



# Childhood Trauma in Patients With PAH—Prevalence, Impact on QoL, and Mental Health—A Preliminary Report

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**Background/Objective:** Child maltreatment is associated with increased risk of psychological consequences, contributes to morbidity and has long lasting effects on mental health and quality of life. Child maltreatment has not been assessed in patients with pulmonary arterial hypertension (PAH). We examined the prevalence of child maltreatment and determined their impact on disease severity in patients with PAH.

**Methods:** A cross-sectional observational multicenter study at two PH centers in Germany was conducted. Patients with a confirmed diagnosis of PAH were given a self-administered questionnaire. Child maltreatment using the Childhood Trauma Questionnaire (CTQ), quality of life (QoL), anxiety, depression, and lifestyle factors were assessed and enhanced by clinical parameters 6-min walk distance (6MWD), WHO functional class (WHO FC), and serum levels of N-terminal fragment of pro-brain natriuretic peptide (NT-proBNP). Prevalence rates of child maltreatment were compared to the general population and impact of child maltreatment on disease severity was calculated by logistic regression analysis.

**Results:** Two-hundred and seventeen patients, 71% female and a median age of 56 years were enrolled in this study. Patients with PAH had higher rates of emotional abuse and lower rates of physical neglect compared to the German population while rates of emotional neglect, physical abuse, and sexual abuse did not differ between patients and German population. Patients with any form of child maltreatment were more likely to be active smokers, had a worse QoL and more anxiety or depression. Moderate associations between child maltreatment, mental health, QoL, lifestyle factors and clinical parameters could be observed. Logistic regression analysis showed a significant impact of CTQ-total score on disease severity with an OR of 1.022 (95%-CI: 1.001–1.042,  $p = 0.035$ ).

**Conclusion:** We found a higher rate of child maltreatment in patients with PAH in comparison to the German population. Correlations suggest moderate associations

between CTQ-scores and mental health as well as QoL. Child maltreatment had significant impact on disease severity. However, effects were moderate. We conclude that child maltreatment has effects on mental health and quality of life in patients with PAH and may have limited effect on disease severity.

**Keywords:** pulmonary arterial hypertension, child maltreatment, mental health, quality of life, prevalence, pulmonary hypertension

## INTRODUCTION

Pulmonary arterial hypertension (PAH) is progressive pulmonary vascular disease. Characterized by remodeling of pulmonary vasculature it leads to increased pulmonary vascular resistance (1, 2). Patients with PAH are experiencing symptoms such as dyspnea on exertion, fatigue and with disease progression potentially clinical signs of heart failure. These debilitating symptoms impair physical activities and quality of life (QoL) (3, 4). While the disease remains fatal as none of the currently available drugs are curative, improvement of therapeutic options, clinical outcomes and life expectancy have put questions of patient's quality of life, mental health, emotional, and social burden are on the forefront of current research (5–8). Data on prevalence of psychiatric disorders in PAH patients (9, 10) is still scarce. Olsson et al. demonstrated a higher prevalence of anxiety and depression disorders with negative impact on QoL in PAH compared to levels in the German population (11, 12). Child maltreatment may pose an additional risk factor associated with lower QoL and mental disorders in patients with PAH. Several studies have identified child maltreatment as an important contributing factor to the incidence and severity of depressive disorders (13). Child maltreatment is defined as the abuse and neglect against a child under the age of 18 by a parent or other caregivers. It includes all types of physical and/or emotional ill-treatment, sexual abuse and neglect which results in actual or potential harm to the child's health, survival, development, or dignity in the context of a relationship of responsibility, trust, or power (14). It has been associated with poorer overall health, greater physical, and emotional functional disability and higher degree of health risk behavior. Patients with multiple types of maltreatment showed greatest worsening of self-reported health symptoms (15). Child maltreatment is associated with various diseases such as the development of cardiovascular diseases, type 2 diabetes or chronic obstructive pulmonary diseases leading to higher mortality (16–18). Proskynitopoulos et al. (19) found increased prevalence of child maltreatment in adults with congenital heart disease compared to the general German population. Higher total Child trauma questionnaire (CTQ) scores correlated with

decreased quality of life, higher rates of anxiety, and depression and contributed to the prediction of New York Heart Association (NYHA) scores (19). The present study aimed to assess the (i) prevalence of child maltreatment in patients with PAH and (ii) to compare this with the prevalence in the German general public as well as (iii) to assess the impact, differences and associations of child maltreatment on disease severity, lifestyle factors, mental health, and QoL in patients with PAH.

## METHODS

This cross-sectional observational multicentre study included patients with a confirmed diagnosis of PAH at two participating PH referral centers (Hannover Medical School and University of Giessen and Marburg, both in Germany). The study concept was developed in cooperation with patient organizations as suggested during the latest Pulmonary Hypertension World Symposium in 2018 (20). All patients gave written informed consent. The study was approved by local institutional review boards (Nr. 8540\_BO\_K\_2019 for Hannover and Nr. 21119 for Giessen and Marburg). Patients were contacted between September 2019 and March 2020. This study was conducted by a self-administrated questionnaire.

### Patient Setting and Clinical Parameters

Patients were selected based on diagnosis of PAH according to current criteria (1) and age  $\geq 18$  years. Assessment included hemodynamics from right heart catheterization at time of diagnosis, 6-minute walk distance (6MWD), WHO functional class (FC), and serum levels of N-terminal fragment of pro-brain natriuretic peptide (NT-proBNP). Risk assessment for our cohort was based on three variables FC, 6MWD, and BNP/NT-proBNP as previously described (21, 22). Each variable was graded with a number as low risk (1), intermediate risk (2), and high risk (3). The average risk was calculated by dividing the sum of the grades by the number of available variables and rounding to the next integer (23).

### Assessment of Child Maltreatment

Child maltreatment was assessed using the German version of the Childhood Trauma Questionnaire CTQ (24). The CTQ consists of a 28-item self-rating scale divided in five subscales inquiring five areas: emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect. The items are rated from 1 (never true) to 5 (very often true). The subscale scores range from 5 to 25 with an overall score from 25 to 125 points. Several studies have supported the reliability and validity of reported childhood trauma obtained with this instrument,

**Abbreviations:** 6MWD, 6-minute walk distance; BNP, brain natriuretic peptide; CTQ, child trauma questionnaire; FC, World Health Organization functional class; HADS, Hospital Anxiety and Depression Scale; NT-proBNP, N-terminal fragment of pro-brain natriuretic peptide; NYHA, New York Heart Association; PAH, Pulmonary arterial hypertension; PEPPAH, Psychische Einschränkungen bei Patienten mit pulmonal arterieller Hypertonie (Prevalence of mental disorders and impact on quality of life in patients with pulmonary arterial hypertension); QoL, quality of life; SD, Standard Deviation.

discriminant validity with structured trauma interviews and corroboration with independent data (24). Thresholds presented by Walker et al. (15) were used to construct groups with either form of maltreatment or no maltreatment. Child maltreatment was classified when threshold scores for emotional abuse (10), emotional neglect (15), physical abuse (8), physical neglect (8), and sexual abuse (8) were met. The CTQ-derived prevalence rates and mean-values of child maltreatment were compared to the German general population described by Iffland et al. (25).

## Assessment of Symptoms of Anxiety and Depression and Quality of Life

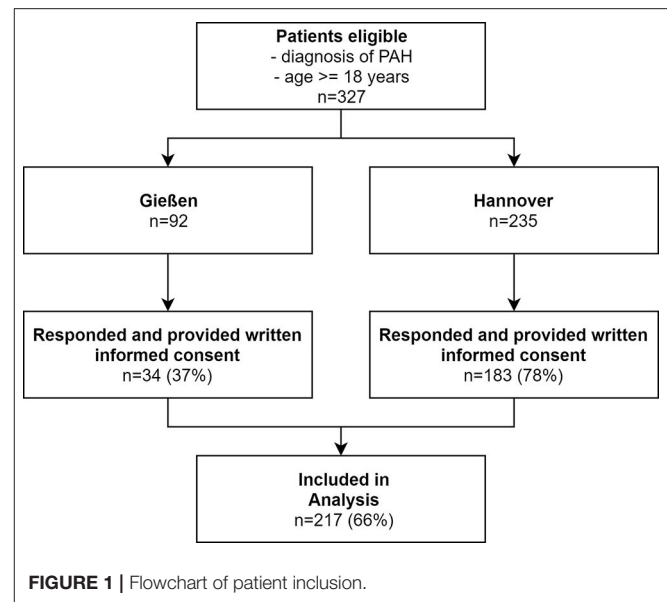
Symptoms of anxiety and depression were assessed with participants completing the Hospital Anxiety and Depression Scale (HADS) (26). The HADS questionnaire is divided into subscales for anxiety (HADS-A) and depression (HADS-D), each containing seven questions for a maximum of 21 points per subscale. The higher score indicating a more severe anxiety or depression. Zigmond et al. (26) proposed a score >11 per subscale to be associated with significant anxiety or depression. A cut-off score of 8 or above for both HADS-A and HADS-D was validated, showing probable signs of anxiety or depression (27, 28). The World Health Organization Quality of Life [WHO-QoL-BREF (29)] was used to assess quality of life.

## Statistical Analysis

IBM SPSS Statistics (version 28.0, IBM Corp., Armonk, New York) and Stata 13.0 (State Corp LP, College Station, Texas, USA) statistical software programs were used for statistical analysis. Continuous parameters are presented as median and interquartile range (Q<sub>25</sub>-Q<sub>75</sub>) or as mean and standard deviation (SD). Categorical variables are presented as number (*n*) and percent (%). Comparisons of continuous parameters were conducted using *t*-test or Mann-Whitney *U*-test (if not normally distributed or ordinal scaled) and comparison of categorical parameters by using Chi-square-test or Fisher's exact test, unless indicated otherwise. Correlations of continuous and ordinal parameters were assessed using Pearson correlation coefficient. Parameters were CTQ-scores, lifestyle factors (exercise, drinks per week, and smoking intensity) and clinical parameters such as BMI, HADS-scores, QoL, 6MWD, and WHO FC. Logistic regression analysis was conducted to assess impact of CTQ-score on clinical outcome parameter WHO FC as surrogate for disease severity (WHO FC I and II vs. WHO FC III and IV was used as binary outcome). Further univariate logistic regression was conducted to assess impact of child maltreatment (any positive CTQ-subscore) on anxiety or depression disorder. Nagelkerke's R<sup>2</sup> was determined to assess model quality. All tests were two-sided, *p* < 0.05 were considered statistically significant. *P*-values of multiple correlations were adjusted using the Benjamini-Hochberg-procedure.

## RESULTS

This patient cohort was previously described in the PEPPAH-study (12). A total of 327 patients were approached in this



study. Two hundred and seventeen patients (66%) agreed to participate and returned the questionnaires (Figure 1). Patient characteristics are shown in Table 1. The majority of patients were female (*n* = 155, 71%); median age was 56 (49-67) years. All patients were treated with PAH medications, most of them (47%) with dual combination therapy. Nearly all patients (96%) fell in the low or intermediate ERS risk score category. Patients with any form of child maltreatment were more likely to be active smokers, had a worse overall QoL and more anxiety and depression. Trends could be observed in 6MWD with more than 30 m difference in patients with or without any form of child maltreatment (Table 1). Disease severity indicated by ERS risk status, WHO FC and NTproBNP, hemodynamics at time of diagnosis, and PAH treatment did not differ between groups.

## Prevalence of Child Maltreatment in Patients With PAH

In this study, child maltreatment with a least one subgroup above threshold was detected in fifty percent of the patients (Table 1). Emotional abuse and emotional neglect were about 2 times more frequent in patients with PAH than in the general population (Table 1; Figure 2). Patients with PAH had a significantly higher total CTQ score (*p* < 0.001), while physical neglect was more prevalent in the general German population (48.4 vs. 36.4%, *p* = 0.041) and physical abuse did not significantly differ between both groups (14.3 vs. 12.0%, *p* = 0.458). Sexual abuse was reported under 10% in both patients with PAH and the general population (Table 2).

## Correlation of CTQ Subscores on Quality of Life, Mental Health, Lifestyle, and Clinical Parameters

Moderate associations between CTQ-scores, mental health, QoL, lifestyle factors, and clinical parameters could be observed (see

TABLE 1 | Patient characteristics.

	All patients <i>n</i> = 217	Patients with any CTQ positive subscore <i>n</i> = 108 (50%)	Patients without any CTQ positive subscore <i>n</i> = 109 (50%)	<i>p</i> -value of group comparison
Age—years	56 (49-67)	55 (41-65)	57 (45-66)	0.422
Sex—female (%)	155 (71%)	74 (69%)	81 (74%)	0.345
BMI (kg/m <sup>2</sup> )	26 (23-31)	26 (23-31)	26 (23-31)	0.813
Time since PAH diagnosis (years)	6 (3-11)	6 (2-11)	7 (4-13)	0.062
<b>Diagnosis—<i>n</i> (%)</b>				
- 1.1 IPAH	122 (56%)	66 (61%)	56 (51%)	0.233 <sup>c</sup>
- 1.2 HPAH	25 (12%)	13 (12%)	12 (11%)	
- 1.4 Associated PAH	70 (32%)	29 (27%)	41 (38%)	
<b>WHO FC</b>				
- I, <i>n</i> (%)	20 (9%)	7 (7%)	13 (12%)	0.439 <sup>c</sup>
- II, <i>n</i> (%)	92 (43%)	45 (42%)	47 (44%)	
- III, <i>n</i> (%)	93 (43%)	51 (47%)	42 (39%)	
- IV, <i>n</i> (%)	10 (5%)	5 (5%)	5 (5%)	
<b>ESC/ERS risk status—<i>n</i> (%)</b>				
- Low	107 (50%)	52 (49%)	55 (52%)	0.799 <sup>c</sup>
- Intermediate	97 (46%)	51 (53%)	46 (47%)	
- High	9 (4%)	4 (44%)	5 (56%)	
6MWD	439 (353–521)	423 (339–502)	454 (371–539)	0.061
NT-proBNP (ng/l), <i>n</i> = 192	184 (88–517)	169 (74–419)	207 (104–586)	0.961
DLCO (% pred.), <i>n</i> = 138	62 (47-74)	64 (42-73)	61 (48-74)	0.844
paO <sub>2</sub> , mmHg	67 (60–75)	67 (60–76)	67 (61–75)	0.788
<b>Hemodynamics at diagnosis</b>				
- mPAP (mmHg)	48 (41-57)	48 (41-58)	49 (41-58)	0.651
- PAWP (mmHg)	9 (6-12)	9 (6-12)	9 (6-12)	0.794
- CI (l/min/m <sup>2</sup> )	2.4 (2.0–2.9)	2.4 (2.0–3.0)	2.4 (2.0–2.7)	0.284
- PVR (dyn·s·cm <sup>-5</sup> )	707 (501–947)	689 (505–951)	752 (498–927)	0.914
<b>PH-therapy—<i>n</i> (%)</b>				
- Monotherapy	44 (20%)	21 (19%)	23 (21%)	0.673 <sup>c</sup>
- Double combination therapy	102 (47%)	54 (50%)	48 (44%)	
- Triple combination therapy	71 (33%)	33 (31%)	38 (35%)	
<b>Smoking status</b>				
- Active, <i>n</i> (%)	24 (11%)	17 (16%)	7 (6%)	0.021 <sup>c</sup>
- Former, <i>n</i> (%)	31 (14%)	19 (18%)	12 (11%)	
- Never, <i>n</i> (%)	162 (75%)	72 (67%)	90 (83%)	
- Packyears	14 (5-25)	15 (6-23)	9 (4-33)	0.495
Alcohol drinking (drinks per week)	0.8 ± 2.0	0.9 ± 2.5	0.8 ± 1.1	0.772 <sup>a</sup>
Exercise score (points)	3 (2-4)	3 (2-3)	3 (2-4)	0.906 <sup>b</sup>
HADS-A (points)	6 (2-9)	7 (3-10)	5 (2-9)	<b>0.034</b>
HADS-D (points)	5 (2-8)	6 (3-9)	4 (2-7)	<b>0.002</b>
QoL-overall (points)	50 (38-75)	50 (38-63)	63 (44-75)	<b>0.026</b>
QoL-psych (points)	71 (58–79)	63 (50-79)	71 (63–83)	<b>0.020</b>
QoL-physical (points)	57 (45-75)	57 (43-71)	64 (50-75)	<b>&lt;0.001</b>
QoL-social (points)	67 (58-83)	67 (58-83)	67 (50-75)	<b>0.009</b>
QoL-environment (points)	78 (69–88)	75 (63–84)	78 (70–88)	<b>0.012</b>

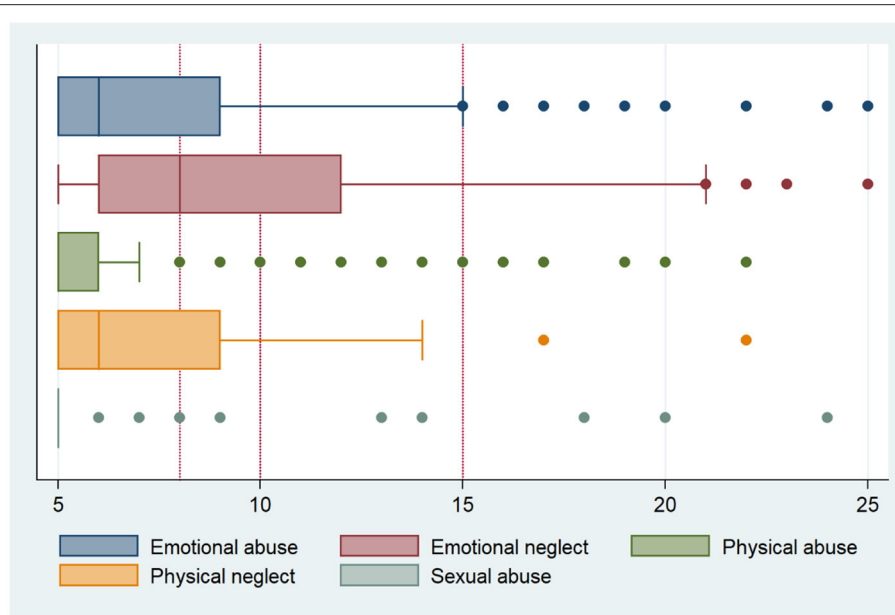
Continuous variables are stated as median and interquartile ranges (IQR) and categorical variables are stated as *n* and percent (%), unless indicated otherwise. All *p*-values were derived using *t*-test, unless indicated otherwise.

<sup>a</sup>Mean and SD because of distribution of the data.

<sup>b</sup>Non-parametric Mann-Whitney *U*-test because of ordinal scale of the variable.

<sup>c</sup>Chi<sup>2</sup>-test because of the categorical scale of the variable.

BMI, body mass index; QoL, quality of life; HADS-A, Hospital Anxiety and Depression Scale—anxiety; HADS-D, Hospital Anxiety and Depression Scale—Depression; I/HPAH, idiopathic or heritable pulmonary arterial hypertension; WHO FC, World Health Organization Functional Class; 6MWD, 6-min walking distance; NT-proBNP, N-terminal fragment of pro-brain natriuretic peptide; DLCO, diffusion capacity of the lung for carbon monoxide; paO<sub>2</sub>, mmHg, arterial pO<sub>2</sub>; mPAP, mean pulmonary arterial pressure; PAWP, pulmonary artery wedge pressure; CI, cardiac index; PVR, pulmonary vascular resistance; IQR, interquartile range. Statistically significant values as bold.



**FIGURE 2 |** Subscores of childhood trauma questionnaire of patients with pulmonary arterial hypertension.

**TABLE 2 |** Scores and prevalence of child maltreatment in patients with PAH compared to German population.

Item	PAH <i>n</i> = 217	German population (25) <i>n</i> = 2,500	<i>p</i>
<b>Comparison of CTQ-scores, Mean (SD)</b>			
- CTQ-total score	41.84 ± 14.43	35.99 ± 10.48	<b>&lt;0.001</b>
- CTQ-emotional abuse	7.68 ± 4.00	6.51 ± 2.60	<b>&lt;0.001</b>
- CTQ-emotional neglect	9.58 ± 4.88	10.09 ± 4.23	0.093
- CTQ-physical abuse	6.19 ± 2.83	5.88 ± 2.17	<b>0.049</b>
- CTQ-physical neglect	7.18 ± 2.75	8.15 ± 3.02	<b>&lt;0.001</b>
- CTQ-sexual abuse	5.54 ± 2.24	5.45 ± 1.66	0.458
<b>Comparison of CTQ-categories, <i>n</i> (%)</b>			
- CTQ-emotional abuse	43 (19.8%)	254 (10.2%)	<b>&lt;0.001</b>
- CTQ-emotional neglect	42 (19.4%)	348 (13.9%)	0.078
- CTQ-physical abuse	31 (14.3%)	301 (12.0%)	0.458
- CTQ-physical neglect	79 (36.4%)	1,210 (48.4%)	<b>0.041</b>
- CTQ-sexual abuse	14 (6.5%)	156 (6.2%)	0.920

Continuous variables are stated as mean and standard deviation and categorical variables are stated as *n* and percent (%).

CTQ, childhood trauma questionnaire; PAH, pulmonary arterial hypertension; SD, standard deviation; Statistically significant values as bold.

**Table 3).** Higher CTQ emotional-, physical, or total scores were correlated with higher HADS depression and anxiety scores ( $r = 0.201$ – $0.401$ ,  $p < 0.001$ ) while being negatively correlated with QoL ( $r = -0.200$  to  $-0.315$ ,  $p < 0.001$ ). History of smoking and WHO FC were positively correlated with emotional and physical CTQ-scores ( $r = 0.113$ – $0.216$ ). Total CTQ-scores were negatively correlated to 6MWD ( $r = -0.145$  to  $r = -0.204$ ,  $p < 0.005$ ) whereas exercise and drinks per week were not significantly related. There were no significant association between CTQ-sexual abuse and any evaluated parameter.

## Impact of CTQ on Disease Severity and Mental Health

Univariate logistic regression analysis on disease severity (WHO FC I+II vs. WHO FC III+IV) revealed a significant impact of CTQ-total score with an OR of 1.022 (95%-CI: 1.001–1.042,  $p = 0.035$ ) while the model describes 2.9% of the independent variable. Further univariate regression analysis showed that patients with reported emotional neglect had a 6.8% higher chance (95%-CI: 1.009–1.131,  $p = 0.023$ ) of being in WHO FC III or IV per CTQ point increase. Model accuracy was 3.3%. Impact of any positive CTQ-subscore on anxiety had an OR of 1.678



**TABLE 3** | Correlations of CTQ-scores in PAH with HADS, QoL, Lifestyle and 6MWD, and WHO FC.

	HADS-D	HADS-A	QoL	BMI	Exercise	Drinks	Smoking	WHO FC	6MWD
CTQ-total score	0.368**	0.351**	-0.315**	0.158*	-0.068	-0.071	0.188*	0.186*	-0.192*
CTQ-emotional abuse	0.388**	0.401**	-0.302**	0.126	-0.039	-0.027	0.181**	0.125	-0.174*
CTQ-emotional neglect	0.316**	0.255**	-0.308**	0.121	-0.056	-0.082	0.113	0.210*	-0.145*
CTQ-physical abuse	0.262**	0.268**	-0.200*	0.139*	-0.081	-0.066	0.157*	0.118*	-0.146*
CTQ-physical neglect	0.251**	0.204*	-0.269*	0.131	-0.041	-0.088	0.216*	0.192*	-0.204*
CTQ-sexual abuse	0.112	0.106	-0.056	0.123	-0.033	0.001	0.021	0.049	-0.097

Pearson correlation coefficient. Statistically significant values are marked using asterisk, \*\* $p < 0.001$ ; \* $p < 0.05$ .

BMI, body mass index; CTQ, childhood trauma questionnaire; QoL, quality of life; HADS-A, Hospital Anxiety and Depression Scale—anxiety; HADS-D, Hospital Anxiety and Depression Scale—Depression; PAH, pulmonary arterial hypertension; WHO FC, World Health Organization Functional Class; 6MWD, 6-min walking distance.

(95%-CI: 0.788–3.574,  $p = 0.179$ ) while impact on depression showed an OR of 2.761 (95%-CI: 1.369–5.209,  $p = 0.004$ ) while model accuracy was 1.5 and 6%, respectively.

## DISCUSSION

To the best of our knowledge this is the first study to assess the prevalence of child maltreatment in patients with PAH. Patients with PAH had a higher overall CTQ-score with fifty percent of our patients exceeding the threshold for any subscore of child maltreatment. In these patients, moderate associations between CTQ-scores and QoL, anxiety and depression, WHO FC, and 6MWD could be detected. Higher prevalence of CTQ-scores were mainly driven by higher subscores in emotional abuse or physical abuse. This is in line with previous observations from patients with congenital heart disease (19). While absolute scores were higher in patients with PAH, both groups reported only moderately elevated scores on the scale of 5–25 points per subscore (as seen in **Figure 2**). Inversely physical neglect was comparatively more frequent in the general population than in patients with PAH. It has been discussed that elderly who experienced privation of (post-)war year were more likely to report physical neglect (25). With comparatively weak psychometric properties and weak internal consistency, comparisons for the physical neglect subscale discussion on impact can only be held cautiously.

Several severe long-term consequences of child maltreatment have been studied and suggested. Ranging from mentioned physical health, psychological to behavioral, and societal consequences. Most children who experienced child maltreatment are often affected by many other adversities such as domestic violence, poverty, and parental substance abuse (30).

Child maltreatment poses a higher risk on the development of mental disorders such as depression (31–34). Olsson et al. have recently demonstrated a higher prevalence of mental disorders in patients with PAH. Our findings indicate a correlation between higher CTQ scores and higher HADS depression and anxiety scores. Gamble et al. (35) in as early as 2006 had described the correlation between childhood trauma and severity of anxiety and depression. Similarly, we demonstrated impact of child maltreatment on the diagnosis of depression, which is in line

with these previous studies. Several studies examining impact of child maltreatment on disease outcomes saw attenuation of the relationship between child maltreatment and disease when adjusting for mental disorder (36). Our data supports existing evidence in indicating that child maltreatment is a risk factor for mental disorders which themselves may be mediators for disease severity of PAH (36).

QoL contributes to the evaluation of emerging PAH treatments as well as disease course. QoL in patients with PAH is severely impaired by clinical symptoms as well as emotional domains (20, 37). Mathai et al. (38) have found QoL to be a predictor of outcomes in PAH and thus a target for therapeutic interventions. Child maltreatment in patients with PAH correlate with worse QoL. This is in line previous studies such as Corso et al. who demonstrated significant and sustained losses of QoL in adulthood of persons who experienced child maltreatment (39, 40).

Several studies have demonstrated association between child maltreatment and cardiometabolic diseases such as systemic hypertension, ischemic heart disease, and chronic heart disease (41, 42). Many authors examined child maltreatment as a composite measure of adversity and reported a dose-response relationship between number of childhood adversities and heightened risk for cardiometabolic diseases. Overall, CTQ scores were associated with disease severity measured by WHO FC. In a subscore analysis of our study, we found that patients with higher scores in emotional neglect had a significantly higher chance of being in a higher WHO FC per CTQ point increase. While this impact might suggest negative influence on disease course, morbidity, and mortality model accuracy is comparatively low. Clinical signs of right heart failure, 6MWD, NT-proBNP/BNP, and WHO FC are strong indicators of disease severity and risk status in patients with PAH (23). Arguably these somatic factors play a more prominent role on disease severity with a minor role of child maltreatment and by association mental disorders.

## Limitations

Our paper has strength and limitations. Data for childhood maltreatment, mental health and QoL were derived using a self-administered, paper-based questionnaire. Reliable measurements of prevalence and severity of child maltreatment have yet relied

on self-reports, showing discrepancies of rates compared to reports of child-protection agencies (43, 44). Median global prevalence rates differ substantially by maltreatment type, gender and by continent with varying number of studies and available data (45). Only two German PH-centers were involved in this study which might cause selection bias. This study was carried out between September 2019 and March 2020. In January, the Corona virus pandemic hit Germany and this study didn't control for any possible impact on mental disease during this time. Of note, Park et al. (46) have studied effects on first waves of corona virus pandemic on a subsample of this cohort and found minor changes in mental health due to the corona virus pandemic. However, a strength is relatively large sample size of PAH patients given that PAH is a rare disease as both participating centers are large university-based tertiary-level referral centers.

## CONCLUSION

In the present study, child maltreatment, in particular, subscores for emotional abuse and physical abuse was more prevalent in patients with PAH than in the general population. The presence of child maltreatment was associated with a higher likelihood of anxiety and depression and reduction in QoL. Child maltreatment in patients with PAH might play a role in disease severity. With wide ranges of long-term consequences of child maltreatment, screening for a history of child maltreatment can help physicians in assessment of patients' needs and treatment options. This should be taken into consideration in addition to more widely acknowledged impact of mental disorders and QoL on PAH. Psychosocial interventions as a treatment approach have been proven effective in patients with a history of child maltreatment (47–49). Integrating past experiences and psychological problems in the care and treatment of patients with PAH is recommended. The lasting consequences of child maltreatment warrant further investigation.

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## 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 Hannover Medical School and University of Giessen and Marburg. The patients/participants provided their written informed consent to participate in this study.

## AUTHOR CONTRIBUTIONS

DHP was responsible for study design, implementation of the study, data collection, data interpretation, and drafting the manuscript. TM was responsible for data collection and revising the manuscript. KK was responsible for study design, data interpretation, and revising the manuscript. JK was responsible for data interpretation and revising the manuscript. MR, HG, and HAG were responsible for implementation of the study and critically revising the manuscript. MH was responsible for implementation of the study, data interpretation, and critically revising the manuscript. KO was responsible for study design, implementation of the study, data interpretation, and critically revising the manuscript. JF was responsible for study design, implementation of the study, data collection, statistical analysis, data interpretation, and drafting the manuscript. All authors contributed to the article and approved the submitted version.

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The remaining 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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