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# PREVALENCE OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY IN CHILDREN WITH SICKLE CELL DISEASE AT TISHREEN UNIVERSITY HOSPITAL IN LATTAKIA

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## ABSTRACT

**Background:** Sickle cell disease(SCD) continues to be a major global public health concern due to lifelong complications associated with SCD. The coincidence of SCD with G6PD deficiency is considered an important problem that worsen the final outcome of children regarding hemolysis. **Objectives**: The aim of current study was to investigate the prevalence of G6PD deficiency in children with sickle cell anemia, and alterations in laboratory investigations according to presence of deficiency. **Materials and Methods:** A Prevalence Descriptive Study (Cross Sectional) was conducted for the period one year (2021- 2022) at Tishreen University Hospital in Lattakia-Syria. The study included group of children with SCD who were screened for G6PD deficiency and laboratory tests were compared between two groups; group I consisted of 31 patients with presence of G6PD deficiency, whereas group II consisted of 221 children without deficiency. **Results:** The prevalence of G6PD deficiency was 12.3% which ranges in severity from moderate (54.9%) to severe (45.1%). In females, we observed only moderate form (9.5%), whereas deficiency of G6PD ranged from moderate (3.5%) to severe (12.2%) in males. There were no significant differences between the two groups regarding age and sex ($p>0.05$). There were significant differences between two groups regarding HGB and MCH (group I versus group II); ($7.17\pm0.7$ versus $9.11\pm0.5$, p:0.0001) and $24.8\pm1.7$ versus $28.7\pm1.4$, p:0.002) respectively and differences regarding HGB and MCH were observed significantly in males and females. **Conclusion:** The current study revealed that deficiency of G6PD was observed in proportion of SCD children and associated closely with the levels of HGB and MCH.

**KEYWORDS:** Sickle cell disease, G6PD deficiency, children, hemolysis.

## INTRODUCTION

Sickle cell disease(SCD) represents the most frequent genetic disorder in red blood cell(RBCs) that result from presence of mutated form of hemoglobin S(HbS).[1] It can be caused by heterozygosity (two different alleles for HbS and another beta-globin especially beta-thalassemia) or homozygosity (two identical alleles for HbS).[2]

SCD is mostly present in blacks, and found with much less frequency in eastern Mediterranean and Middle East population, without sex predilection since SCD is not an X-linked disease.[3] HbS polymerizes under some conditions such as low oxygen, acidosis, or in the setting of pyrexia or dehydration leading to deformed RBCs and reduced life span).[4] Patients experience a spectrum of symptoms that related to hemolytic anemia, vaso-occlusion and hemolysis correlates with several SCD complications such as leg ulcers, kidney disease, hypertension, stroke, and death).[5,6]

Glucose -6-phosphate dehydrogenase (G6PD) deficiency is an X-linked hereditary disorder and represents a global public health concern in which children are at high risk of developing hemolytic anemia following exposure to certain food, bacterial infections, and certain drugs such as primaquine and tefenoquine.[7,8] The global prevalence of G6PD deficiency is estimated to be 10% which approximate 400 million children worldwide with wide geographical distribution that correlates with presence of malaria, in which highest prevalence was in Africa,

followed by Middle east, Asia, and some areas of the Mediterranean.[9] According to World Health Organization(WHO), different G6PD variants were classified depending on the degree of deficiency and severity of hemolysis into classes I to V and class II represented G6PD editerranean deficiency.[10] The deficiency of G6PD will induce an accelerated rate of hemolysis, and concomitant G6PD deficiency in patients with SCD might increase severity of clinical manifestations with conflicting results.[11] Absence of local studies in Syria prompt us to carry out this study. Therefore, the aims of this study were: 1- to investigate the prevalence of G6PD deficiency in children with a diagnosis of SCD. 2- to determine the association between presence of deficiency and alterations in laboratory tests related to red blood cells.

**Patients and Methods Study Population**

After approval by local research ethics committee, a cross sectional descriptive study was conducted in patients seen at Pediatric General Clinic, Tishreen University Hospital over a period of one year from June 2021 to July 2022.

**Inclusion Criteria were as follows:** Children of both sexes and aged 2 to 12 years with proven diagnosis of SCD. **Exclusion Criteria:** Patients with one of the following: hemolytic crisis or blood transfusion in the past three months.

Complete history, review of systems and physical examination were performed for all patients. Blood samples were collected for measurement of complete blood count(CBC), White blood cell(WBC), neutrophil(NEUT), hemoglobin(HGB), total bilirubin(TB), mean corpuscular volume(MCV), MCHC (mean corpuscular hemoglobin concentration), MCH (mean corpuscular hemoglobin) and reticulocyte count. Patients were classified depending on the status of G6PD as follow: with G6PD deficiency (31 cases), without deficiency (221 cases) and laboratory tests of the study population were compared between two groups.

**Statistical Analysis**

Statistical analysis was performed by using IBM SPSS version20. Basic Descriptive statistics included means, standard deviations (SD), median, Frequency and percentages. To examine the relationships and comparisons between the two group, chi-square test was used. Independent t student test was used to compare 2 independent groups. All the tests were considered significant at a 5% type I error rate($p<0.05$), β:20%, and power of the study:80%.

**RESULTS**

The baseline characteristics of patients were as shown in Table (1). Among the 252 study participants,45.6% were males and 54,4% were females with an average age of the children was 8.17±2.4 years. Age group 10-12 years represented the most frequent age group (35.3%), followed by 8-10 (23.8%), 6-8(23.4%),4-6(12.3%) and 2-4(5.2%). The overall prevalence of G6PD deficiency was 12.3%(31/252) which is classified to moderate (17 cases) and severe form (14 cases). Severe forms were observed only in males (12.2%), whereas moderate forms were detected in males (3.5%) and females (9.5%).

**Table 1: Demographic characteristics of the study population.**

| Variable | Result |
|---|---|
| **Gender (n,%)** | |
| Male | 115(45.6%) |
| Female | 137(54.40%) |
| **Age (years)** | 8.17±2.4(2.5-12) |
| **Age groups (n,%)** | |
| 2-4 | 13(5.2%) |
| 4-6 | 31(12.3%) |
| 6-8 | 59(23.4%) |
| 8-10 | 60(23.8%) |
| 10-12 | 89(35.3%) |
| **G6PD deficiency** | |
| Present | 31(12.3%) |
| Absent | 221(87.7%) |
| **Severity of G6PD deficiency** | |
| Moderate | 17(54.9%) |
| Severe | 14(45.1%) |

As shown in table (2), there was no significant difference between two groups regarding age (8.03±3.1 years in group I versus 8.19±2.3 in group II, p:0.7). In group I, age group 10-12 years represented the most frequent age group (38.7%), followed by 8-10 (25.8%), 2-4(16.1%),6-8(9.7%), and 4-6(9.7%), whereas age group 10-12 years represented the most frequent group in children without G6PD deficiency (34.8%) followed by 6-8(25.3%), 8-10(23.5%),4-6(12.7%) and 2-4(3.6%), p:0.06. 58.1% of the children with deficiency of G6PD were males and 41.9% were females, p:0.07.

There were no significant differences between two groups regarding laboratory investigations except of HGB and MCH which were significantly lower in group I; (7.17±0.7 versus 9.11±0.5, p:0.0001) and (24.8±1.7 versus 28.7±1.4,p:0.002).

**Table 2: Characteristics of the study population by comparison of the two group.**

| Variables | Group I Patients with G6PD deficiency (n=31) | Group II Patients without G6PD deficiency (n=221) | P value |
|---|---|---|---|
| **Age (years)** | 8.03±3.1 | 8.19±2.3 | 0.7 |
| **Age groups(n,%)** | | | |
| 2-4 | 5(16.1%) | 8(3.6%) | 0.06 |
| 4-6 | 3(9.7%) | 28(12.7%) | |
| 6-8 | 3(9.7%) | 56(25.3%) | |
| 8-10 | 8(25.8%) | 52(23.5%) | |
| 10-12 | 12(38.7%) | 77(34.8%) | |
| **Gender** | | | |
| Male | 18(58.1%) | 97(43.9%) | 0.07 |
| Female | 13(41.9%) | 124(56.1%) | |
| **Laboratory investigations** | | | |
| WBC | 8193.5±1715.9 | 8634.3±4.3 | 0.1 |
| Neut | 59.19±9.05 | 57.9±8.1 | 0.9 |
| HGB | 7.17±0.7 | 9.11±0.5 | 0.0001 |
| MCV | 78.9±4.3 | 79.52±3.5 | 0.2 |
| MCHC | 32.9±1.2 | 35.3±2.8 | 0.06 |
| MCH | 24.8±1.7 | 28.7±1.4 | 0.002 |
| TB | 1.25±0.2 | 1.29±0.6 | 0.5 |
| Reticulocyte count | 3.22±1.2 | 2.52±0.9 | 0.08 |

In males, there were no significant differences between patients according to the severity of deficiency regarding laboratory investigations except of HGB and MCH which were significantly lower in severe forms; (6.6±0.8 versus 9.2±0.3 in patients without deficiency, p:0.0001) and (22.9±0.8 versus 28.2±1.3 in children without deficiency, p:0.0001) respectively. In addition to, there were significant differences between females regarding HGB and MCH according to the severity of disease which were significantly lower in moderate forms; (7.9±0.4 versus 8.9±0.7, p:0.0001) and(25.9±0.7 versus 28.5±2.1,p:0.0001) respectively.

**Table 3: Laboratory investigations of the study population according to presence of G6PD deficiency.**

| | Laboratory investigations | | | | |
|---|---|---|---|---|---|
| | **HGB** | **MCV** | **MCH** | **MCHC** | **Reticulocyte count** |
| **Males** | | | | | |
| **G6PD deficiency (-)** | 9.2±0.3 | 79.9±3.2 | 28.2±1.3 | 33.2±1.3 | 2.23±1.1 |
| **Moderate deficiency** | 7.1±0.7 | 80.1±3.5 | 25.3±0.3 | 32.9±1.1 | 2.51±0.8 |
| **Severe deficiency** | 6.6±0.8 | 79.7±2.9 | 22.9±0.8 | 31.1±0.8 | 2.9±0.2 |
| **P value** | 0.0001 | 0.2 | 0.0001 | 0.06 | 0.07 |
| **Females** | | | | | |
| **G6PD deficiency (-)** | 8.9±0.7 | 79.4±3.8 | 28.5±2.1 | 34.1±1.3 | 2.6±0.5 |
| **Moderate deficiency** | 7.9±0.4 | 78.9±2.9 | 25.9±0.7 | 31.7±1.7 | 2.7±0.5 |
| **P value** | 0.0001 | 0.5 | 0.0001 | 0.09 | 0.4 |

## DISCUSSION

This cross sectional descriptive, single-center study investigated the prevalence of G6PD deficiency among children with SCD due to the fact that both are inheritable diseases of the red blood cells that can co-exist in an individual. In addition to, determining the differences in laboratory investigations between children according to presence of deficiency. The present study revealed the main findings: first, an age group 10-12 years represented the most frequent group followed by 8-10 and 6-8 years. Second, SCD was observed in 55% of females. Third, G6PD deficiency was detected in 31 cases on average 12.3% which ranges in severity from moderate to severe in males with only moderate form in females. In addition to, there were no significant differences between children regarding age and sex depending on presence of deficiency. Finally, levels of HGB and MCH were significantly lower in patients with presence of G6PD deficiency which increased with increasing the severity of deficiency in males. The results of current study are consistent with the previous studies.

Mohammad et al (1998) demonstrated in a study performed in Bahrain which included 125 children (60 males, 65 females) with a diagnosis of SCD that prevalence of G6PD deficiency was 46.45%(59 cases) on average 47% in males and 19% in females. By comparison with the current study, occurrence of G6PD deficiency was lower (7.1% in males and 5.2% in females) which might be explained by increasing of

consanguineous marriage.[12]

Simpore et al (2007) found in a study performed in Italy which included 74 children with SCD that prevalence of G6PD deficiency was 27.03% and incidence was increased with advanced age;8.4% in the age group 6-9 years versus 20.9% in the group 10-12 years. In addition to, there were significant differences between two groups only regarding HGB and MCH values. By comparison with the current study, occurrence of G6PD deficiency was higher in Simpore et al study (27% versus 12.3%) with agreement between two studied regarding laboratory findings.[13]

Baffour et al (2019) demonstrated in a study conducted in Ghana included 120 children with SCD that prevalence of G6PD deficiency was 35.38% which ranges in severity from moderate (8.33%) to severe (13.3%) in males and only moderate form in females (14.17%).[14] By comparison with the current study, occurrence of G6PD deficiency was higher in Baffour et al study (35.38% versus 12.3%) with agreement between two studied regarding presence severe form of deficiency only in males. Higher prevalence of deficiency might be explained particularly by high incidence of malaria.

Ogunkanbi et al (2019) showed in a study conducted in Nigeria included 115 children with SCD who compared with matched healthy control group (115) that prevalence of G6PD deficiency was 6.1% in cases versus 7% in the control group, p:0.7, and the deficiency was observed more frequently in advanced age and in males but without significant difference($p>0.05$).[15] By comparison with the current study, occurrence of G6PD deficiency was lower in Ogunkanbi et al study (6.1% versus 12.3%) and all children in the current study were with a diagnosis of SCD.

In summary, coexistence of G6PD deficiency with SCD might worsen final outcome of the patients, so that early detection of deficiency and avoidance factors that might induce hemolysis due to presence of G6PD deficiency is considered crucial to improve prognosis.

**Declarations Competing of Interests**
All the authors do not have any possible conflicts of interest.

**Ethical consideration**
After discussing the study with the parents, all of them gave a complete and clear informed consent to participate in the study. This study was performed in accordance with the Declaration of Helsinki.

**Availability of data and materials**
Most of the data was in the article, and other data can be asked from the corresponding author.

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**Author contributions**
All authors performed the measurements and wrote the article. Literature review was done by Dr. Seba Ali Ebrahim, and all authors performed analytic calculations and performed the numerical simulations.

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