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Prevalence and Hematological Characteristics of G6PD Deficiency Among Children at a Tertiary Hospital in Madinah, Saudi Arabia: A Three-Year Retrospective Study

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Abstract **Background:** Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency is the most common enzyme disorder worldwide and an X-linked hereditary condition that can result in hemolytic anemia, particularly in response to oxidative stress. While G6PD deficiency is prevalent in the Middle East, regional and gender-specific pediatric data remain limited. This study aimed to assess the prevalence and hematological profile of G6PD deficiency among children in Madinah, Saudi Arabia. **Methods:** A retrospective cross-sectional study was conducted among 3,623 children aged 10 years and below who visited the Maternity and Children Hospital in Madinah between January 2020 and January 2023. G6PD status was assessed using a qualitative fluorescent spot test. Hematological parameters including RBC count, Hemoglobin (Hb), Hematocrit (Hct), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC) and red blood cell distribution width (RDW) were recorded. Statistical analysis was performed using SPSS v26; group comparisons were conducted using independent sample t-tests, with significance set at $p \leq 0.05$. **Results:** The overall prevalence of G6PD deficiency was 9.88% (n = 358), with a significantly higher prevalence in males (7.48%) than females (2.40%) ($p<0.001$). G6PD-deficient children showed reduced Hb (11.39±2.55 g/dL), Hct (38.46±6.22%) and MCH (28.17±1.67 pg), while other red cell indices remained within reference ranges. Hematological parameters were significantly higher in deficient females compared to males ($p<0.05$). **Conclusion:** G6PD deficiency is relatively common among children in Madinah and disproportionately affects males. Given its role in neonatal jaundice and hemolytic crises, early detection is critical. The findings support implementing region-wide newborn screening and premarital counseling programs as part of Saudi Arabia's public health strategy.

Key Words G6PD deficiency, Prevalence, Children, Saudi Arabia, Hematology, Screening

INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most prevalent enzymatic disorder in humans, affecting over 400 million people globally [1]. The condition is particularly common in regions historically exposed to malaria, including Africa, the Middle East, Southern Europe, Southeast Asia and parts of the Pacific Islands [2]. Due to population migration, G6PD-deficient alleles are now also present in the Americas and Northern Europe.

G6PD deficiency is an X-linked hereditary disorder caused by mutations in the G6PD gene, resulting in varying levels of enzyme activity. G6PD plays a central role in the pentose phosphate pathway, which is essential for the production of nicotinamide adenine dinucleotide phosphate (NADPH) [3]. NADPH maintains glutathione (GSH) in its reduced form, protecting red blood cells (RBCs) from oxidative damage. In deficient individuals, reduced GSH levels lead to increased vulnerability to oxidative stress, hemoglobin denaturation and potential hemolysis. Severe cases may result in the formation of Heinz bodies-aggregates of denatured hemoglobin-and can lead to acute hemolytic crises.

While many individuals with G6PD deficiency remain asymptomatic, oxidative triggers such as certain drugs, infections or ingestion of fava beans can precipitate hemolysis. Clinically, this may manifest as anemia, jaundice or back pain. Laboratory findings typically include elevated indirect bilirubin, lactate dehydrogenase and reticulocyte

counts [4]. In neonates, G6PD deficiency is a significant cause of early-onset jaundice, typically appearing within the first four days of life [5].

In Saudi Arabia, the prevalence of G6PD deficiency varies significantly by region and sex. AlShomar *et al.* [6] reported a prevalence of 2.9% in the Al-Qassim region, while Hamali documented an 8.4% prevalence among males in Jazan [7]. Albagshi *et al.* [4] found a much higher overall prevalence of 25% in Eastern Saudi Arabia, with 19.1% in males and 5.9% in females. These disparities highlight the importance of localized epidemiological data.

Despite its known clinical significance and regional variation, there is a lack of recent prevalence data specific to pediatric populations in Madinah. Furthermore, few studies have explored the associated hematological parameters in G6PD-deficient children in this region. Addressing this gap is crucial for informing public health initiatives such as newborn screening and preventive education.

Therefore, this study aimed to determine the prevalence of G6PD deficiency and evaluate associated hematological profiles among children aged 10 years and below attending the Maternity and Children Hospital in Madinah, Saudi Arabia, from January 2020 to January 2023.

METHODS

Study Design and Population

This retrospective cross-sectional study included 3,623 children aged 10 years and below who visited the Maternity and Children Hospital in Madinah, Saudi Arabia, over a three-year period from January 2020 to January 2023. The study was approved by the Ethics Committee of King Salman bin Abdulaziz Medical City (Ref: IRB23-025).

Inclusion criteria

- Children aged ≤10 years
- Children with a documented family history of G6PD deficiency
- Children diagnosed with G6PD deficiency or G6PD deficiency presenting with acute hemolytic anemia

Exclusion criteria

- Children aged >10 years
- Children diagnosed with anemia of other causes (e.g., iron deficiency, thalassemia)

Data Collection

Demographic data (sex) and laboratory data were extracted from the hospital's electronic medical records. Laboratory parameters included:

- G6PD enzyme activity determined by the qualitative fluorescent spot test
- Complete blood count (CBC) parameters including:
  - Red blood cell count (RBC; $\times 10^6/\mu L$)
  - Hemoglobin (Hb; g/dL)
  - Hematocrit (Hct; %)
  - Mean corpuscular volume (MCV; fL)
  - Mean corpuscular hemoglobin (MCH; pg)
  - Mean corpuscular hemoglobin concentration (MCHC; g/dL)
  - Red blood cell distribution width (RDW; %)

All hematological tests were conducted using standardized protocols in a single hospital laboratory with calibrated equipment. Internal quality control measures were performed daily in accordance with hospital laboratory policy. Data entry was double-checked to minimize errors. Duplicates and incomplete records were excluded. The normal reference ranges for all laboratory values were based on age-specific standards adopted by the hospital's clinical laboratory.

Sampling Approach

Children included in this study were selected from the total pediatric population visiting the hospital during the study period. Although a random sampling technique was not employed, the large and consecutive nature of the sample aimed to ensure a representative cross-section of the pediatric population in Madinah. Age-stratified data, however, were not separately analyzed in this phase of the study, which is acknowledged as a limitation.

Statistical Analysis

Data were recorded in Microsoft Excel and analyzed using IBM SPSS Statistics version 26. Descriptive statistics included frequencies, percentages, means and standard deviations. The Shapiro-Wilk test was applied to assess the normality of distribution for continuous variables; a p-value>0.05 indicated a normal distribution. For comparative analysis, independent sample t-tests were used to evaluate differences in hematological parameters between G6PD-deficient males and females. Statistical significance was set at $p \leq 0.05$. Effect sizes and confidence intervals were not included in this phase but are recommended for future analyses to enhance interpretability of clinical significance.

RESULTS

This retrospective study analyzed 3,623 pediatric patients aged 10 years and below who visited the Maternity and Children Hospital in Madinah, Saudi Arabia, between January 2020 and January 2023. Among the total participants, a slightly higher proportion were male, comprising 54.3% (n = 1,968), while females accounted for 45.7% (n = 1,655). These demographic details are summarized in Table 1.

The overall prevalence of G6PD deficiency in the study population was 9.88% (n = 358). A significantly higher prevalence was observed among males, with 271 out of 1,968 (7.48%) testing positive for G6PD deficiency, compared to 87 out of 1,655 females (2.40%). The sex-based difference was statistically significant ($p<0.001$), which is consistent with the X-linked inheritance pattern of the disorder. The prevalence rates by gender and deficiency status are detailed in Table 2.

Table 1: Demographic Characteristics of Study Participants

Gender	Frequency	Percentage
Male	1,968	54.3%
Female	1,655	45.7%
Total	3,623	100%

Table 2: Prevalence of G6PD Deficiency by Gender

Gender	G6PD Deficient	G6PD Normal	Total	Prevalence (%)
Male	271	1,697	1,968 (54.3%)	7.48
Female	87	1,568	1,655 (45.7%)	2.40
Total	358	3,265	3,623 (100%)	9.88

Table 3: Hematological Parameters in G6PD-Deficient Children (n = 358)

Blood Parameter	Normal Range	Mean±SD
RBC (×10⁶/μL)	3.90-5.40	4.44±0.65
Hemoglobin (g/dL)	11.6-14.0	11.39±2.55
Hematocrit (%)	42-52	38.46±6.22
MCV (fL)	72.0-104.6	98.70±98.14
MCH (pg)	31-34	28.17±1.67
MCHC (g/dL)	31-36	33.75±2.19
RDW (%)	11.5-15.0	12.54±1.73

Table 4: Comparison of Hematological Parameters in G6PD-Deficient Males and Females

Blood Parameter	Gender	Mean±SD	p-value
RBC (×10⁶/μL)	Male	4.38±0.63	0.001
	Female	4.65±0.65	
Hemoglobin (g/dL)	Male	11.27±2.57	0.023
	Female	11.76±2.46	
Hematocrit (%)	Male	38.22±6.60	0.006
	Female	39.21±4.82	
MCV (fL)	Male	96.88±92.27	0.017
	Female	104.35±114.93	
MCH (pg)	Male	28.11±1.54	0.014
	Female	28.34±2.07	
MCHC (g/dL)	Male	33.67±2.20	0.050
	Female	34.00±2.16	
RDW (%)	Male	12.52±1.67	0.001
	Female	12.62±1.92	

Next, hematological profiles were examined for the 358 children with G6PD deficiency. As shown in Table 3, the mean hemoglobin (Hb) level was 11.39±2.55 g/dL and hematocrit (Hct) was 38.46±6.22%, both below the lower limit of normal. The Mean Corpuscular Hemoglobin (MCH) was 28.17±1.67 pg, also below the reference range, suggesting mild anemia or hypochromia. Other parameters such as RBC count, MCV, MCHC and RDW remained within normal reference ranges. These findings reflect mild but clinically relevant hematologic alterations among G6PD-deficient children.

To explore sex-based hematological differences among G6PD-deficient children, male and female subgroups were compared. As presented in Table 4, all hematological parameters were significantly higher in females. Female patients had higher mean values for RBC count (4.65 vs. 4.38 ×10⁶/μL), hemoglobin (11.76 vs. 11.27 g/dL), hematocrit (39.21 vs. 38.22%) and MCV (104.35 vs. 96.88 fL), with p-values<0.05 for all parameters. These differences may be attributable to biological variation, including lyonization (X-chromosome inactivation) in heterozygous females. Although fewer in number, female patients exhibited hematological indices that suggest stronger compensatory responses than their male counterparts.

In summary, the findings indicate that G6PD deficiency is significantly more prevalent in male children and while most hematological values remain within normal limits, Hb, Hct and MCH are consistently lower, suggesting mild anemia. Female patients, although less commonly affected, demonstrate higher hematologic indices, likely due to genetic mosaicism, highlighting the importance of gender-specific interpretation in G6PD screening and diagnosis.

DISCUSSION

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most prevalent enzymatic disorder in humans, affecting over 400 million individuals worldwide [1]. It plays a key role in protecting red blood cells from oxidative stress. In newborns, G6PD deficiency can cause neonatal jaundice and increase the risk of kernicterus. This underscores the need for early detection and screening in high-risk populations.

In the current study, we assessed the prevalence of G6PD deficiency among children under 10 years of age at the Maternity and Children Hospital in Madinah. We found an overall prevalence of 9.88%, with a significantly higher rate among males (7.48%) compared to females (2.40%), ($p<0.001$). This sex-based difference aligns with the X-linked inheritance pattern of G6PD deficiency. According to the Lyon hypothesis, heterozygous females may also exhibit symptoms due to random X-chromosome inactivation [1].

Our findings are in agreement with a study conducted by Albagshi *et al.* [4], which reported a prevalence of 18.8% in Eastern Saudi Arabia (26% in males, 9.9% in females). The lower prevalence observed in our study may be attributed to regional differences, sample size or genetic variation in Madinah. In contrast, AlShomar *et al.* [6] reported a lower prevalence of 2.9% in the Al-Qassim region, highlighting the wide geographic variation within Saudi Arabia. According to Hamali [7], the national prevalence among Saudi males is estimated to be around 8.4%, which is consistent with our male subset.

Despite the high national prevalence, Saudi Arabia lacks a universal newborn screening program for G6PD deficiency. This is concerning, especially considering the recommendation by the American Academy of Pediatrics to screen neonates with a family history of jaundice or poor phototherapy response [8]. Given the severity of potential complications, such as hemolytic anemia and kernicterus, routine screening could have a significant public health impact [10,11].

In addition to prevalence, our study evaluated hematological parameters among G6PD-deficient children. We found that hemoglobin (Hb), hematocrit (Hct) and Mean Corpuscular Hemoglobin (MCH) levels were below the reference range, suggesting mild anemia. These findings are consistent with previous studies by Gupte *et al.* [12] and Sagiv *et al.* [13], who also observed reduced red cell indices in G6PD-deficient populations. Notably, in our study, we excluded cases with other types of anemia, such as iron deficiency or thalassemia, to isolate the effects of G6PD deficiency more accurately.

Interestingly, female patients exhibited significantly higher hematologic values than males across all measured parameters, including RBC count, Hb, Hct, MCV, MCH, MCHC and RDW. This observation may be explained by X-chromosome lyonization, resulting in mosaic expression and partial compensation in heterozygous females [1,14]. Elevated MCV levels in G6PD-deficient children may also reflect folate deficiency or bone marrow compensation, as previously suggested by Gupte *et al.* [12].

While literature indicates that RDW tends to be lower in G6PD-deficient individuals-implying a more uniform RBC population-our findings showed RDW within the normal range, possibly due to the steady-state condition of the patients and absence of acute hemolysis.

Despite strong results, our study has limitations. It was conducted at a single center, which may limit generalizability. In addition, we did not analyze age-stratified or seasonal trends, nor did we perform genotypic analysis to identify specific G6PD variants. These limitations should be addressed in future multi-center studies to better understand the full clinical and genetic spectrum of G6PD deficiency in Saudi Arabia.

CONCLUSIONS

This study demonstrated a 9.88% prevalence of G6PD deficiency among children in Madinah, with males significantly more affected due to the X-linked nature of the condition. Hematological analysis revealed trends of mild anemia and all evaluated blood parameters were significantly higher in G6PD-deficient females than males, likely due to X-inactivation patterns.

These findings emphasize the need for G6PD screening in newborns, particularly in high-prevalence regions. We recommend that the Saudi Ministry of Health implement newborn screening programs, promote premarital testing and invest in public health education regarding triggers of hemolysis. Future research should incorporate genotype-phenotype analysis, include multiple centers and explore longitudinal outcomes to advance the understanding and management of G6PD deficiency in Saudi Arabia.

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Conflicts of Interest

The authors declare that there are no conflicts of interest related to the conduct, authorship or publication of this research.

Ethical Approval

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board (IRB) of King Salman bin Abdulaziz Medical City, Madinah, Saudi Arabia, under reference number IRB23-025. Due to the retrospective nature of the study and use of anonymized data, the requirement for informed consent was waived by the IRB. All patient data were fully de-identified prior to analysis to ensure confidentiality and privacy.

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