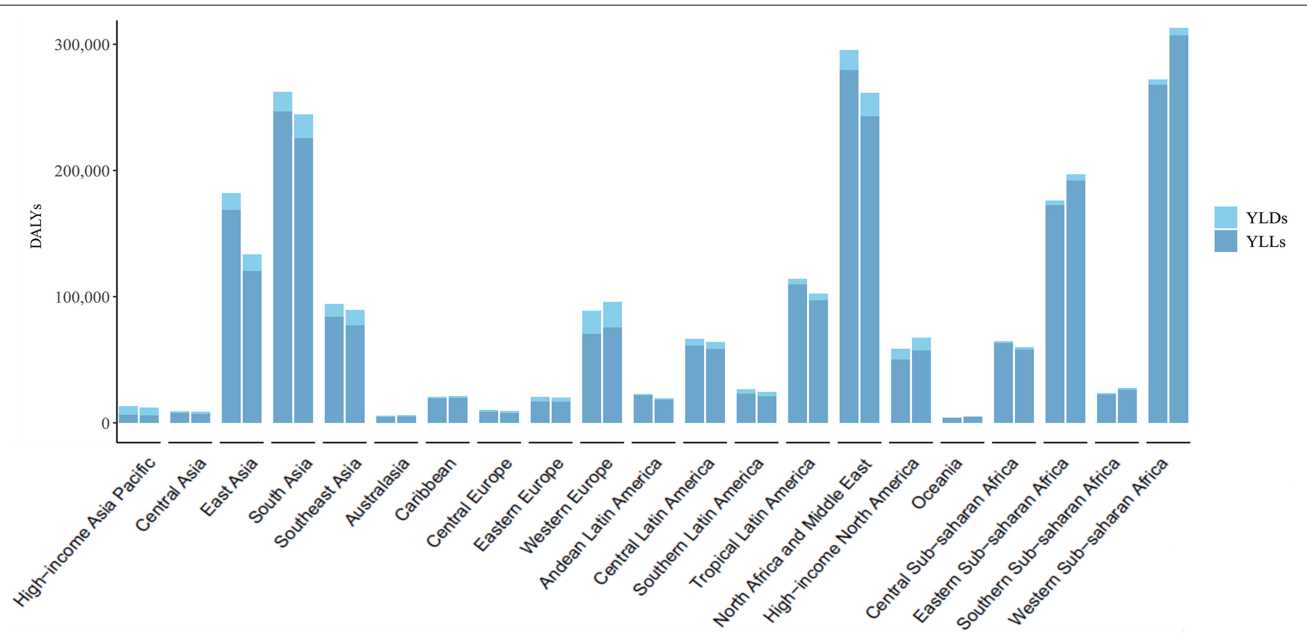

FIGURE 2 | The DALYs, YLDs, and YLLs of Down syndrome at a regional level. The left column in each group is the data in 2010 and the right column in 2019. DALYs, disability-adjusted life years; YLDs, years lived with disability; YLLs, years of life lost.

complications, and it is more difficult to establish a complete set of technical methods for these complications than using neonatal screening to prevent DS death in areas with low SDI.

In addition, The DALY rates in this study were mostly attributable to the YLL rates of people younger than 1 year, and so more attention to screening DS-related diseases or

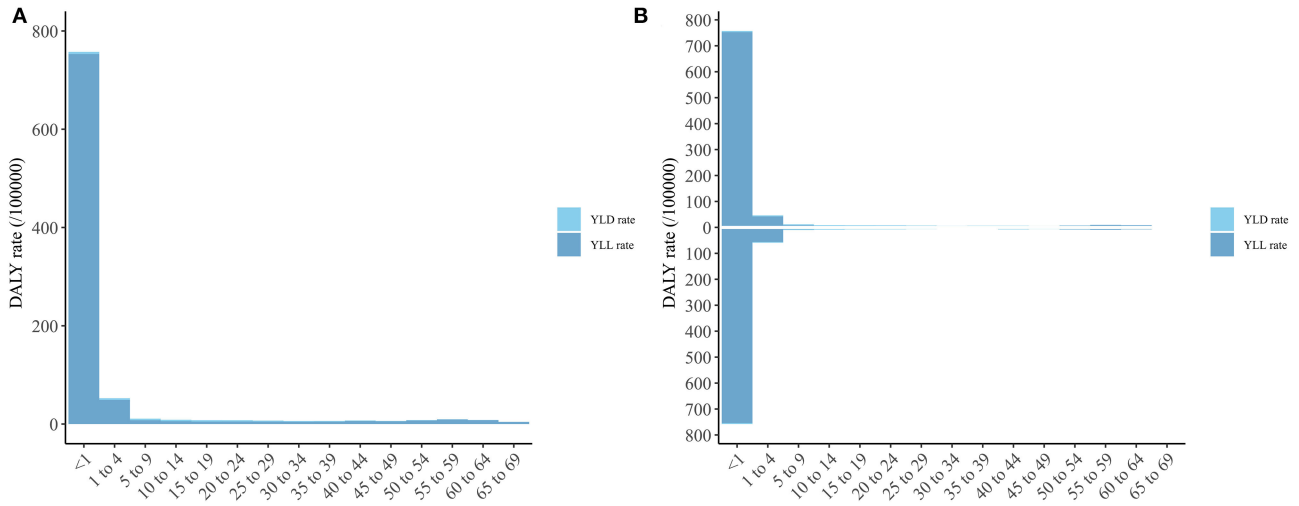

FIGURE 3 | The DALY, YLD, and YLL rate of Down syndrome of different age group. **(A)** Both sexes; **(B)** Male and Female (The column above is for male and the column below is for female). DALY, disability-adjusted life year; YLD, year lived with disability; YLL, year of life lost.

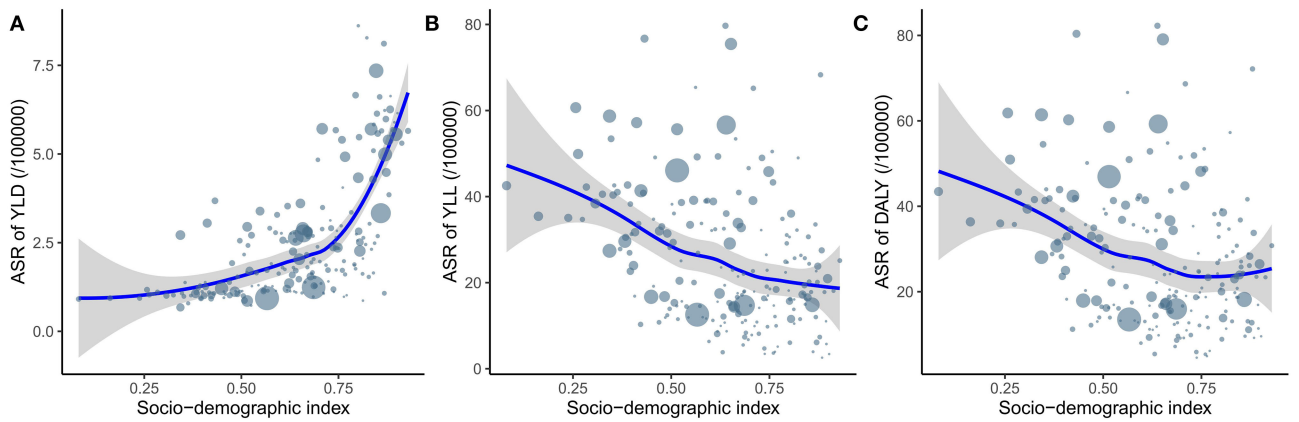

FIGURE 4 | The relationship between ASR of YLD **(A)**, YLL **(B)** and DALY **(C)** and SDI. ASR, age-standardized rate; YLD, year lived with disability; YLL, year of life lost; DALY, disability-adjusted life year; SDI, socio-demographic index.

death risk in this age range may be more effective in reducing YLL rates. For example, DS can present alongside various congenital malformations including congenital heart disease, was well as abnormalities of the digestive system, musculoskeletal, respiratory, and urinary systems (22). Congenital heart disease is the most common of these conditions, being present in 40∼60% of DS cases, and is the most-common cause of death in patients with DS (23). Due to the characteristics of heart defects and respiratory hypoplasia, children with DS are prone to early pulmonary hypertension formation, leading to pulmonary vascular disease and heart failure, which seriously affect the prognoses of patients with DS. Early diagnosis and intervention of congenital heart disease is therefore very important for prolonging the survival of children with DS (24); this may reduce the YLL rate, in turn decreasing the disease burden of DS. Notably, although high-SDI regions had the lowest DS DALY rates among the five SDI regions, they were the only regions with increasing trends in YLL and YLD rates from 2010 to 2019. More research is required to explain the cause of this phenomenon, which is currently unknown. Of course, SDI is only one of the factors affecting the disease burden of DS. For example, social values are another factor affecting its disease burden. For the population with DS diagnosed via neonatal disease screening, pregnancy termination is the most-effective means to reduce the disease burden of DS, but pregnancy termination is affected by variations in social values (e.g., law, morality, religion, and ethics) among countries or regions. This can also partly be explained by how regions and countries with similar SDIs have relatively large differences in the disease burden of DS.

This study was subject to some notable limitations. First, only the global disease burden of DS was analyzed, with the different risk factors for DS in different countries and regions not being

addressed. Because the risk factors affecting YLD, YLL and DALY rate of DS cannot be extracted in the GHDx. Second, EAPC estimation comes from point estimate with CI rather than the interval estimate with UI. EAPC with CI calculated based on GBD data is not appropriate because the estimates of GBD data are from interval estimation with UI. In addition, in order to make the DS burden trend obtained by EAPC more conservative, we use DS burden change with UI to control it.

This study performed the most-comprehensive assessment of the disease burden of DS from 2010 to 2019. Although the global DS DALY rate was found to be stable, there were significant differences for DS burden among regions or countries. Future analyses of how to control the burden of DS should pay attention to DS-related deaths in children younger than 1 year and the DS burden in low-SDI regions and countries. The information yielded by this study should help in understanding the global disease burden of DS and in the establishment of more-effective and targeted strategies or measures that could further reduce the DS burden.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

This study was performed in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Xi'an Children's Hospital.

AUTHOR CONTRIBUTIONS

QB and ZP: study design and data extraction. ZP: statistical analysis. QB, RQ, HCheng, AW, HChen, and ZP: manuscript draft. All authors approved the final version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fped.2022.882722/full#supplementary-material

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ORIGINAL RESEARCH
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The Economic Burden of Hospital Costs on Families With Type 1 Diabetes Mellitus Children: The Role of Medical Insurance in Shandong Province, China

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Objective: This study estimates the economic burden imposed on families by comparing the hospitalization costs of T1DM children with and without medical insurance in Shandong province.

Methods: Our data comprised 1,348 T1DM inpatient records of patients aged 18 years or younger from the hospitalization information system of 297 general hospitals in 6 urban districts of Shandong Province. Descriptive statistics are presented and regression analyses were conducted to explore the factors associated with hospitalization costs.

Results: Children with medical insurance had on average total hospitalization expenditures of RMB5,833.48 (US$824.02) and a hospitalization stay of 7.49 days, compared with the children without medical insurance who had lower hospitalization expenditures of RMB4,021.45 (US$568.06) and an average stay of 6.05 days. Out-of-pocket expenses for insured children were RMB3,036.22 (US$428.89), which is significantly lower than that of the uninsured children ($P < 0.01$). Out-of-pocket (OOP) expenditures accounted for 6% of the annual household income of insured middle-income families, but rose to a significant 25% of the annual income for low-income families. These OOP expenditures imposed a heavy economic burden on families, with some families experiencing long-term financial distress. Both insured and uninsured families, especially low-income families, could be tipped into poverty by hospitalization costs.

Conclusion: Hospitalization costs imposed a significant economic burden on families with children with T1DM, especially low-income insured and uninsured families. The significantly higher hospitalization expenses of insured T1DM children, such as longer

hospitalization stays, more expensive treatments and more drugs, may reflect both excess treatment demands by parents and over-servicing by hospitals; lower OOP expenses for uninsured children may reflect uninsured children from low-income families forgoing appropriate medical treatment. Hospital insurance reform is recommended.

Keywords: hospitalization costs, childhood type 1 diabetes, T1DM children, economic burden, medical insurance

INTRODUCTION

Diabetes mellitus is a complex chronic non-communicable disease with acute and long-term consequences and it is becoming an increasingly important global health issue (1, 2). The global prevalence of diabetes is expected to increase from 171 million in 2000–366 million by 2030 (3, 4). In 2015, the absolute global cost of diabetes was US$1.31 trillion or 1.8% of global gross domestic product, and is projected to reach US$2.5 trillion by 2030 based on past trends (5, 6). Moreover, the health complications arising from diabetes, such as cardiovascular disease, pose an obvious and rising health cost on diabetes sufferers and a nation's health care system (7).

A unique subset of diabetes sufferers are children. The changes in children's lifestyle and entertainment trends, high calorie intake and reduction in energy expenditure has contributed to an obesity pandemic and increased prevalence of type 1 diabetes (T1DM) in children (8, 9). A study in The Lancet showed that the incidence of T1DM continues to increase, especially in young children from high- and middle-income countries (10). According to a study comprising 13 cities from different Chinese provinces, the estimated incidence of T1DM for ages 0–14 years old in Jinan, Shandong's provincial capital, was 2.18 per 100,000 person years (11). The same study estimated T1DM incidence rates of 1.02 per 100,000 person years for 15–29 year olds, and 0.51 per 100,000 person years for those older than 30 years old between 2010 and 2013 (11). The evidence shows that the incidence of childhood type 1 diabetes mellitus in those <18 years old is significantly higher than other age groups in China. This trend is not limited to China. An America study argued that over the last 3 decades, T1DM, a disease which previously only affected adults, had an increasingly noticeable prevalence among children and adolescents (12). Evidence from Africa showed that the prevalence of T1DM in children under 5 was increasing (13) and in Taiwan between 1999 and 2010, the incidence rate of type 1 diabetes mellitus was highest when the age was <15 years old (14). The growing number of children with diabetes pose a global health economic challenge, including financial burden to a country's health system and economic stress to families with T1DM children.

Shandong was one of China's developed eastern coast industrial provinces, where roughly 40% of the adult population had 12 years or more of education and the province's per capita gross domestic product of RMB72,200.00 (US$11,352.00) ranked the 11th highest in China (15). According to China's seventh national census for Shandong Province, the number of children between 0 and 14 years old was 19.01 million, roughly 18.8% of the total population, comprising 64.01 million urban residents and 37.51 million rural residents. Due to the specific needs of a child's growth and development, the treatment for T1DM children is quite different from that of adults, and the cost of medical treatment is relatively high, which imposes a heavy economic burden on families, the health system and the medical insurance system (16). China has not yet established a comprehensive government-funded child health insurance system that could meet the medical welfare needs of this growing group of T1DM children and protect their families from the economic burden of T1DM hospital costs. We explore the hospitalization costs incurred by T1DM children and the economic burden on families, with and without medical insurance.

Early diabetes studies focused on the composition of hospitalization costs for adult diabetic patients (17), explored the factors which influenced these hospitalization costs (18, 19) and quantified the economic burden of hospitalization cost for adult patients (20–23). One study distinguished the hospitalization costs between adult sufferers with and without medical insurance (24). In China, there is a gap in the literature on the hospitalization costs imposed on families with children with type 1 diabetes mellitus. This lack of data constrains policymakers in their development of nationwide child diabetes strategies and proposed changes to China's national health insurance schemes (25). Using data from Shandong province, we address this lacuna by conducting a cross-section study comparing the hospitalization costs burden on families with T1DM children, with and without medical insurance.

MATERIALS AND METHODS

Settings and Data Source

In Shandong Province, a 3-stage cluster sampling was used to select sampling sites. First, all cities in Shandong Province were stratified into three groups by the status of their economic development. As shown in **Figure 1**, two cities were selected in each group, with Qingdao and Weifang being selected from the eastern region, Jinan and Linyi being selected from the middle region and Dezhou and Jining being selected from the western region. We then selected four districts from each city on the basis of GDP per capita. Finally, six sub-districts or townships were selected from each chosen district. This yielded 6 cities, 24 districts and 192 sub-districts or townships as sampling sites. From these sampling sites, we chose 297 medical facilities as sampling institutions, including general hospitals, traditional Chinese medicine hospitals, maternal and child health hospitals, specialist hospitals, community health service centers and township health centers. From 297 medical

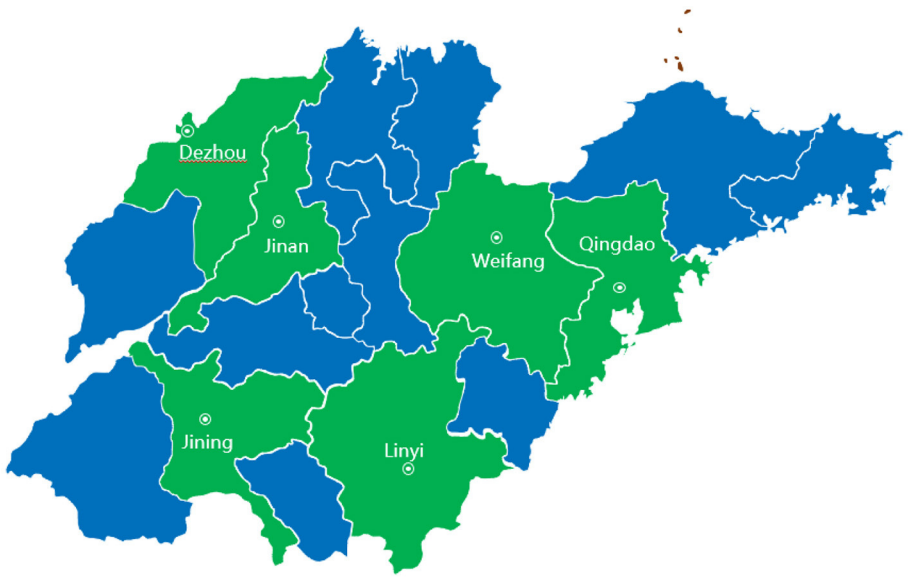

FIGURE 1 | Sampling cities of this study in Shandong Province.

institutions, we extracted data on all inpatients from January 1 to December 31, 2017.

Study Population

Hospitalized T1DM inpatients were identified when the primary discharge diagnosis corresponded to the 10th edition of the International Classification of Diseases (ICD-10) E10 diabetes codes. Using the electronic system of the medical institution, trained medical staff uniformly reported ICD-10 codes. In order to reduce any errors, all ICD-10 codes for 2017 were proofread using a special computer program developed by the National Health and Wellness Development Committee. Inpatients aged <18 years with at least 1 day of hospitalization were included, yielding a sample of 1,348 qualified type 1 diabetes mellitus children in 297 medical institutions across Shandong province. All inpatients had complete information recorded regarding their demographics, regional distribution of cities, comorbidities, sex, age, health insurance, hospitalization costs, insurance reimbursements and the information about the health facilities.

China is in the process of integrating the New Cooperative Medical Scheme (NCMS) for its rural population, and the Urban Residents Basic Medical Insurance System (URBMI) for its urban out-of-workforce population. This involves integrating urban children, students, the unemployed and the disabled into the Urban and Rural Medical Insurance Scheme (IURMI). By the end of 2020, the National Healthcare Security Administration reported 1.02 billion IURMI participants, of which 246 million (24.2%) were children (26). Compared to adults under the IURMI, children experienced lower participation rates, lesser compensation for medical expenses and differentiated levels in medical security protection caused by varying insurance policies (27). In addition, child T1DM inpatients were likely to have lower hospital expenses compared to adults, but will incur significant on-going costs during their lifetime (27). Shandong province completed China's IURMI reforms in 2015, with children under the age of 18 only having IURMI or no insurance. Compared to insured children, uninsured children came from households with lower self-reported family income, higher non-enrollment in education, migrants and poor parental awareness and decision-making (28, 29).

Statistical Analysis

Statistical analysis was performed using STATA Version 14.0 and statistical significance was set at the 5% significance level. For continuous variables, the *p*-value was calculated using Student's *t*-test; and for categorical variables, the *p*-value was calculated using the chi-square test. We used a multivariate linear regression model to analyze relationships between hospitalization costs and potential influential factors. We specified the following regression model:

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_m X_m + e$$

where the dependent variable (Y) was hospitalization costs and the independent variables were age, sex, with or without medical insurance, severity of illness represented by with or without comorbidities, regional distribution of cities, geographical location of the medical institution and whether the medical institution was public or private.

RESULTS

Basic Information of the Participants

As displayed in **Table 1**, the study included a total of 1,348 inpatient children with type 1 diabetes, with a mean age of 8.97 years ± 0.16 and 52.89% were male. Of these child inpatients, 998 or 74.04%, were identified as having medical insurance, with the remaining 350 (25.96%) without medical insurance. We

TABLE 1 | Baseline and demographic characteristics.

		Medical insurance			
	***N* (%)**	**No (%)**	**Yes (%)**	X^2	***P***
Observations	1,348 (100)	350 (25.96)	998 (74.04)		
Sex				0.3679	0.5440
Males	713 (52.89)	190(26.65)	523 (73.35)		
Females	635 (47.11)	160(25.20)	475 (74.80)		
Age				25.7463	**0.0000**
0–5	470 (34.87)	152 (32.34)	318 (67.66)		
6–11	430 (31.90)	118 (27.44)	312 (72.56)		
12–18	448 (33.23)	80 (17.86)	368 (82.14)		
Location				114.2038	**0.0000**
Urban	1186 (87.98)	252 (21.25)	934 (78.75)		
Rural	162 (12.02)	98 (60.49)	64 (39.51)		
Comorbidity				14.8313	**0.0000**
Yes	468 (34.72)	92 (19.66)	376 (80.34)		
No	880 (65.28)	258 (29.32)	622 (70.68)		
Regional distribution				7.3364	**0.0260**
East	460 (34.12)	140 (30.43)	320 (69.57)		
Middle	538 (39.91)	129 (23.98)	409 (76.02)		
West	350 (25.97)	81 (23.14)	269 (76.86)		
Type of health facility				0.0406	0.8400
Public	1,319 (97.85)	342 (25.93)	977 (74.07)		
Private	29 (2.15)	8 (27.59)	21 (72.41)		

Bold values are statistically significant p values at the 5% level.

TABLE 2 | Hospitalization costs of children with type 1 diabetes (RMB).

Variable	All (mean ± SD)	Inpatient with medical insurance (mean ± SD)	Inpatient without medical insurance (mean ± SD)	*t*-value	*p*-value
Age	8.97 ± 0.16	9.39 ± 0.18	7.79 ± 0.29	4.4983	**0.0000**
Length of stay	7.11 ± 0.14	7.49 ± 0.17	6.05 ± 0.24	4.5645	**0.0000**
Total costs	5,363.00 ± 171.00	5,833.48 ± 220.63	4,021.45 ± 176.66	4.6819	**0.0000**
Treatment costs	824.87 ± 40.60	908.89 ± 52.11	585.30 ± 46.41	3.5095	**0.0005**
Drug costs	934.80 ± 42.20	1,041.16 ± 55.29	631.48 ± 34.80	4.2842	**0.0000**
Bed fees	325.71 ± 11.37	340.25 ± 13.59	284.28 ± 20.25	2.1614	**0.0308**
Diagnosis fees	122.31 ± 5.23	134.33 ± 6.35	88.05 ± 8.51	3.9034	**0.0001**
Check-up fees	373.43 ± 18.02	397.85 ± 22.76	303.79 ± 24.23	2.2925	**0.0220**
Surgery costs	75.64 ± 11.30	84.23 ± 14.66	51.13 ± 12.07	1.2843	0.1993
Test costs	1,064.74 ± 33.97	1,154.19 ± 42.29	809.67 ± 48.32	4.4776	**0.0000**
Nursing fees	163.85 ± 6.92	166.48 ± 8.54	156.35 ± 10.86	0.6416	0.5213
Other costs	541.51 ± 46.16	563.61 ± 60.59	478.47 ± 41.93	0.8086	0.4189
Out-of-pocket costs	3,292.03 ± 89.26	3,036.22 ± 102.25	4,021.45 ± 176.66	4.8803	**0.0000**

Bold values are statistically significant p values at the 5% level.

categorized children into three age groups, where those <6 years (34.87%), between 6 and 11 years (31.90%) and 12 years and older (33.23%), each accounting for about one third of the sample. Children under 6 most likely to be uninsured. The proportion of child inpatients from urban areas (87.98%) was significantly larger than rural inpatients (12.02). In our sample, two-thirds (65.28%) of the inpatient children were without comorbidities; 1,319 were treated at national public hospitals and 29 were treated at private health facilities; and the number of patients from the eastern, middle and western region was roughly the same.

Hospitalization Costs of Type 1 Diabetes in Children With and Without Medical Insurance

As shown in **Table 2**, the type 1 diabetes mellitus inpatients with medical insurance had significantly higher total hospital

TABLE 3 | Regression coefficients and standard errors for major factors associated with hospitalization costs.

Factors	Coefficients	SE	*t*-value	*p*-value
Comorbidities	3,078.3660	353.5739	8.7100	**0.0000**
Location	2,764.0280	535.8362	5.1600	**0.0000**
Medical insurance	949.8624	394.1617	2.4100	**0.0160**
Regional distribution	241.6070	218.1295	1.1100	0.2680
Age-group	213.2196	204.5707	1.0400	0.2970
Gender	140.4322	327.9564	0.4300	0.6690
Type of health facility	247.9743	1,137.1560	0.2200	0.8270

Bold values are statistically significant p values at the 5% level.

expenditure (RMB5,833.48 ± 220.63/US$824.8 ± 31.2) than those without medical insurance (RMB4,021.45 ± 176.66/US$568.6 ± 24.98, $p < 0.001$) and had a longer stay in hospital (7.49 ± 0.17 days) than those without medical insurance (6.05 ± 0.24 days, $p < 0.001$). Breaking down the specific hospital expenditures, the treatment costs, drug costs, bed fees, diagnosis fees, check fees and test expenditure were all significantly higher for children with medical insurance than those without medical insurance. Other health cost, including surgery costs and nursing costs were not significantly different between the insured and uninsured children.

Factors Associated With Hospitalization Costs

Table 3 shows the results of the multivariate regression analysis for the major factors associated with hospitalization costs, listed in the decreasing order of their absolute *t*-value. The most significant influential factors for hospitalization costs were with or without medical insurance, urban-rural location of the medical institution and severity of illness represented by with or without comorbidities. Sex, regional distribution of cities, age group and type of medical institution were not significantly related to the total cost of hospitalization.

DISCUSSION

This is the first cross-sectional study of the hospital costs incurred by Chinese type 1 diabetes mellitus children with or without medical insurance. The results show that the median hospitalization costs for T1DM children was RMB5,363.00 (US$757.79), which was lower than RMB7,996.11 (US$1,162.53) found in people of all ages with diabetes in Beijing (17). Median hospitalization costs was also lower than the US$863.2 found by a rural southwest China study for population aged 18 or over (4) and lower than the US$1,655 found for adults in a provincial capital city in east China (30). A Chinese study estimated the median hospitalization costs for diabetes mellitus adult inpatients with medical insurance was RMB9,458 (US$1,407) and RMB9,104 (US$1,354) without medical insurance (24). The international average annual treatment and management cost for people with diabetes was US$1,622–2,886 per person in 2015 (31). Our focus on children with type 1 diabetes had its own specific characteristics: compared with adults, children with diabetes have fewer complications, lower severity and shorter hospital stays and, therefore, lower hospitalization costs. Of course, we did not calculate the ongoing costs of child diabetes sufferers, where under 18 years old children would accumulate hospitalization expenses over their lifetime.

Children with medical insurance had significantly higher total hospital expenditures for various services, such as treatment, drug costs, bed fees, diagnosis fees, check-up fees and test costs, and longer hospital stays than children without insurance. Part of this difference was related to parents with medical insurance seeking better quality and a greater quantity of medical services and treatments for their children (24). From the supply side, children with insurance may be over-serviced, reflected in excessive hospital services and longer hospital stays. Parental demands of insured children for more medical care, and more frequent doctor visits, will encourage over-servicing, including more treatments, drugs, surgery and test fees. For families without medical insurance, we suggest a medical services self-selection bias effect, with parents demanding lower levels of hospital care and shorter stays for uninsured children.

From **Table 2**, diabetes mellitus inpatients with medical insurance had significantly lower out-of-pocket expenses (RMB3,036.22 ± 102.25) than inpatients without medical insurance (RMB4,021.45 ± 176.66, $p < 0.001$), which is consistent with previous studies (24, 32). Lower out-of-pocket expenses also encouraged higher consumption of hospital stays and medical treatments for insured inpatients. It was also the case that children with poor health were more likely to participate in medical insurance schemes (33), which makes some medically insured children more likely to incur excessive hospitalization costs due to greater severity of illness caused by more comorbidities. Of course, not all costs were related to insurance status, with surgery, nursing and other costs not significantly different for insured and uninsured inpatients.

Medical insurance reduced, but did not do away with, the economic burden of hospital costs on families, while those without medical insurance faced significant hospital and health care costs that severely strained average household budgets. In 2015, the average annual income of middle-income households in China was RMB49,809.73 (US$7,239.05) and that of low-income households was only RMB12,048.79 (US$1,751.10). Out-of-pocket expenses of RMB3,036.22 (US$429.01) for insured middle-income families accounted for about 6% of yearly family income, but 25% of low-income insured families' yearly family income. For uninsured families, out-of-pocket expenses of RMB4,021.45 (US$568.23) for middle-income families was 8% of the yearly family income and 33% of the yearly family income for low-income families. Both insured and uninsured families with type 1 diabetes children faced an economic burden imposed by hospital costs, with low-income families' financial resources severely impacted by out-of-pocket hospital expenses. Many insured and uninsured families would deplete family savings, sell assets or borrow to pay for out-of-pocket hospitalization expenses. Some families faced long-term economic distress, and some families were tipped into poverty, when over 40% of their

yearly non-food budget was accounted for by out-of-pocket hospital expenses (34).

There are some limitations in our study. First, it was a cross-section study, and the relationship between hospitalization costs and other factors cannot be interpreted as cause and effect. Second, there was a lack of information on the detailed symptoms of inpatients, so we were unable to analyze whether the hospital costs were "reasonable" for the treatment required. Additional data on the inpatients' medical conditions should be collected in follow-up studies. Our data only included single visit hospitalization costs. Annual hospitalization costs of insured and non-insured inpatients should be collected in future studies. Also, the addition of hospital levels in the analysis of cost factors should be included in future studies. Further studies should also include more socioeconomic factors, including family income and household savings data, which will allow the full economic impact of the hospitalization costs of T1DM children on families to be evaluated, and also allow more in-depth policy research and health economics evaluations. While we are confident that we drew a representative sample from Shandong province, data from other provinces, especially in less developed regions, are required to confirm our data are representative of all Chinese provinces.

CONCLUSIONS

This study assessed the economic burden imposed on families by comparing the hospitalization costs of T1DM children with and without medical insurance in Shandong province. Based on our results, we recommend further reform to the medical insurance system in China, providing equity and better accessibility to more families; providing additional protection to vulnerable low-income families; and to allow families to purchase child medical insurance. The different cost structures between insured and uninsured type 1 diabetes mellitus children suggest the need for further investigations of treatment regimes, including over-demand by parents for treatment of their children and over-supply of treatment by medical staff. Most worrying is the self-treatment bias for children by uninsured parents. Many parents with uninsured children faced high out-of-pocket expenses, which may have encouraged parents to curtail the medical treatment of their children. This is supported by the evidence that uninsured children had shorter hospital stays, less drugs and fewer tests, which may have imposed a significant potential health risk to T1DM children. Inadequate childhood diabetes treatment likely increased the costs of adulthood diabetes treatment, with negative effects on both individual diabetes sufferers and on the Chinese health system.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

SW and YG contributed to the conception and design of the manuscript. YG wrote the first draft. SW wrote sections of the manuscript. JS contributed toward the article by collecting data. SN, EM, and AL contributed to the manuscript revision. All authors read and approved the final version of the manuscript.

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Social and Regional Disparities in Utilization of Maternal and Child Healthcare Services in India: A Study of the Post-National Health Mission Period

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Background: India has enjoyed enhanced economic growth, but has fared poorly in human development indicators and health outcomes, over the last two decades. Significant health inequities and access to healthcare continue to exist and have widened within communities across states. This study examine the changes and disparities in maternal and child healthcare (MCH) among disadvantaged and advanced social groups in three states of India.

Data and Methods: Four rounds of National Family Health Survey data were used to measure infant mortality rate (IMR) and under-five mortality rate (U5MR) according to the social groups for the selected states. This study investigates the socio-economic inequities manifested into caste and class differentials and inequities in availability, utilization, and affordability of maternal and healthcare services. Descriptive statistics and the logistic regression model were used. Individual- and household-level covariates were employed to understand the differentials in healthcare utilization.

Results: The probability of not receiving full antenatal care (ANC) or full immunization for the children was highest among the Scheduled Caste/Scheduled Tribe (SC/ST) families, followed by economic class, mother's education and residence. Tamil Nadu showed the highest utilization of public health facilities, while Bihar was the poorest in terms of health outcomes and utilization of MCH care services even after the pre-National Health Mission (NHM) period. Bihar and West Bengal also showed private healthcare dependence.

Conclusion: This study detected the presence of significant caste/tribe differentials in the utilization of MCH care services in the selected states of India. Limited accessibility and unavailability of complete healthcare were the foremost reasons for the under-utilization of these services, especially for people from disadvantaged social groups. The result also suggested that it is perilous to confirm "Health for All" immediately. It will be the efficiency with which India addresses inequities in providing healthcare services and guarantees quality care of health services.

Keywords: inequalities, maternal health, child health, healthcare utilization, NHM

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BACKGROUND

India has enjoyed enhanced economic growth, but has fared poorly in human development indicators and health outcomes, over the last two decades. Health outcome indicators, such as child and maternal health, remain unsatisfactorily high compared with south and east Asian countries with similar income levels and economic growth rates. Aside from the low population level indicators, worrying inequities in health concur with the multiple axes of caste, class, gender, and geographical differences that have also been acknowledged (1–3).

Significant health inequities and access to healthcare continue to exist and have widened within communities and across states. In India, caste is an essential determinant of socio-economic inequities in nearly all wellbeing spheres. The constitution of India grouped various castes and tribes into four broad categories: Scheduled Castes (SCs), Scheduled Tribes (STs), Other Backward Classes (OBCs), and others. The SCs are castes that have historically faced social exclusions; they constitute about 16.6% of the Indian population, a large percentage of those live in rural areas and are mainly landless agricultural laborers. Like SCs, STs are a marginalized community and have been subjected to deprivation and discrimination for centuries and are also called Adivasis. As per Census 2011 figures, they comprised about 8.6% of India's population. OBCs and general castes together account for 71% of India's total population (4).

Several researchers found that various health outcome dissimilarities occur primarily from disparities in availability, accessibility, affordability, quality, and utilization of healthcare services (5, 6). Further, the inequalities in healthcare services lead to overall health disparities across regions and states of the population (6, 7).

Inequities in health are the unfair distribution of healthcare due to insufficient social arrangements and in India, this is a harsh reality. The recent round of the National Family Health Survey (8) data reveals sharp geographic and socio-economic divides in health outcomes. The deprived castes, the underprivileged and the less developed states excessively bear the burden of mortality. High rates of infant mortality (IMR) and under-five mortality (U5MR) and maternal mortality, in general, are inversely associated with income. These inequities are also accompanied by wide gaps across gender and caste (3, 9). However, reducing maternal and premature deaths by providing financial risk protection are key health-related targets of sustainable development goals (SDGs) (10). To achieve health-related SDGs, it requires substantial investment on maternal and child health (MHC) to protect households from high out-of-pocket payment shocks. High out-of-pocket expenditure (OOPE) is positively associated with limited access to healthcare, increases untreated morbidity, reduces consumption of goods and services, and leads to long-term disadvantage (11). The level of OOPE differs across socio-economic groups and type of health services (12–15).

MATERNAL AND CHILD HEALTH IN THE POST-NATIONAL HEALTH MISSION PERIOD IN INDIA

The healthcare system in India is categorized into two healthcare providers—public healthcare services, which are manifested in central, state, and local government, and private healthcare services. Fifteen years earlier in India, maternal and child deaths were very high with poor MCH indicators, especially in socially deprived groups. As a policy response, to reduce maternal and child mortality and reduce OOPE on MCH care, in 2005, the Government of India launched the National Rural Health Mission (NRHM) Program (16). The program intended to develop the health system by providing universal access to equitable, affordable, and quality maternal and child healthcare services. The NRHM was a wide-ranging, centrally driven government maternal and child health program that tried to address serious inequities such as under-investment, lack of human resources, infrastructure and some aspects of quality of care in the public healthcare sector (17–19). Initially, the NRHM was started in rural areas of 18 states, including 8 Empowered Action Group (EAG) states, with poor health infrastructure and the worst health indicators. Enjoying success in rural areas, the program was simultaneously started in urban areas and extended to non-EAG and other remaining states. Afterwards, the program was renamed as the National Health Mission (NHM). The two most critical apparatuses of the NHM are—Janani Suraksha Yojana (JSY) and Janani Shishu Suraksha Karyakaram (JSSK). The JSY is a cash enticement scheme provided to mothers for delivering at public health centers for the first or second time who are economically weaker (16). The incentive differed between rural and urban areas and state-to-state based on their performance and it covered the incentive to Accredited Social Health Activist (ASHA) workers too. The JSSK scheme was launched in 2011 and enabled all economically weaker pregnant women to deliver in public health facilities for no cost and free treatment for infants for a year (20). There has been significant progress in maternal and child health, after the implementation of the NHM in 2005. Trends in IMR and U5MR suggest (**Figure 1**) extensive improvements in the post-NHM period. Still, at the same time, inequalities in utilization of MCH care and health outcomes among the social groups have not been narrowed down.

Along with the child mortality rate, maternal mortality has also declined. JSY significantly impacted increasing natal care and JSSK has shown significant institutional delivery progression. The NHM proposed reducing the OOPE, besides improving maternal and child survival. The OOPE on delivery care largely diverges across states, classes and castes (21). Various studies explained that MCH care in India placed a high financial liability on households and it has also been recommended to reduce out-of-pocket payment to benefit disadvantaged groups (22–25).

However, some regions showed much progress in reducing maternal and child mortality and increasing access to MCH

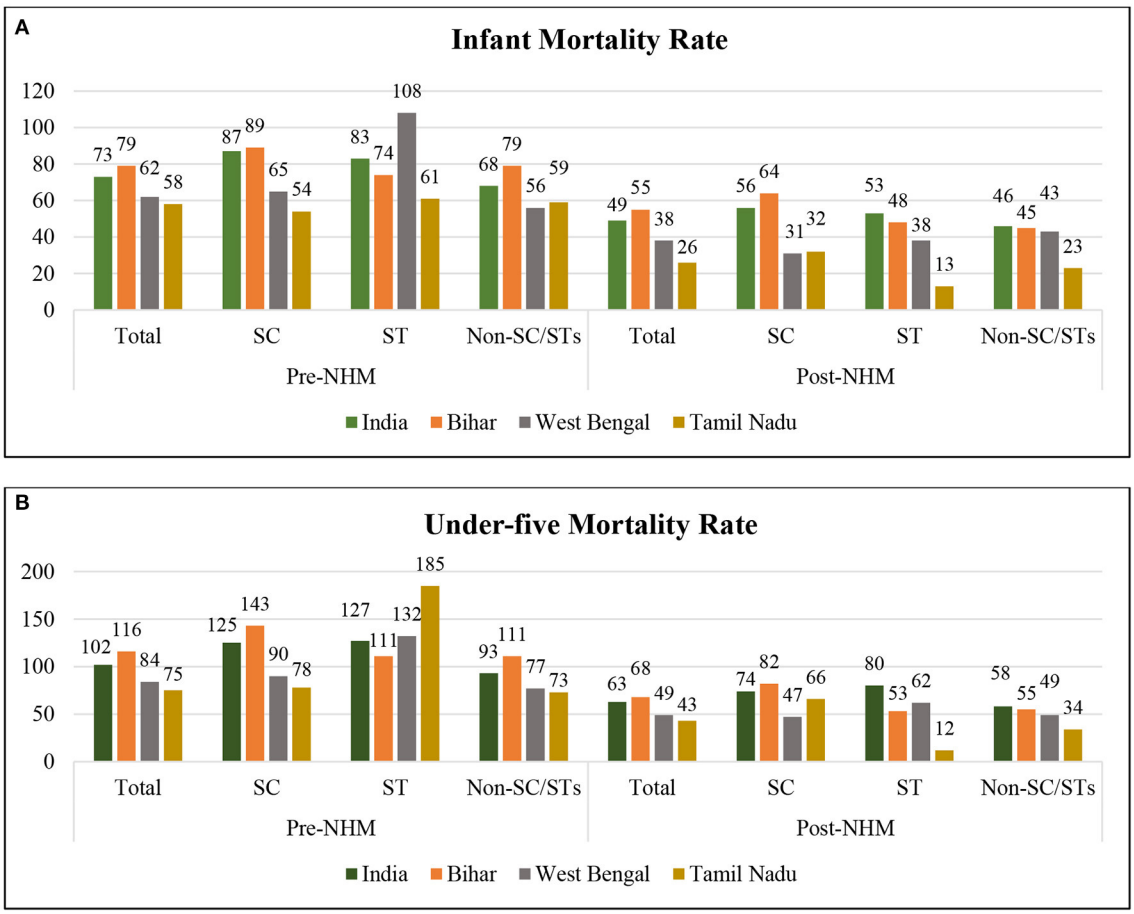

FIGURE 1 | Social gap in **(A)** infant mortality rate (IMR) and **(B)** under-five mortality rate (U5MR) during the pre- and post-National Health Mission (NHM) periods. Authors estimated IMR and U5MR per 1,000 live births for the 5-year period preceding the survey. Average death rates have been calculated. For the pre-NHM period (1992–1999), NFHS 1 and 2, and for post-NHM period (2005–2016), NFHS 3 and 4 have been combined.

care. Nevertheless, progress has not been equitable and many women from deprived groups still lack access to maternal and child healthcare (26). This article aims to understand geographic and socio-economic inequalities in the selected states of India manifested in caste and class differentials and inequalities in the utilization, availability, and affordability of maternal and child health services in the post-NHM period.

METHODS

Data

This study is based on the publicly available data from the fourth round of the National Family Health Survey (NFHS) conducted between 2015 and 2016. The NFHS 4 (8, 27) was conducted on behalf of the Ministry of Health and Family Welfare (MOHFW) and carried out by the International Institute for Population Sciences. This survey is an Indian version of the Demographic and Health Survey (DHS). This survey was conducted in over 29 states and 7 union territories (UTs). This survey was based on 1,315,617 births from 601,509 households with women aged 15–49 years old. The NFHS survey adopted a two-stage stratified random sampling approach by selecting primary sampling units (PSUs) and covering all 640 census enumeration blocks (CEBs) for urban areas and villages for rural areas with the probability proportional to population size (PPS) strategy. In the next stage, a systematic random sample selection of 22 households (HHs) was made for each PSU and CEB, respectively. Lastly, data from Central Bureau of Health Intelligence (CBHI) (28) 2016, Rural Health Statistics (RHS) (29) 2018–2019, and the Sample Registration System (SRS) maternal mortality ratio (MMR) Bulletin 2016–2018 (30) were also exploited.

State Selection

We restricted our analysis to three states, namely, Bihar, West Bengal, and Tamil Nadu. Extreme health outcome variations and three kinds of health systems were identified between these three states. The third most populous state in India is Bihar, where around 40% of its population is below the poverty line. The state's significant health and demographic indicators, such as child mortality, MMR and birth rates, are much higher than the

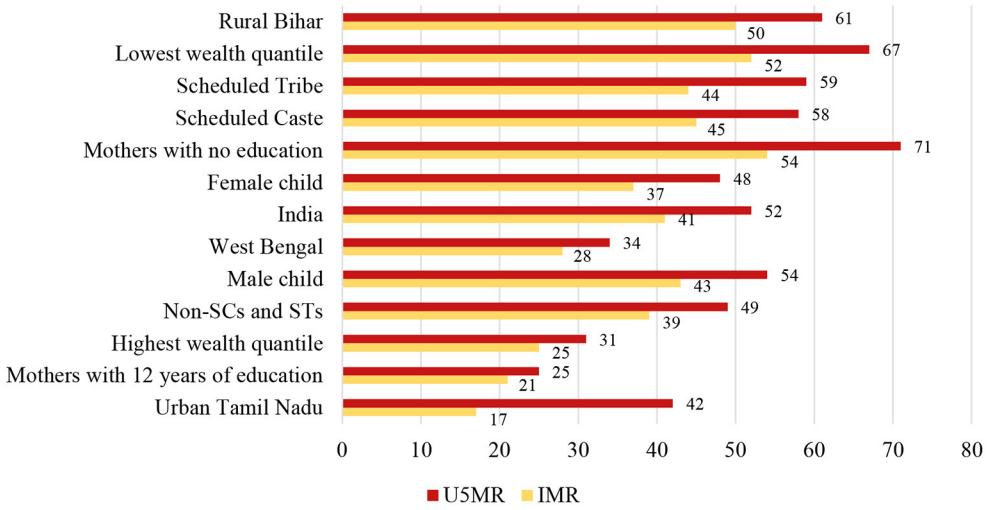

FIGURE 2 | Inequalities in infant and under-five mortality in India, 2015–2016.

national level and replicate poor health outcomes. Bihar has been the lowest in the Human Development Index (HDI) for the last three. Substantial gaps in the health sector have also been found in infrastructure and essential health requirements (31).

On the other hand, Tamil Nadu is often ranked the best among the well-performing states in India, especially in public health delivery, next only to Kerala in terms of various health indicators and the HDI. The state is renowned for its low mortality rates, adequate healthcare infrastructure, and human health resources. Tamil Nadu has adopted various new approaches to improve access to good-quality healthcare services at an affordable cost. The public healthcare system in the state has enhanced over the last few decades, with more people having better access to medical care services, whereas in West Bengal, the healthcare system is a mix of public and private care, and the private healthcare system is flourishing at secondary and tertiary healthcare levels. To show inter-state differences, the said states were compared. The former had among the best and moderate indicators and the latter the worst indicators of health outcomes. In 2000, Jharkhand was removed from the southern portion of Bihar. For NFHS 1 and 2, the districts of the present Bihar state were combined to make it universal for the rest of the rounds (the districts under Jharkhand state were removed). For trend analysis, only the previous three rounds of NFHS data were utilized.

Statistical Analysis

Descriptive statistics and the logistic regression model were used in these analyses. Individual- and household-level covariates were also utilized. The household characteristics pertained to the head of the household, while individual characteristics pertained to women (aged 15–49 years). The covariates were—age (15–24, 25–34, and 35–49 years), place of residence (urban, rural), caste (SC, ST, and non-SC/STs), religion (Hindu, Muslim, Christian, and others), wealth quantile (poor, middle, and rich), educational attainment (primary, secondary, and higher), husband's occupation (not working, professional or clerical, agricultural workers, and services), and place of delivery (public and private).

RESULTS

Determining Factors of Health Inequalities

Among the SCs and STs, infant and under-five deaths were higher among the latter than the former. The averages for infant and under-five deaths decreased from 73 to 49 and 102 to 63, respectively, during the pre- to post-NHM period in India and all the selected states. However, this period was marked with increasing inequalities in child deaths among social groups, as shown in **Figures 1A,B**. Post-NHM, the IMR and U5MR showed a considerable decline in Tamil Nadu (23, 32) compared to other states. At the same time, India witnessed a tremendous social inequality in child deaths.

The recent round of NFHS data (2015–2016) acknowledged the sharp socio-economic and regional disparities in infant and under-five deaths and showed that those from deprived castes and poor and backward states bore the higher burden of mortality. However, the risks of mortality burden before reaching 1 or 5 years were higher among boys (43 and 54%, respectively) than girls (37 and 48%, respectively). Again, a persuasive mortality burden were shown to be higher among Scheduled Caste and Scheduled Tribe communities than non-SC/STs, followed by rural Bihar (the state with the poorest health indicators in India) than urban Tamil Nadu. However, mothers with 12 years of education had lower mortality among younger than 1- (21%) or 5-year-old (25%) children in India. Further, it can be explained from **Figure 2** that economic status can be a significant indicator of infant and under-five deaths in India. Child deaths for the lowest income quantile earners were two times higher than that for the highest income quantile.

TABLE 1 | Selected socio-economic and health indicators of India, Bihar, West Bengal, and Tamil Nadu.

Indicators	India	Bihar	West Bengal	Tamil Nadu
Population (in crores)	121	10	9	7
Sex Ratio (females per 1,000 males)	943	918	950	996
Per capita net state domestic product (Rs.)	86,879	36,143	78,903	128,366
Percentage of population below poverty line	22	34	20	11
Female literacy rate (%)	65	52	71	73
Average life expectancy (in years)	57	54	64	60
Infant mortality rate (per 1,000 live births)	41	48	28	20
Under-five mortality rate (per 1,000 live births)	52	59	34	45
Maternal mortality rate (per 100,000 live births)	113	149	98	60
Population covered by a sub-center	5,616	10,626	6,070	4,172
Population covered by a PHC	35,567	55,670	69,231	25,561
Population served per government hospital	64,425	70,701	138,792	58,697
Population per government hospital bed	1,678	8,789	1,341	1,170
Percentage of births delivered in a health facility	79	64	75	99
Percentage of deliveries attended by health professional	81	70	82	99
Percentage of mothers received JSY assistance after giving birth	43	57	30	31
Percentage of children (0–59 months) fully immunized	50	48	69	60

National Family Health survey (NFHS-4) 2015-16; Central Bureau of Health Intelligence (CBHI) 2016; Rural Health Statistics (RHS) 2018-19; and SRS MMR Bulletin 2016-18.

Inequalities in Availability of Care Services

The availability of public health services is not even across the states of India (**Table 1**). Inequalities in public health infrastructure, resources (economic and human), and bed:population ratios have been recognized. Here, we compared Bihar, West Bengal, and Tamil Nadu based on public health infrastructure and availability of care services. Despite the rise in private healthcare facilities in Tamil Nadu, there were relatively better functioning primary public healthcare centers and better health outcomes in Tamil Nadu than Bihar and West Bengal or other states in India. This improvement might be due to the state government's investment in the health sector.

Along with the best health indicators, Tamil Nadu also had the best the socio-economic development in terms of—per capita income, sex ratio and female literacy. On the other hand, Bihar presented high poverty levels, poor health outcomes, inadequate public health facilities, utilization (population covered by a PHC, population:bed ratio, number of immunized children, and deliveries attended by a health professional), and poor social development. In comparison, West Bengal presented a mixed scenario of these two, with better use of public health facilities and availability of care services with improved social indicators.

Inequalities in Utilization of Preventive and Curative Services

All India rates for receiving full antenatal care (ANC) increased to 14% in 2015–2016 from 8% in 2005–2006 (**Figure 3**), with an urban–rural differential of 23 and 11%, respectively. Unfortunately, for Tamil Nadu, a sharp 12% decline in full ANC coverage was reported, six percentage points less than the national level. In Bihar, the overall figure was lowest (2%) in 2015–2016, with a fall of 1% in 10 years, with a strident urban–rural difference of 4 and 2%. For West Bengal, a positive trend (with an increase of 10%) was recognized in full ANC coverage. Among the social caste categories (**Table 2**), the Scheduled Tribe population had the lowest percentage of receiving full ANC care in all the selected states. Again, there was considerable variation in the economic groups. The percentage of received ANC was highest among the richest quantile (25%) compared to the poorer section (7%) followed by mothers with a higher level of education (31%) in India. In contrast, data of full ANC coverage showed an upward trend in all the states, with some notable declines recognized among the top performers such as Tamil Nadu.

The all-India average for full immunization coverage for 2005–2006 was 37% with an improvement of 50% for 2015–2016, with a four percentage point rural–urban difference. An intra-state variation was shown between Bihar, West Bengal, and Tamil Nadu. The overall full immunization coverage for Tamil Nadu was 60%, while the overall full immunization coverage for Bihar and West Bengal was 48 and 69%, respectively. A substantial percentage difference was recognized among the socio-economic groups. The coverage was lowest among SCs (59%) and STs (45%) compared to non-SC/STs (61%). In comparison, the coverage was highest in the wealthiest quantile (63%). However, the gap between the socio-economic groups has not been narrowed down even a decade after the NHM and Tamil Nadu showed a drop in full immunization coverage.

Inequalities in Maternal and Child Health Expenditure Burden

The evidence (**Figure 4**) from recent years showed a dependence on the private sector (53%); this may be due to India's weak public health delivery systems, while rural dependency on the

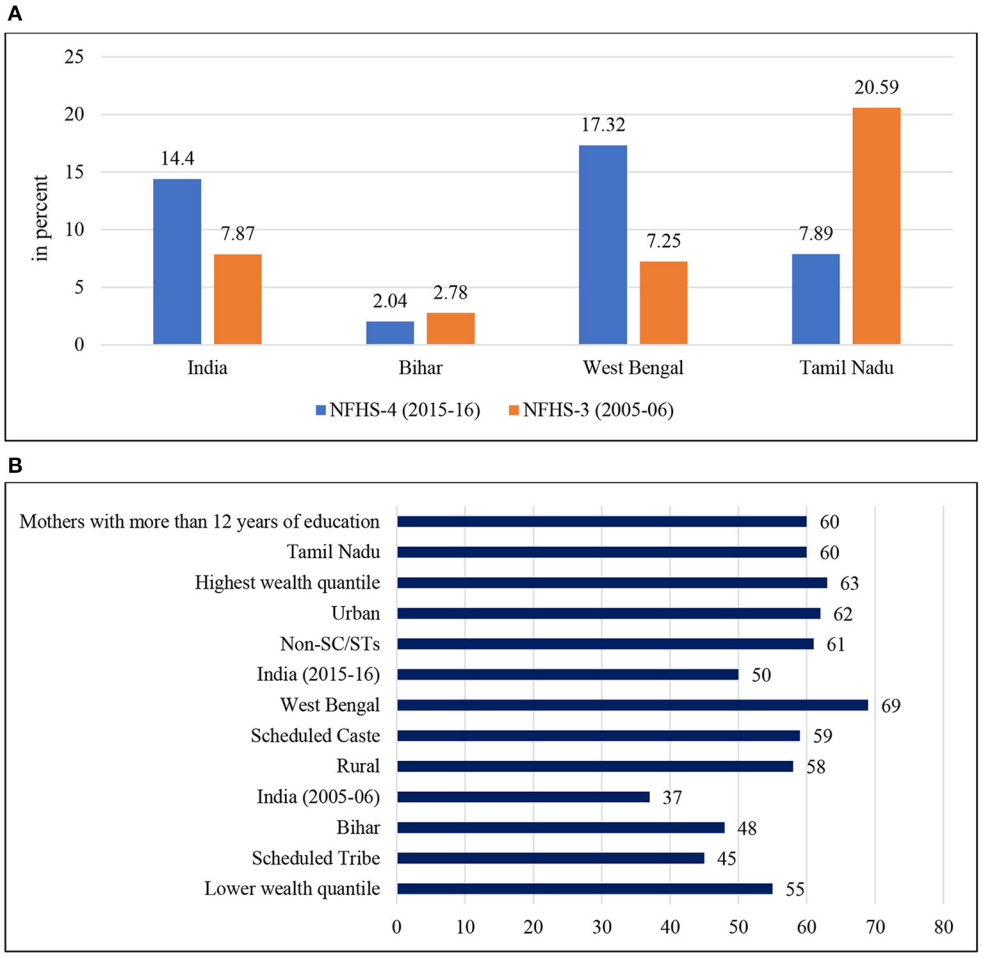

FIGURE 3 | (A) Inequalities in receiving full antenatal care (women aged 15–49 years) in India. Full Antenatal Care comprises 4+ANC visits, 2+TT injections, and 100+IFA tablets. **(B)** Inequalities in immunization rate (full immunization of children aged 0–59 months) in India. Full immunization covers three injections each of DPT and Polio, and one injection each of BCG and Measles.

public sector has been recognized. Further, intra-state variations occurred in the utilization of healthcare services.

Tamil Nadu had better developed and administrated services at the primary level, showing a higher level of utilization of the public sector (77%) even more than the national level. In contrast, a poorer state such as Bihar showed a lower utilization of the public health sector (22%). In West Bengal, this percentage was mixed with more utilization of the public sector (55%).

Expectedly, expenditure on childbirth was higher in the private health sector than in the public health sector (**Figure 5**). A considerable difference in public–private expenditure was also seen nationally and across the states, Bihar and Tamil Nadu poses the least expenditure in public healthcare whereas West Bengal shows comparatively higher cost for the last birth. On the other hand, in private healthcare the cost was the highest in Tamil Nadu along with West Bengal, even more than the national level. Moreover, it can be seen that out-of-pocket costs in urban places were higher than those in a rural setting (**Figure 6**); therefore, it is also evident that people living in rural areas had a higher burden to access healthcare. In contrast, urban areas had better access to public and private healthcare services with a 1.5 times lower expenditure than rural counterparts (**Figure 7**).

An adverse socio-economic differential (**Table 3**) in OOPE demonstrated that people from the rural setting were more likely to spend more than urban households. Further, due to the absence of financial risk protection, high OOPE affected the poorer wealth quantile and the people from the deprived caste badly. While age (0.04), level of education (0.19), caste (0.0), religion (0.1), and wealth quantile (0.12) directly affected expenditure, husband's profession (−0.02), and place of residence (−0.0) did not show a consistent effect on OOPE.

The analysis (**Figure 8**) from NFHS data showed that the high burden of the healthcare expenditure by the poorest quantile was financed primarily in two ways—by their savings (66%) and borrowing from friends or relatives (32%). In rural areas, a substantial proportion of the health expenditure for the last live birth was financed by borrowing money from others or selling

TABLE 2 | Inequalities in receiving full antenatal care (women aged 15–49 years) by background characteristics in India, 2015–2016.

Background characteristics	Full Antenatal Care			
	India	Bihar	West Bengal	Tamil Nadu
Place of residence				
Urban	22.58	4.27	19.68	33.01
Rural	11.2	1.78	16.41	29.11
Caste				
Scheduled caste	12.85	0.94	18.67	29.27
Scheduled tribe	10.87	0.6	14.78	22.47
Non-SC/STs	15.48	2.44	18.28	31.85
Religion				
Hindu	14.45	2.1	19.25	30.84
Muslim	11.88	1.76	12.95	33.95
Christian	23.83	#	12.49	30.44
Others	20.9	#	11.16	#
Wealth quantile				
Poor	6.66	1.05	14.02	28.21
Middle	15.56	3.64	19.21	28.39
Rich	24.84	9.49	25.18	33.38
Mother's educational attainment				
No education	5.24	0.76	11.75	28.42
Primary	9.76	1.55	14.92	27.64
Secondary	18.06	3.44	18.16	29.75
Higher	30.99	12.82	34.18	36.02

Full Antenatal Care comprises 4+ANC visits, 2+TT injections, and 100+IFA tablets.
#Not enough samples.

property in the poorer sections. In contrast, this percentage for urban households was comparatively low. Though in India, to minimize the financial shock for the poorer section, the government launched health insurance schemes, unfortunately, a negligible proportion (0.5%) was identified.

DISCUSSION

The NHM in India aimed to increase the utilization and access of maternal care, reduce maternal and child deaths and institutional deliveries, and reduce the out-of-pocket expenditure on maternal care. However, evidence suggests a surge in the utilization of maternal and child care services and reduction in maternal and child deaths in the post-NHM period (22, 33–35); there are limited studies that have exploited the effectiveness of the program. This study presents a comprehensive picture of the availability, utilization, and expenditure of MCH care in the pre-NHM period.

In this study, we assessed the population-level impact of the NHM on maternal and child healthcare. Caste and economic status are the two strongest socio-economic determinants of health in the setting of India (36). Overall, we found positive impacts of the NHM on delivery care, but at the same time, a sharp socio-economic inequality persisted in the post-NHM period. Several studies also reported considerably lower beneficial impacts among the low socio-economic population groups.

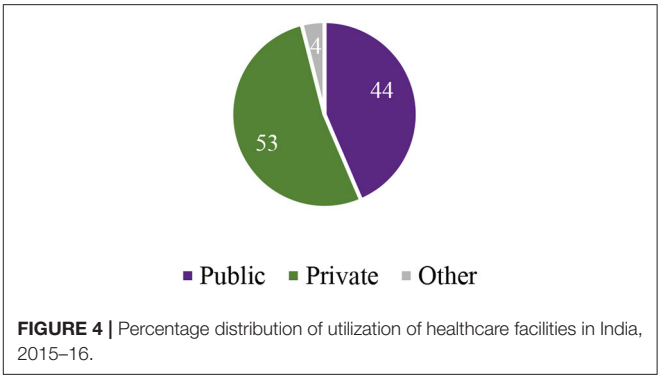

FIGURE 4 | Percentage distribution of utilization of healthcare facilities in India, 2015–16.

Besides, that caste is a factor of inequity in health has been revealed in other previous studies conducted in India. Women belonging to lower social groups (SC, ST) are less likely to be assisted by a skilled birth attendant (32). A study conducted in Kerala concluded that caste-based inequity in household health expenditure reproduces unequal access to general healthcare among different caste groups (36). A review of social exclusion, caste, and health concluded that the health outcomes and healthcare-seeking behavior of SCs and STs indicate both their social exclusion and the strong association between poverty and health for this population (37). In the examination presented in this article, we specify that caste may impact access to healthcare and the quality of care received. A substantial inter-state variation in the impacts of the NHM was found. Lower performing states such as Bihar showed a higher mortality rate, under-utilization of ANC and immunization care, and a minimal percentage of institutional births. However, states such as Tamil Nadu and West Bengal showed better MCH utilization. However, it is surprising to note that higher-performing state such as Tamil Nadu had a substantial decline in ANC and immunization care over the period (7). Moreover, conducting state-wise comprehensive evaluation studies and using quantitative and qualitative methods to identify the primary reasons for the inter-state variations in utilization of MCH care services would help to formulate practical policy guidelines.

Results confirm the growth of private healthcare (53%) across the nation's states. The National Sample Survey (NSS) stated that "not satisfied with medical treatment" ranked primarily in rural and urban areas. The reason "not satisfied with medical treatment" was followed by "lack of availability of services" in rural and "long waiting time" in urban settings. Besides, the latest NFHS data showed that the observation of "poor quality of care" was one of the most critical reasons across the states of India. A recent study suggested that the element of quality of care included interpersonal and clinical magnitudes, which stimulated the choice and utilization of healthcare (38).

The percentage of institutional deliveries doubled between 2005–2006 and 2015–2016, from 39 to 79%, and after that, interventions through the NHM contributed to a significant increase. Almost 100% of births in Tamil Nadu took place in a health facility. Rural–urban differences have also narrowed over the period (14%). A study carried out on EAG states found an

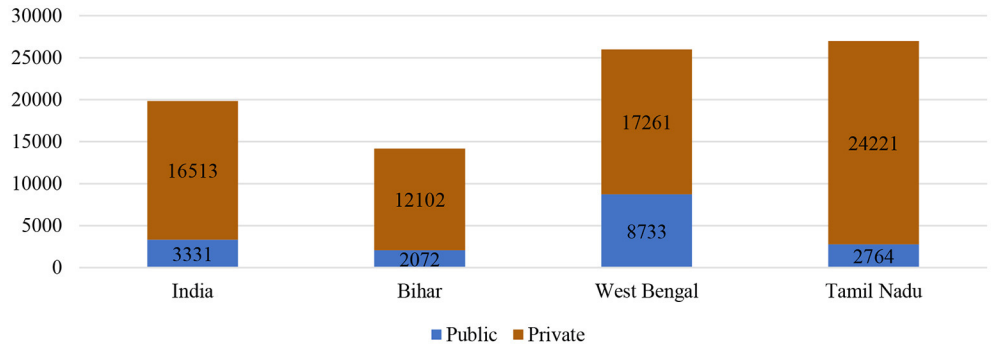

FIGURE 5 | Burden of out-of-pocket expenditure (in rupees) for delivery of the most recent live birth among women aged 15–49 years in India and selected states, 2015–2016.

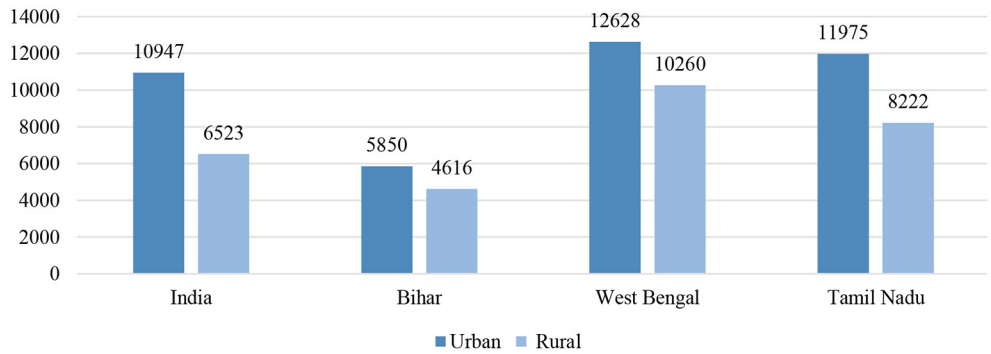

FIGURE 6 | Urban–rural differences in average out-of-pocket cost (in rupees) paid for delivery of the most recent live birth among women aged 15–49 years in India and selected states, 2015–2016.

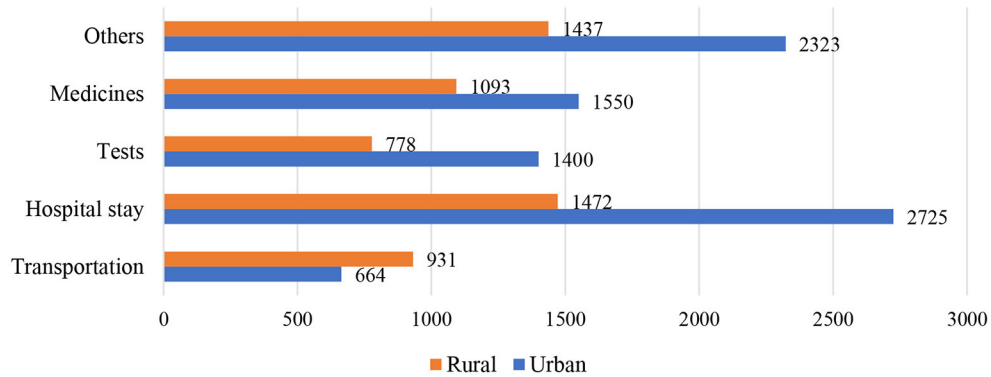

FIGURE 7 | The urban–rural difference of average out-of-pocket expenditure (in rupees) of transportation, hospital stays, tests, medicines and other costs paid for delivery of the most recent live birth among women aged 15–49 years in India and selected states, 2015–2016.

enormous socio-economic inequity in the uptake of institutional delivery, preferring higher socioeconomic groups, in the pre-NHM period. A similar pattern was observed in the post-NHM period, but the magnitude of inequity in institutional delivery dropped considerably. On one hand, the JSY contributed to institutional delivery and ANC uptake. Unfortunately, states such as Bihar showed a decline in full ANC care. But, studies revealed equity and uptake of ANC improved in most states in the late post-NHM period and socio-economic inequalities also narrowed down (39).

A substantial component of total health expenditure in India comes from out-of-pocket payments. These payments include—consultation charges, investigative testing, hospital stay, medications and conveyance. The NHM was launched

TABLE 3 | Regression coefficient and 95% CI of out-of-pocket expenditure (OOPE) (in rupees) of the most recent live birth among women aged 15–49 years according to background characteristics in India, the National Family Health Survey-4 (NFHS-4) (2015–2016).

Background characteristics	Coef.	Std. Err.	*t*	*P* > *t*	(95% Conf. Interval)
Age (15–24, 25–34, 35–49)	0.04	0.01	3.54	0.00	0.02–0.07
Place of residence (urban, rural)	−0.00	0.02	−0.00	1.00	0.0–0.04
Education (primary, secondary, higher)	0.19	0.01	20.68	0.00	0.17–0.21
Wealth quantile (poor, middle, rich)	0.12	0.01	10.67	0.00	0.10–0.14
Caste (SC, ST, non-SC/Ts)	0.00	0.01	0.28	0.78	0.0–0.02
Religion (Hindu, Muslim, Christian, others)	0.10	0.01	9.84	0.00	0.08–0.12
Husband's occupation (not working, professional or clerical, agricultural workers, services)	−0.02	0.01	−2.69	0.01	−0.04–(−0.01)
Place of delivery (public, private)	1.79	0.02	103.32	0.00	1.76–1.80
Constant	2.99	0.07	41.99	0.00	2.85

*Note: *p < 0.05, **p < 0.01, ***p < 0.001.*

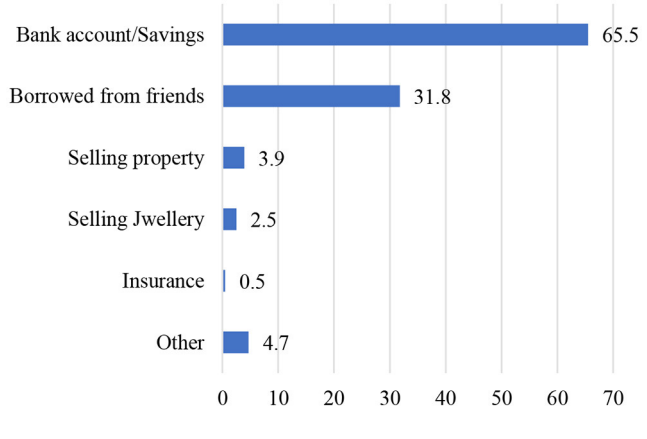

FIGURE 8 | The nature of out-of-pocket cost (in rupees) paid for delivery for the most recent live birth among women aged 15–49 years in India by the poorest quantile, 2015–2016.

with the aim to cut down the out-of-pocket expenditure by providing better MCH care in the public sector. The NFHS showed that the average out-of-pocket cost for delivery for the most recent live birth was Rs. 7,938. The usual cost was five times higher in private healthcare facilities (Rs. 16,522) than the public healthcare facilities (Rs. 3,198) in the post-NHM period. The differentials in OOPE on delivery care between public and private health centers have massively enlarged; this is possibly because of the increasing incidence of cesarean deliveries across the states of India (22). One of the most significant elements of OOP expenditure is obtaining medications. The NSS (1999–2000) estimate showed that more than two-thirds of the total OOP expenditure in urban and more than three-quarters in rural areas was spent on medications. The negative socio-economic discrepancy in out-of-pocket payments was revealed because the poorest quintile in rural areas spends around 87% of OOPE on medications (40).

In contrast, the richest quintile in urban areas paid relatively less, 65% (41) for the equivalent expenditure. The high OOP payment adversely affected the deprived sections because of the absence of financial risk protection. After adjusting for health expenditure due to OOP payments, an additional 3.5% of the population fell below the poverty line, grounded on estimates for 2005–2006 (42); comparatively, a slight rising trend was observed when 3.25% fell below the poverty line from the estimate made in 1999–2000 (41, 43). Numerous observations were documented by a study of 482 poor households in Udaipur, Rajasthan, which showed that a little less than one-third of the households identified a huge health expenditure as one of the reasons for economic pressure (44). Facing this certainty, the poor often finance rising healthcare costs by cutting down consumption level expenditures for other household members (45). Thus, an ailment of a household member could have noxious consequences toward further destitution of the households (39, 41).

CONCLUSION

To conclude, the NHM effectively increased the utilization continuation of maternal and child care services in public health centers and minimized expenditure on delivery care. Though the magnitude of intra-state and socio-economic inequalities has reduced, people from deprived social groups and poor developing states are still experiencing inequality. However, results also indicated that overcoming structural barriers through programs focusing on lower socio-economic groups rather than the psychological outlooks of poor people will likely to reduce inequities and indorse the uptake of maternal and child healthcare services.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

This analysis utilizes a secondary dataset with no identifiable information on the survey participants. This dataset is available

in the public domain for study use; hence, no approval was required from any institutional review board, as there is no question of human subject protection in this case.

AUTHOR CONTRIBUTIONS

MB and SG conceptualized the article. MB analyzed the data and wrote the manuscript. SG edited the article. All authors approved the final version of the manuscript.

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