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Management of secondary immunodeficiency in hematological malignancies: a Delphi consensus from the Middle East

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Secondary immunodeficiency (SID), acquired hypogammaglobinemia, is an immunodeficiency caused by different factors like diseases, medications, and/or nutrition disorders. Most patients with hematological malignancies (HM), namely chronic lymphocytic leukemia (CLL) and multiple myeloma (MM), experience such SID. These patients have a consistently high risk of infection throughout the disease course. Traditional chemotherapy and novel agents used to treat HM may further increase infection susceptibility. Immunoglobulin replacement therapy (IgRT) is an effective management option for SID. The prevalence of SID in the Middle East needs better documentation. Healthcare providers should consider and evaluate SID in patients at risk, monitor for infection occurrence, and treat accordingly (including initiating IgRT when indicated). A Delphi initiative was conducted by a consensus panel of 15 experts from the Middle East who have over 20 years of experience in actively managing patients with SID. The modified Delphi process was used, and 16

questions reached a consensus on managing SID patients with IgRT. In addition, the consensus panel of Middle East experts recommended real-world practice recommendations regarding initiating, dosing, and discontinuing IgRT in managing SID. This consensus recommendation aims to assist healthcare practitioners in the Middle East in evidence-based clinical decision-making for better management of SID.

KEYWORDS

secondary immunodeficiency, Middle East, Delphi consensus, immunoglobulin replacement therapy, acquired hypogammaglobinemia

1 Introduction

Secondary immunodeficiency (SID), mainly in the form of acquired hypogammaglobulinemia in hematological malignancies (HMs), can develop due to either the underlying disease or as a consequence of therapy (1, 2). Patients with SID may experience increased susceptibility to infections, ranging from mild to severe, including opportunistic bacterial, viral, and fungal infections (3, 4). The spread of multidrug-resistant organisms such as multidrug-resistant gram-negative bacteria, vancomycin-resistant enterococcus, and methicillin-resistant Staphylococcus aureus further increases the incidence of severe infections and mortality (3).

Management of SID requires a thorough evaluation of the patient's clinical and laboratory profiles to determine the most effective interventions. These interventions may include patient education, immediate access to antibiotics in emergencies, preventive antibiotic treatment, vaccination, and reduced immunosuppression or treatment of the underlying condition when feasible (5). The recently updated European Medicines Agency (EMA) guidelines have expanded the indication for the usage of immunoglobulin replacement therapy (IgRT) in SID to include a wide range of patients, such as those with various HMs, individuals undergoing B cell-depleting therapy and people experiencing hypogammaglobulinemia after bone marrow or solid organ transplantation. This is in addition to the previous EMA indication that included only chronic lymphocytic leukemia (CLL) and multiple myeloma (MM) patients (6). Selected patients who suffer from severe or recurrent infections despite appropriate prophylactic antibiotics and vaccination and have low levels of quantitative serum immunoglobulin G (IgG) may be recommended for management with IgRT. Several studies have reported that IgRT effectively reduces severe infection rates in CLL or MM patients (7–9). However, other published research has not consistently replicated these results (10, 11). Data from a market research study analyzing secondary specialty pharmacies found that CLL and MM were the primary causes of secondary antibody deficiency leading to IgRT use, with approximately 39.2% to 54.9% of patients receiving IgRT for this condition (10). Acknowledging the complexity of the decision to use IgRT to manage SID is essential as it is multifactorial and involves physician-patient interaction and consensus. Additionally, more evidence that describes real-world practices around the initiation, dosing, and discontinuation of IgRT, specifically in managing patients with SID in the Middle East, is warranted. Therefore, developing evidence-based, region-specific recommendations from real-world experts for treating SID using IgRT is crucial. To achieve this goal, we present a set of consensus recommendations for managing SID with IgRT in the Middle East.

Wherever the term "HM patients at risk" is used, this implies CLL patients, MM patients, patients with B-lymphoproliferative neoplasms, patients on B-cell depleting therapies, hemopoietic stem cell transplant (HSCT) recipients, and patients on CAR T-cell therapies.

2 Materials and methods

The Middle East SID consensus recommendations were generated using a modified Delphi Method. A panel of 15 experts from the Middle East region, along with an international expert in IgRT and SID, was selected based on their expertise in managing patients with SID and their regional practice. The experts agreed upon the four most crucial areas of SID management that needed systematic literature review and detailed discussion to understand regional practices around a) Evaluation and diagnosis of SID, b) Prophylactic treatment of patients with SID, c) Monitoring Ig levels, d) Initiating, dosing, and discontinuation of IgRT. Eighteen (12) questions related to the four sections were generated through a modified Delphi process and distributed to all panel members via email in January 2023. Responses were collected within 30 days, and in March 2023, two virtual meetings were held to reach a consensus on managing SID in the Middle East. Experts voted anonymously

Abbreviations: CAR, Chimeric Antigen Receptor; CLL, Chronic Lymphocytic Leukemia; DLBCL, Diffuse Large B-Cell Lymphoma; fSCIg, Facilitated Subcutaneous Immunoglobulin; HM, Hematological Malignancies; IgRT, Immunoglobulin Replacement Therapy; IVIG, Intravenous IgG; SCIg, Subcutaneous Immunoglobulin; SID, Secondary Immunodeficiency.

on each recommendation statement presented in the multiple-choice format, and those with ≥70% agreement were included in the consensus. Statements not receiving agreement were discussed, revised if necessary, and re-voted.

The study was carried out in compliance with the standards outlined in the Declaration of Helsinki (11).

3 Results and discussion

The Delphi panel from the Middle East consisted of Hematologists and Immunologists with extensive experience (average experience: 25 (35/15) years) in managing SID (Table 1). A total of 16 questions (12 + 2 questions written as two sub-questions each) with two or more statements are included after the agreement of the experts from the Middle East (Table 2).

3.1 Evaluation and diagnosis of SID

Lymphoid malignancies are frequently associated with SID, with reported incidences of some forms of hypogammaglobulinemia in newly diagnosed CLL, MM, and diffuse large B-cell lymphoma (DLBCL) reaching up to 25%, 80%, and 22%, respectively (13–15). The incidence of hypogammaglobulinemia increases during disease evolution in CLL patients. Therefore, infectious complications are common in CLL patients, with up to 80% of them experiencing such complications at some point during their disease (16). Severe or significant infections are experienced by 20% of CLL patients, accounting for an estimated 60% of deaths (16, 17).

Experts recommend that clinicians investigate SID in all HM at-risk patients through appropriate laboratory and clinical evaluations. In HM patients at risk without a history of infection, it would be prudent to obtain baseline quantitative serum IgG levels and then monitor the patient periodically during the natural course of the disease.

3.2 Primary and secondary prophylaxis in SID in patients with HMs

Experts from the Middle East typically recommend antimicrobial prophylaxis based on the patient's underlying risk of infection (disease, type of therapy, etc.) as the primary prophylaxis for SID in these patients. Vaccination is also advised as a preventive measure to reduce the risk of infections in this population. To ensure early reporting of conditions in SID patients and timely initiation of treatment, patients, parents, and caregivers should receive education. Early recognition and management of infections are vital in reducing the morbidity and mortality associated with SID in patients with HMs. Therefore, appropriate prophylactic measures, vaccinations, and patient education are essential to optimize the management of SID in this patient population.

The role of IgRT as primary prophylaxis (before any infectious occurrence) for HM patients at risk with hypogammaglobulinemia is unclear. An international survey reported that the prescription practice for prophylactic IgRT in patients with SID varies among countries (12). The difference in IgRT usage between Italy, Germany, Spain, the United States, and the UK in patients with SID is more prevalent in the former four countries compared to the UK (12, 18). In 85% of cases, IgRT was prescribed after two or more severe infections, whereas in 65% of cases, it was prescribed after the first severe infection (secondary prophylaxis).In this study, IgRT was the primary prophylaxis given in 24% of the patients (18).

3.3 Monitoring IgG levels

Experts from the Middle East discussed in detail the practices carried out in everyday clinical practice regarding monitoring of IgG levels in patients with SID and unanimously recommended that regular evaluation and monitoring for hypogammaglobulinemia should be considered in CLL patients without a history of infection since they may develop SID during the natural course of the disease. Quantitative serum IgG levels should be determined at diagnosis and before initiation of treatment in all HM patients at risk. Additionally, IgG levels should be evaluated in patients who develop at least one episode of severe bacterial infection, and further testing is recommended in patients who develop recurrent or persistent infections. Routine baseline checking of IgG and the uninvolved immunoglobulin subtypes is recommended in MM patients with recurrent infections. If IgG levels are normal, no further testing is recommended unless the patient develops recurrent infections despite adequate antibiotic treatment. Repeating testing of uninvolved immunoglobulin and IgG levels is recommended in these patients. In addition, evaluation of the antibody titers to vaccination is advisable. An increased frequency of monitoring or monthly monitoring is recommended in patients with recurrent or persistent infections, delayed improvement, or complications.

The IgRT is recommended to be used in hypogammaglobulinemia patients with severe or recurrent

TABLE 1 Expert panel details*.

Region	UAE	Saudi Arabia	Lebanon	Kuwait	Oman	Qatar
Immunologists (N)	1	1	1	1	1	
Hemato-oncologists (N)	3	3	1	1	1	1
Total (N)	4	4	2	2	2	1

This expert panel had Dr. Maria Dimou (Hemato-oncologists) from Greece as moderator.

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TABLE 2 Middle East consensus recommendations for the management of SID (percentage agreement).

Consensus Statement	Consensus Percentage
Q1. How do you evaluate early and diagnose hypogammaglobulinemia/secondary immunodeficiency (SID) in your patients with hematological malignancies such as Lymphoproliferative diseases, B cell malignancies, bone marrow transplant and those receiving immunotherapy such as monoclonal antibodies, antibody drug conjugates, Bi-specific monoclonal antibody, and CAR-T cell therapy?	
A. All patients with HMs should be suspected of having some degree of SID	93
B. Confirmed diagnosis of HM as mentioned above (with no infection history)	73
C. Patients who are admitted with a serious infection or who have persistent or recurrent infections should have SAD ruled out by appropriate laboratory and clinical evaluations.	100
D. Even in the event of a no infection history and wait and watch strategy being employed, it is recommended to conduct a thorough hypogammaglobulinemia/SID evaluation, as the natural course of the disease might further increase the immunodeficiency.	80
E. The overall aim of testing should be to help characterize a patient's infection risk, including IgG concentration, functional IgG, B-cell counts, and T-cell counts.	93
Q2. When would you typically check or recommend IgG levels in a patient with hematological malignancies?	
A. Estimation of baseline IgG is recommended in all patients with hematological malignancy at diagnosis	73
B. Before initiating treatment	87
C. In patients who develop at least 1 episode of infection	80
D. Additional testing is recommended in patients who develop recurrent infections	92
Q3. Do you routinely check/recommend uninvolved immunoglobulin subtypes in your patients with myeloma to look for hypogammaglobulinemia/secondary immunodeficiency (SID)?	
A. Routine baseline checking of IgG and the uninvolved immunoglobulin subtypes is recommended in patients with recurrent infections	80
B. If the levels are normal, no further testing is recommended unless the patient develops recurrent infections despite adequate antibiotic treatment, then repeat testing of Immunoglobulins, along with IgG levels and antibody titers to vaccination	87
Q4. What treatments do you use or recommend for primary prophylaxis in secondary hypogammaglobulinemia/secondary immunodeficiency (SID) in patients with HMs?	
A. Antimicrobial prophylaxis for at risk patients as indicated	93
B. Vaccination	93
C. Education of patients, parents, and caregivers	100
Q5.[A]. In which patients with hematological malignancies and low immunoglobulin do you routinely use or recommend immunoglobulin replacement therapy?	
A. Patients with hypogammaglobulinemia with recurrent infections despite receiving appropriate anti-infective therapy	100
B. Patients with hypogammaglobulinemia after a single severe infection or recurrent or persistent infections.	100
Q5.[B]. In which patients with HMs who have hypogammaglobulinemia and recurrent infections, do you consider the usage of immunoglobulin replacement therapy as primary prophylaxis?	
A. Patients with HM with hypogammaglobulinemia receiving CAR-T cell therapy	93
B. Patients with lymphoproliferative disorders and hypogammaglobulinemia with high comorbidity ≥6 and low immunoglobulin IgG level <4	79
Q6. How do you estimate kidney loss of Immunoglobulin in patients with HM and hypogammaglobulinemia?	
A. To assess urine protein loss, perform urine protein creatinine ratio and 24 hour urinary protein.	93
Q7. What are the barriers to check and initiate prophylactic immunoglobulin replacement therapy (IgRT) [IVIg/SCIg/fSCIg] for patients with HM and isolated low serum IgG level who do not have a history of recurrent or severe infection?	
A. Cost of therapy	80
B. Lack of enough scientific evidence	87
Q8. Which of the routes of administration [IVIg/SCIg/fSCIg] do you prefer to use for immunoglobulin replacement therapy (IgRT) in your patients with HM and hypogammaglobulinemia?	
A. In patients who are willing to self-infuse, fSCIg is preferred.	93
B. Depends on the availability of Immunoglobulin replacement therapy (IgRT)	87
Q9.[A] **Which factors affect choice of immunoglobin in your patients with HM and hypogammaglobulinemia?**	
A. The physician's judgment.	87
B. Patient's preferences.	100
C. Patient's previous experience with home-based treatment.	93
D. Patient's medical needs.	87
E. Individual needs.	100
F. Cost of formulations and insurance coverage.	100
Q9. [B] What are the switch criteria for IgRT in your patients with HM and hypogammaglobulinemia?	
A. Patient preference for less frequent injections due to a busy schedule.	100
B. Patients who want to bear the responsibility of their own health.	87
C. Optimum Ig serum concentrations are not reached with other formulations.	73
D. Shortage of certain Ig formulations.	100
Q10. Do you monitor or recommend IgG levels during immunoglobulin replacement therapy (IgRT) [IVIg/SCIg/fSCIg], and if so, how often in your patients with HM and hypogammaglobulinemia?	
A. Monitoring should be performed every three months initially, then every six months, and then if the levels	87

(Continued)

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TABLE 2 Continued

Consensus Statement	Consensus Percentage
remain stable, monitoring is recommended annually. B. More frequent monitoring (monthly) is especially useful in patients with recurrent/persistent infections or with delayed improvement or complications.	93
Q11. What serum Ig trough level do you aim for immunoglobulin replacement therapy (IgRT) in your patients with HM and hypogammaglobulinemia?	
A. 6–15 g/L for SCIg/fSCIg	80
Q12. How do you determine the dose of Immunoglobulin replacement therapy (IgRT) [IVIg/SCIg/fSCIg] in your patients with HM and hypogammaglobulinemia?	
A. Dose based on the actual weight B. 0.4 g/kg body weight every four weeks as initiation therapy C. Starting dose of IgRT (IVIG dose of 0.4 g/kg body weight, SCIg/fSCIg dose of 0.2 -0.4g/kg) given once, followed by maintenance dose D. Maintenance dosing of IgRT (IVIG-0.4-0.8 g/kg Every 3–4 weeks, SCIg -0.2 -0.4 g/kg weekly/bi-weekly, fSCIg - No specific maintenance dose follows a standard dose of 0.2-0.4 g/kg every 3-4 weeks) E. Follow a tailored approach to maintenance dosing of IgRT. F. To determine maintenance dosing, after a period of approximately 5–6 administrations of the new IgG product, trough levels and treatment intervals should be measured.	80 87 73 73 73 87
Q13. When do you stop immunoglobulin replacement therapy (IgRT) [IVIg/SCIg/fSCIg] in your patients with HM and hypogammaglobulinemia?	
A. After 12 months with close monitoring. B. If a patient fails two trials of IgRT withdrawal (e.g., a two-year interval), no further trials of treatment should be undertaken unless there is clear evidence of immune reconstitution.	70 73
Q14. How frequently do you monitor immunoglobulin replacement therapy (IgRT) [IVIg/SCIg/fSCIg] in your patients with HM and hypogammaglobulinemia?	
A. Unscheduled monitoring of IgG levels for patients with breakthrough infections. B. Following IgRT discontinuation, infection rates, and IgG levels every three to six months (or reflecting local clinical practice, e.g., timing of regular visits, including assessment of B-cell counts every six months for patients with NHL).	93 86

infections, and monitoring of therapy through IgG trough levels is advisable: initially, every three months, followed by subsequent monitoring every six or more months if IgG trough levels have reached the preferable level. One possible approach is to check IgG levels monthly during treatment and every 3 to 6 months or annually. However, this approach is not recommended by the experts (Table 3).

Early diagnosis and management of SID in high-risk HM patients are essential to minimize the risk of infectious complications and improve patient outcomes. These recommendations are in line with international guidelines.

TABLE 3 Middle East recommendations for the management of SID that did not reach consensus (percentage agreement).

Consensus Statement	Consensus Percentage
Q1. How do you evaluate early and diagnose hypogammaglobulinemia/secondary immunodeficiency (SID) in your patients with hematological malignancies such as Lymphoproliferative diseases, B cell malignancies, bone marrow transplant and those receiving immunotherapy such as monoclonal antibodies, antibody drug conjugates, Bi-specific antibody, and CAR T cell therapy?	
A. Evaluation of response to vaccines (with recommended vaccines) is a useful tool to help guide diagnosis of SAD and should be used where available to assess functional antibody status.	60
Q2. When would you typically check or recommend IgG levels in a patient with hematological malignancies?	
A. During treatment every month and then subsequently every 3 to 6 months B. Annually	47 53
Q3. Do you routinely check/recommend uninvolved immunoglobulin subtypes in your patients with myeloma to look for hypogammaglobulinemia/secondary immunodeficiency (SID)?	
A. Checking IgG and uninvolved immunoglobulin subtypes every 3 to 6 months along with IgG depending on the underlying risk factors and history of the patient B. Rarely indicated	67 20
Q4. What treatments do you use or recommend for primary prophylaxis in secondary hypogammaglobulinemia/secondary immunodeficiency (SID) in patients with HMs?	
A. Immunoglobulin replacement therapy	29
Q5.[A]. In which patients with hematological malignancies and low immunoglobulin do you routinely use or recommend immunoglobulin replacement therapy?	
A. Patients whose IgG levels are <4 g/L with no history of infection B. All patients with IgG <2.5g/L, regardless of history of infections	21 43
Q6. How do you estimate kidney loss of Immunoglobulin in patients with HM and hypogammaglobulinemia?	
A. Serum and urine protein electrophoresis. B. If the liver function test indicates albumin and globulin are low, it is suggestive of protein loss.	60 60
Q7. What are the barriers to check and initiate prophylactic immunoglobulin replacement therapy (IgRT) [IVIg/SCIg/fSCIg] for patients with HM and isolated low serum IgG level who do not have a history of recurrent or severe infection?	
A. The availability of Immunoglobulin replacement therapy	47
Q8. Which of the routes of administration [IVIg/SCIg/fSCIg] do you prefer to use for immunoglobulin replacement therapy (IgRT) in your patients with HM and hypogammaglobulinemia?	
A. IVIg in majority of patients	47

(Continued)

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TABLE 3 Continued

Consensus Statement	Consensus Percentage
Q10. Do you monitor or recommend IgG levels during immunoglobulin replacement therapy (IgRT) [IVIg/SCIg/fSCIg], and if so, how often in your patients with HM and hypogammaglobulinemia?	
A. Every 2- 6 months	40
Q11. What serum Ig trough level do you aim for immunoglobulin replacement therapy (IgRT) in your patients with HM and hypogammaglobulinemia?	
A. More than 5 g/L. for IVIg B. More than 6 g/L for IVIg C. Higher than 15 g/L for SCIg/fSCIg	53 40 0
Q12. How do you determine the dose of Immunoglobulin replacement therapy (IgRT) [IVIg/SCIg/fSCIg] in your patients with HM and hypogammaglobulinemia?	
A. Individualising the starting dosage of IgRT based on measured serum IgG levels and the clinical response is a more appropriate method of dosing.	33
Q13. When do you stop immunoglobulin replacement therapy (IgRT) [IVIg/SCIg/fSCIg] in your patients with HM and hypogammaglobulinemia?	
A. In patients with no infections for ≥ 6 months.	67
Q14. How frequently do you monitor immunoglobulin replacement therapy (IgRT) [IVIg/SCIg/fSCIg] in your patients with HM and hypogammaglobulinemia?	
A. More regular monitoring (every 4–6 weeks) for patients with infection and during periods of increased risk (e.g., initiation of new therapies and winter months) is recommended.	64

Additionally, several methods were listed in the questionnaire to estimate kidney loss of immunoglobulin in patients with HM and hypogammaglobulinemia. To rule out organic causes of immunoglobulin loss, experts recommend evaluating urine protein loss, urine creatinine ratio, and 24-hour urine protein. Serum and urine protein electrophoresis can also be performed, detecting a loss of up to 60% of immunoglobulin. Liver function tests indicating low albumin and globulin levels are not recommended as suggestive of protein loss.

3.4 Initiating, dosing, and discontinuation of IgRT

Insufficient data are available on the occurrence of SID with new treatments. IgRT is recommended in patients with hematological malignancies and low immunoglobulin levels who have recurrent infections despite appropriate anti-infective treatment or who have had a single severe infection or recurrent or persistent infections. In addition, experts have reached a consensus that IgRT is also recommended as primary prophylaxis in specific subgroups of patients, including those with hypogammaglobulinemia receiving CAR (chimeric antigen receptor) T-cell therapy and those with lymphoproliferative disorders and hypogammaglobulinemia with comorbidities and IgG<4 g/l. However, there is no consensus on using IgRT in other HM patients whose IgG levels are <4 g/L or even <2.5 g/L with no history of infection (19).

The expert recommendation suggests a serum Ig trough level of 6-15 g/L when administering IgRT to patients with hematological malignancies and hypogammaglobulinemia via subcutaneous immunoglobulin (SCIg)/facilitated subcutaneous immunoglobulin (fSCIg).

In patients with hematological malignancies and isolated low serum IgG levels without a history of recurrent or severe infections, barriers to initiating prophylactic IgRT include cost and lack of adequate scientific evidence. The cost of IgRT is documented to be substantial and adds to the burden on healthcare systems (e.g., 100-150,000 USD per year in the United States) (20). Although IgRT tends to decrease respiratory infections and hospitalizations, it is not universally effective across all treatment groups or disease stages. Expert recommendations emphasize the need for more robust randomized controlled trials to evaluate the efficacy and safety of IgRT in this patient population. Moreover, the availability of IgRT is considered a minor barrier. Nevertheless, the use of IgRT presents considerable obstacles, such as an annual 6-8% rise in worldwide demand and an uneven distribution of global supply (21). The experts acknowledge that the limited availability of IgRT during the COVID pandemic was a challenge in the Middle East, but not now.

According to expert recommendations, the preferred route of administration for IgRT in patients with hematological malignancies and hypogammaglobulinemia depends on certain factors. For example, if patients are willing to self-infuse, then SCIG or fSCIg is the preferred route of administration. The availability of IgRT is also a determining factor. In summary, the choice of immunoglobulins is based on the physician's judgment, the patient's preference, the patient's previous experience with home-based treatment, the patient's medical needs, the specific individual needs of the patients, and the cost of the formulations and availability of insurance coverage.

Furthermore, there is a need to change the definition of the dosing and discontinuation of IgRT (3). Expert recommendation for determining the dose of IgRT in patients with hematological malignancies and hypogammaglobulinemia includes initiating therapy with a dose of 0.4 g/kg body weight every 3-4 weeks, followed by maintenance dosing of 0.4-0.8 g/kg every 3-4 weeks for intravenous IgG (IVIG) and 0.2-0.4 g/kg weekly/bi-weekly for SCIg, while fSCIg does not follow a specific maintenance dose but a standard dose of 0.2-0.4 g/kg every 3-4 weeks. Alternatively, a tailored approach can be used to determine maintenance dosing based on trough levels and treatment intervals measured after approximately 5-6 administrations of the new IgG product. Breakthrough infections could also be another important reason for tailored IgRT doses and infusion intervals (e.g., increased doses and/or more frequent infusions). Dosing based on actual weight is recommended, while individualizing the starting dosage based on measured serum IgG levels and clinical response is not recommended.

Expert recommendation for the switch criteria for IgRT in patients with HMs and hypogammaglobulinemia consists of factors such as the patient's preference for the frequency and number of

infusions, their willingness to take charge of their health, the failure to achieve adequate IgG levels with other forms of treatment, and the unavailability of specific immunoglobulin formulations.

In the case of IgRT discontinuation, it is essential to monitor infection rates and IgG levels every three to six months. This can be based on local clinical practice and may include an assessment of B-cell counts every six months for patients with B-lymphoproliferative neoplasms to monitor B-cell reconstitution. However, per EMA recommendations, more regular IgG monitoring must be followed in the Middle East every 4-6 weeks for patients with infection and during periods of increased risk, such as initiation of new therapies and winter months.

Expert recommendations suggest that patients with hematological malignancies and hypogammaglobulinemia should be carefully monitored for when to stop IgRT using IVIg, SCIg, or fSCIg. Experts did not agree on IgRT discontinuation after 12 months of close monitoring or in patients who have not had any infections for at least six months. Experts agreed that if a patient fails two trials of IgRT withdrawal (e.g., a two-year interval), no further trials of treatment should be undertaken unless there is clear evidence of immune reconstitution. This approach is intended to avoid potential relapse or worsening of the condition and ensure that patients receive optimal long-term care.

4 Conclusion

This is the first consensus on guidance for managing SID in the Middle East. Adapting the global recommendations for the Middle East region can optimize the SID management approach and improve the overall standard of healthcare provided to these patients across the region.

Author contributions

MD: Conceptualization, Data curation, Formal analysis, Methodology, Supervision, Writing – original draft, Writing – review & editing. MAb: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. MAA: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. KA: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. AAlh: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. FA: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. AAls: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. MAl: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. AB: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. HC: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. RE: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. CI: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. FK: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. IN: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. HO: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. MS: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing.

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Conflict of interest

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Publisher's note

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