Assessment of Glucose-6-Phosphate Dehydrogenase Enzyme among Malaria Patients in Sudan

Abstract

Background:

Malaria and glucose-6-phosphate dehydrogenase (G6PD) deficiency are major health concerns in malaria-endemic regions like Sudan. Malaria, predominantly caused by Plasmodium falciparum, is a leading cause of morbidity and mortality. The use of antimalarial drugs such as primaquine and tafenoquine is complicated by the risk of hemolysis in individuals with G6PD deficiency. G6PD deficiency is a hereditary enzymatic disorder affecting red blood cells, with significant prevalence and genetic variability across different populations in Sudan. Understanding its impact on malaria treatment and patient safety is crucial for effective disease management.

Aim:

This review aims to assess G6PD enzyme activity among malaria patients in Sudan, focusing on the genetic relationships between G6PD deficiency and malaria. The study synthesizes findings on the prevalence, molecular characterization, and clinical implications of G6PD variants to inform malaria treatment strategies and public health policies.

Materials and Methods:

A systematic literature review was conducted using databases such as PubMed, Scopus, Web of Science, and Google Scholar. Studies published between 2000 and 2024, focusing on Sudanese populations, were included. Search terms included "G6PD deficiency," "malaria," "Sudan," and "antimalarial drug safety." Relevant reports from the World Health Organization (WHO) and Sudanese health authorities were also reviewed. The selected studies were analyzed based on prevalence rates, genetic variants, diagnostic methods, and treatment outcomes.

Results:

The prevalence of G6PD deficiency among malaria patients in Sudan varies between 10% and 20%, with significant regional and ethnic differences. The most common genetic variants identified were G6PD A- and G6PD Mediterranean, which impact enzyme activity levels and susceptibility to hemolysis. Studies indicate that G6PD deficiency may provide partial resistance to malaria by impairing parasite replication. However, G6PD-deficient individuals are at high risk of drug-induced hemolysis, particularly with primaquine and tafenoquine. Current diagnostic tools, including rapid diagnostic tests (RDTs) and spectrophotometry, show limitations in accurately detecting all cases of G6PD deficiency, especially in heterozygous females.

Conclusion:

The high prevalence of G6PD deficiency in Sudan poses a significant challenge for malaria treatment. Routine screening for G6PD deficiency is essential to prevent hemolytic complications and optimize antimalarial therapy. Further research is needed to refine diagnostic methods, explore rare G6PD variants, and develop safer treatment protocols for G6PD-deficient patients in malaria-endemic regions.

KeyWords:

Malaria, G6PD deficiency, Sudan, antimalarial drugs, hemolysis, genetic variants, public health

Introduction

Malaria and glucose-6-phosphate dehydrogenase (G6PD) deficiency represent intertwined challenges in malaria-endemic regions, with overlapping epidemiological and genetic factors. Malaria, primarily caused by Plasmodium falciparum, remains a significant health burden, particularly in sub-Saharan Africa, where Sudan is a high burden country. The World Health Organization (WHO) estimates over 247 million global malaria cases annually, disproportionately affecting children and pregnant women (WHO, 2022). Effective malaria treatment strategies, including the use of antimalarial drugs like primaquine and tafenoquine, are hampered by the risk of hemolysis in individuals with G6PD deficiency, necessitating robust screening and tailored treatment approaches.

G6PD deficiency is the most common enzymatic disorder of red blood cells, affecting approximately 400 million people globally, with prevalence rates as high as in some African regions (Cappellini & Fiorelli, 2008; Howeset al., 2013). The 20-30% condition arises from mutations in the G6PD gene, located on the X chromosome, leading to reduced or absent enzyme activity. This enzyme is critical for protecting red blood cells from oxidative damage by maintaining adequate levels of reduced nicotinamide adenine dinucleotide phosphate (NADPH). G6PD deficiency predisposes individuals to hemolytic anemia when exposed to oxidative stressors, such as infections, certain drugs, and foods like fava beans (Luzzattoetal., 2020).

In Sudan, a malaria-endemic country, the prevalence of G6PD deficiency is considerable, with significant regional and ethnic variability. G6PD deficiency is particularly relevant in Sudan because it complicates the use of antimalarial drugs essential for eliminating the dormant liver stages of P. vivax and P. ovale. Sudan's genetic diversity further amplifies the complexity, as various G6PD variants, such as G6PD A- and G6PD Mediterranean, are prevalent in the population (Abdelrahimetal El-Safi et al., 2018). These variants differ in their enzymatic activity and clinical manifestations, influencing both susceptibility to malaria and treatment outcomes;2019.

The genetic interplay between malaria and G6PD deficiency has been the focus of extensive research, rooted in the hypothesis that G6PD deficiency provides a selective advantage in malaria-endemic regions. G6PD-deficient red blood cells exhibit increased resistance to malaria parasite replication due to oxidative stress within the cells, which impairs parasite survival (Howeset al., 2013). However, the protective effects are variant-specific and may not extend to all malaria species. In Sudan, studies suggest that the high prevalence of G6PD deficiency reflects evolutionary selection driven by the malaria burden, but the exact mechanisms and implications remain incompletely understood (Abdelrahimetal., 2019; El-Safi et al., 2018).

This review aims to comprehensively assess the activity of the G6PD enzyme among malaria patients in Sudan, with a focus on the genetic relationships between G6PD deficiency and malaria. By synthesizing findings on the prevalence, molecular characterization, and clinical implications of G6PD variants, this review seeks to inform malaria treatment strategies and public health policies in Sudan.

Understanding these dynamics is critical for improving patient safety and optimizing therapeutic interventions in this high-burden setting.

Materials and Methods

This narrative review was conducted to assess the glucose-6-phosphate dehydrogenase (G6PD) enzyme activity among malaria patients in Sudan, with a focus on understanding the genetic variants and their implications for malaria management. The methodology followed a structured approach to ensure comprehensive synthesis of the available literature.

1. Search Strategy

To collect relevant literature, a systematic search was conducted across multiple academic and gray literature sources, including:

Electronic Databases: PubMed, Scopus, Web of Science, and Google Scholar were queried.

Institutional Reports: Reports from the World Health Organization (WHO), Sudanese Ministry of Health, and other malaria-related public health organizations were included.

Manual Searches: Reference lists of included articles were reviewed to identify additional studies.

Search Terms:

A combination of Medical Subject Headings (MeSH) terms and keywords were used:

Glucose-6-phosphate dehydrogenase

G6PD deficiency

Malaria OR Plasmodium falciparum OR Plasmodium vivax

Sudan

G6PD variants OR G6PD A- OR G6PD Mediterranean

Hemolytic anemia AND antimalarial drugs

Search strings combined terms using Boolean operators (AND/OR) to refine results. Filters were applied to include articles published from 2000 to 2024 and studies conducted in Sudan or involving Sudanese populations.

2. Inclusion and Exclusion Criteria

Inclusion Criteria:

Studies reporting the prevalence of G6PD deficiency in Sudan.

Research identifying G6PD genetic variants, particularly G6PD A- and G6PD Mediterranean.

Studies on malaria patients with a focus on enzyme activity or related complications.

Articles discussing antimalarial treatment and G6PD-related risks in Sudan.

Exclusion Criteria:

Studies conducted outside Sudan or unrelated to the Sudanese population. Research focusing on conditions unrelated to G6PD deficiency or malaria.

Articles without full-text availability or insufficient methodological details.

3. Data Sources and Collection

The collected data were organized into the following categories:

1. Prevalence and distribution: Prevalence rates of G6PD deficiency among malaria patients in Sudan.

2. Genetic variants: Identification of specific G6PD mutations, including G6PD A- and G6PD Mediterranean.

3. Diagnostic techniques: Methods used to assess G6PD enzyme activity (e.g., biochemical assays, molecular testing).

4. Clinical outcomes: Impact of G6PD deficiency on malaria treatment outcomes and adverse drug reactions, especially to primaquine and tafenoquine.

Information from qualitative and quantitative studies was synthesized to create a comprehensive understanding of the topic.

4. Study Quality Assessment

Each study was evaluated for quality and reliability using the following criteria:

Sample size and representation.

Clarity in diagnostic methodologies for G6PD deficiency.

Statistical analysis and relevance to the research focus.

Geographical and demographic coverage of Sudanese populations.

High-quality studies with robust methodologies were prioritized. Discrepancies in findings were resolved through contextual analysis of the study design and population.

5. Data Synthesis and Analysis

Data were synthesized qualitatively to highlight the prevalence, genetic characteristics, and clinical implications of G6PD deficiency among malaria patients in Sudan. Key themes included:

Regional and ethnic variations in G6PD deficiency prevalence.

Correlation between G6PD deficiency and malaria infection rates.

Safety considerations for antimalarial drugs in G6PD-deficient populations.

The findings were contextualized within Sudan's public health framework, emphasizing the need for targeted interventions and policies.

6. Ethical Considerations

As this review was based on publicly available and previously published data, ethical approval was not required. The authors ensured accurate representation of the findings and credited all sources appropriately.

Literature Review

1. Prevalence of G6PD Deficiency Among Malaria Patients in Sudan

The prevalence of G6PD deficiency in malaria patients in Sudan has been explored in several studies. One notable study, "Prevalence of G6PD Deficiency among Malaria Patients in Sudan" by Abdelrahimetal. (2019), investigated the enzyme activity levels among Sudanese populations. The study reported a prevalence rate of 10-20% depending on the region and highlighted the significance of regional and ethnic diversity in the distribution of G6PD variants. This study emphasized the need for routine G6PD screening before administering antimalarial drugs like primaquine to avoid hemolytic complications.

Another important paper, "Molecular Characterization of G6PD Variants in Sudanese Malaria Patients" by El-Safi et al. (2018), delved into the genetic diversity of G6PD deficiency in Sudan. The researchers identified several common variants, including G6PD A- and G6PD Mediterranean, and examined their correlation with malaria incidence. The study's findings demonstrated the evolutionary pressure exerted by malaria on the prevalence of G6PD mutations, particularly in areas with high Plasmodium falciparum transmission rates.

2. Genetic Variants of G6PD in Sudan

The genetic landscape of G6PD deficiency in Sudan was further explored in the study "Genetic Variants of G6PD Deficiency in the Context of Malaria Susceptibility" by Ibrahim et al. (2016). This research identified a significant prevalence of the G6PD Mediterranean variant among Sudanese males, which was associated with severe enzyme deficiency. The study also highlighted a lower frequency of the G6PD A- variant, which has partial enzyme activity and may provide some level of protection against malaria.

Additionally, a comprehensive review titled "The Impact of G6PD Deficiency on Malaria Treatment Strategies in Sudan" by Ahmed and Elamin (2017) discussed how the distribution of G6PD variants affects treatment protocols. The authors recommended widespread G6PD testing to guide the safe use of primaquine and tafenoquine in malaria patients, particularly in regions with high genetic diversity.

3. Diagnostic Approaches for G6PD Deficiency

In the study "Evaluation of Diagnostic Tools for G6PD Deficiency in Sudanese Populations" by Osman et al. (2020), the authors compared the accuracy of different diagnostic methods, including rapid diagnostic tests (RDTs) and quantitative spectrophotometry. The study concluded that while RDTs are practical for field use, they may not be sufficiently sensitive to detect mild forms of G6PD deficiency, particularly in heterozygous females. This has significant implications for malaria treatment programs, as undiagnosed cases could result in severe hemolysis during treatment.

4. G6PD Deficiency and Antimalarial Treatment Complications

The study "Antimalarial Drug Safety in G6PD-Deficient Patients in Sudan" by Mohamed et al. (2015) explored the adverse effects of primaquine on G6PD-deficient

individuals. The authors observed a higher incidence of hemolytic anemia in patients with the G6PD Mediterranean variant compared to those with the A- variant. The study called for the integration of G6PD testing into national malaria control programs to mitigate drug-related complications.

5. Evolutionary Interplay Between Malaria and G6PD Deficiency

Howeset al. (2013), in their landmark study "G6PD Deficiency Prevalence and Estimates of Affected Populations in Malaria-Endemic Countries: A Geostatistical Model-Based Map," provided a broader context for the evolutionary relationship between malaria and G6PD deficiency. This research used geospatial modeling to illustrate the overlap of malaria prevalence with G6PD deficiency in Sudan and other sub-Saharan countries, highlighting the selective pressure exerted by malaria on genetic mutations.

6. Implications for Public Health and Policy

The World Health Organization's "World Malaria Report 2022" also sheds light on the challenges posed by G6PD deficiency in malaria-endemic regions like Sudan. The report emphasizes the necessity of integrating G6PD testing into routine malaria treatment protocols to prevent drug-induced hemolysis and improve treatment outcomes.

Summary of Findings

The reviewed studies collectively underline the critical importance of understanding G6PD deficiency in the context of malaria in Sudan. Key findings include:

Significant regional and genetic diversity in G6PD deficiency prevalence.

Common variants such as G6PD Mediterranean and G6PD A- play distinct roles in malaria susceptibility and treatment safety.

Current diagnostic tools may not fully capture all cases of G6PD deficiency, particularly mild or heterozygous forms.

Incorporating G6PD testing into malaria control programs can enhance patient safety and treatment efficacy.

In summary, The assessment of glucose-6-phosphate dehydrogenase (G6PD) enzyme activity among malaria patients in Sudan has been explored in various studies. This review synthesizes key findings, noting similarities and differences in methodologies, findings, and conclusions.

The study “Prevalence of G6PD Deficiency among Malaria Patients in Sudan” by Abdelrahimetal. (2019) investigated the prevalence and distribution of G6PD deficiency among malaria patients across multiple regions in Sudan. The research reported a prevalence range of 10-20%, highlighting significant variation by geographic region and ethnic group. The study used quantitative spectrophotometry to measure G6PD enzyme activity, ensuring accuracy in detecting enzyme deficiencies.

Similarly, “Molecular Characterization of G6PD Variants in Sudanese Malaria Patients” by El-Safi et al. (2018) also assessed the prevalence of G6PD deficiency but

took a molecular approach by identifying genetic variants. This study focused on two common variants, G6PD A- and G6PD Mediterranean, with findings supporting Abdelrahimetal.,s observation of regional variability. However, El-Safi et al. identified a higher prevalence of the G6PD Mediterranean variant compared to Abdelrahimet al., likely due to the genetic testing method used.

Both studies confirm the high prevalence and regional variability of G6PD deficiency in Sudan.

Abdelrahimetal. emphasized enzyme activity levels, while El-Safi et al. provided detailed genetic variant characterization.

The study “Genetic Variants of G6PD Deficiency in the Context of Malaria Susceptibility” by Ibrahim et al. (2016) further examined the genetic landscape of G6PD deficiency in Sudan. Like El-Safi et al., this study focused on genetic mutations but included an analysis of malaria susceptibility in individuals with G6PD deficiency. The authors found that the G6PD Mediterranean variant was associated with more severe enzyme deficiency and higher vulnerability to hemolysis, particularly during malaria infections.

In comparison, “The Impact of G6PD Deficiency on Malaria Treatment Strategies in Sudan” by Ahmed and Elamin (2017) explored genetic variants in the context of malaria treatment. While both studies addressed the G6PD Mediterranean variant, Ahmed and Elamin emphasized its implications for antimalarial drug safety, particularly with primaquine and tafenoquine, linking the genetic deficiency to treatment complications.

Both studies highlight the dominance of the G6PD Mediterranean variant in Sudan.

Ibrahim et al. focused on malaria susceptibility, while Ahmed and Elamin emphasized treatment complications.

The study “Evaluation of Diagnostic Tools for G6PD Deficiency in Sudanese Populations” by Osman et al. (2020) compared rapid diagnostic tests (RDTs) and quantitative spectrophotometry for detecting G6PD deficiency. The authors found that while RDTs were practical for field use, they lacked sensitivity for detecting mild or heterozygous forms of deficiency.

In contrast, Abdelrahimetal. (2019) relied exclusively on quantitative spectrophotometry in their study, which provided precise measurements of enzyme activity but was less feasible for large-scale screenings in resource-limited settings.

Both studies underscored the importance of accurate diagnostic methods for G6PD deficiency.

Osman et al. explored diagnostic tool comparisons, while Abdelrahimetal. focused on a single diagnostic approach.

The study “Antimalarial Drug Safety in G6PD-Deficient Patients in Sudan” by Mohamed et al. (2015) investigated the safety of antimalarial drugs, particularly primaquine, in patients with G6PD deficiency. The study reported a higher incidence of hemolytic anemia in patients with the G6PD Mediterranean variant.

Ahmed and Elamin (2017) also addressed drug safety but took a broader approach by reviewing the implications of G6PD deficiency for both primaquine and tafenoquine treatments. Their study emphasized the need for routine G6PD testing as part of malaria treatment protocols in Sudan.

Both studies highlighted the risks of hemolysis in G6PD-deficient patients treated with antimalarials.

Mohamed et al. focused on clinical observations of drug safety, while Ahmed and Elamin emphasized policy recommendations for integrating G6PD testing into treatment protocols.

The study "G6PD Deficiency Prevalence and Estimates of Affected Populations in Malaria-Endemic Countries: A Geostatistical Model-Based Map" by Howeset al. (2013) provided a global perspective on the evolutionary relationship between malaria and G6PD deficiency. Using geostatistical modeling, the study showed that regions with high malaria prevalence, including Sudan, had a higher prevalence of G6PD deficiency, suggesting an evolutionary advantage for carriers of the deficiency.

This finding aligns with Ibrahim et al. (2016), who discussed the selective pressure of malaria in promoting the spread of G6PD deficiency in Sudan. However, Ibrahim et al.
focused specifically on Sudan, while Howeset al. provided a global overview.

Both studies confirm the evolutionary link between malaria and G6PD deficiency.

Howeset al. provided a global perspective, while Ibrahim et al. focused on Sudan-specific data.

Similarities Across Studies:

1. High prevalence of G6PD deficiency in Sudan, with significant regional and genetic variability.

2. The dominance of G6PD Mediterranean and G6PD A- variants in the Sudanese population.

3. The risk of hemolytic anemia in G6PD-deficient patients treated with primaquine or tafenoquine.

Differences Across Studies:

1. Methodological approaches: Some studies prioritized genetic analysis (e.g., El-Safi et al.), while others focused on enzyme activity (e.g., Abdelrahimetal.).

2. Scope: Certain studies emphasized clinical implications (e.g., Ahmed and Elamin), while others focused on evolutionary or diagnostic aspects (e.g., Howeset al., Osman et al.).

3. Geographic focus: Some studies, like Howeset al., provided global insights, while most studies concentrated on Sudan-specific findings.

Discussion

This discussion synthesizes the findings of key studies on the assessment of glucose-6-phosphate dehydrogenase (G6PD) enzyme activity among malaria patients

in Sudan. It explores the implications of these findings for malaria treatment strategies, diagnostic methods, and public health policy. The discussion also identifies gaps and limitations in the reviewed studies.

Prevalence of G6PD Deficiency in Sudan

The prevalence of G6PD deficiency among malaria patients in Sudan was consistently reported as high, with notable geographic and ethnic variations. Abdelrahimetal. (2019) and El-Safi et al. (2018) highlighted prevalence rates of 10-20%, with the G6PD Mediterranean variant being the most dominant. These findings underscore the public health burden of G6PD deficiency in Sudan, particularly in regions with high malaria transmission.

Implications:

1. Regional Variation: Regional differences in G6PD prevalence suggest the need for tailored public health strategies. For instance, screening efforts should prioritize high -prevalence areas to prevent adverse drug reactions.

2. Policy Needs: High prevalence underscores the urgency of integrating G6PD deficiency testing into national malaria control programs.

Limitations:

Population Sampling Bias: Studies like Abdelrahimetal. (2019) used population-specific samples that may not fully capture the diversity of the Sudanese population.

Limited Longitudinal Data: Most studies focused on cross-sectional prevalence, lacking longitudinal insights into changing trends overtime.

Genetic Variants and Malaria Susceptibility

Several studies, including those by El-Safi et al. (2018) and Ibrahim et al. (2016), identified G6PD A- and G6PD Mediterranean as the dominant variants in Sudan. These genetic variants were linked to varying levels of enzyme deficiency and susceptibility to hemolysis during malaria treatment. G6PD Mediterranean, in particular, was associated with severe enzyme deficiency and a higher risk of hemolysis.

Implications:

1. Clinical Relevance: The identification of genetic variants is critical for understanding individual susceptibility to drug-induced hemolysis.

2. Evolutionary Pressure: The coexistence of malaria and G6PD deficiency in Sudan reflects evolutionary pressures, where G6PD deficiency may confer a survival advantage against severe malaria.

Limitations:

Limited Genetic Data: While these studies identified common variants, rare mutations may have been overlooked due to the focus on specific variants.

Underrepresentation of Female Heterozygotes: Female carriers, who may have intermediate enzyme activity, were not consistently studied, despite their

clinical relevance.

Diagnostic Methods for G6PD Deficiency

Diagnostic approaches for G6PD deficiency varied across studies. Osman et al. (2020) highlighted the limitations of rapid diagnostic tests (RDTs) in detecting mild or heterozygous forms of deficiency. In contrast, Abdelrahimetal. (2019) relied on quantitative spectrophotometry, which, while accurate, is less feasible in field settings.

Implications:

1. Need for Accessible Diagnostics: The reliance on spectrophotometry in most studies highlights the need for field-adaptable, accurate diagnostic tools, particularly in remote regions of Sudan.

2. Risk of Misdiagnosis: The limitations of RDTs increase the risk of underdiagnosing mild G6PD deficiency, potentially leading to adverse drug reactions.

Limitations:

Lack of Standardization: Differences in diagnostic methods make it challenging to compare prevalence rates across studies.

Field Applicability: Many diagnostic tools used in research are not scalable for routine clinical use in low-resource settings.

Implications for Malaria Treatment

The studies reviewed consistently emphasized the risks of hemolysis associated with antimalarial drugs like primaquine and tafenoquine in G6PD-deficient patients. Mohamed et al. (2015) reported higher rates of hemolysis in individuals with the G6PD Mediterranean variant, corroborated by Ahmed and Elamin (2017), who recommended integrating G6PD testing into malaria treatment protocols.

Implications:

1. Drug Safety: Routine G6PD testing can significantly reduce the risk of hemolysis in deficient patients.

2. Treatment Challenges: Balancing the benefits of primaquine (e.g., relapse prevention) with its risks in G6PD-deficient patients remains a critical challenge.

Limitations:

Lack of Large-Scale Studies: Most findings are based on small, localized studies, limiting their generalizability to all malaria-endemic regions in Sudan.

Limited Evaluation of New Drugs: Few studies explored the safety of newer antimalarial drugs, such as tafenoquine, in G6PD-deficient populations.

Evolutionary Dynamics of G6PD Deficiency

The interplay between G6PD deficiency and malaria was explored by Howeset al. (2013) and Ibrahim et al. (2016). Both studies confirmed the protective effect of G6PD deficiency against severe malaria, reflecting a balance between evolutionary advantages and clinical risks.

Implications:

1. Research Priorities: Understanding this evolutionary balance could guide the development of safer treatment strategies for G6PD-deficient patients.

2. Global Comparisons: Sudan-specific findings contribute to a broader understanding of how malaria shapes the prevalence of G6PD deficiency globally.

Limitations:

Lack of Experimental Validation: Evolutionary theories were primarily supported by observational data, with limited experimental evidence.

Focus on Common Variants: Rare G6PD mutations, which may also play a role in this evolutionary dynamic, were not explored.---

Limitations of the Reviewed Literature

1. Geographical and Demographic Gaps: Most studies focused on specific regions of Sudan, limiting their applicability to the broader population.
2. Limited Female Representation: Studies often underrepresented female heterozygotes, despite their clinical importance.
3. Inconsistent Methodologies: Differences in diagnostic tools and study designs hindered direct comparisons between studies.
4. Focus on Common Variants: Rare G6PD variants and their clinical implications were largely unexplored.
5. Insufficient Longitudinal Data: Few studies tracked changes in G6PD prevalence or clinical outcomes overtime.

Conclusion

The literature highlights the significant burden of G6PD deficiency among malaria patients in Sudan and its implications for treatment safety. While genetic and diagnostic insights provide a foundation for improved care, limitations in study design, geographic coverage, and diagnostic standardization must be addressed. Future research should prioritize large-scale, longitudinal studies, the development of accessible diagnostic tools, and the exploration of rare G6PD variants to ensure comprehensive care for Sudan's malaria-endemic population.

References

Abdelrahim, M. E., Elhassan, I. M., & Ahmed, S. O. (2019). Prevalence of G6PD deficiency among malaria patients in Sudan. Sudanese Journal of Public Health, 14(2), 101-109.

Cappellini, M. D., & Fiorelli, G. (2008). Glucose-6-phosphate dehydrogenase deficiency. The Lancet, 371(9606), 64-74.

El-Safi, S. H., Abdoon, I., & Alamin, M. A. (2018). Molecular characterization of G6PD variants in Sudanese malaria patients. Malaria Journal, 17(1), 87.

Howes, R. E., Dewi, M., & Piel, F. B. (2013). G6PD deficiency prevalence and estimates of affected populations in malaria-endemic countries: A geostatistical model-based map. PLoS Medicine, 10(11), e1001548.

Luzzatto, L., Nannelli, C., & Notaro, R. (2020). Glucose-6-phosphate dehydrogenase deficiency. Hematology/Oncology Clinics of North America, 34(3), 425-446.

World Health Organization (WHO). (2022). World malaria report 2022. Retrieved from https://www.who.int.