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Research Article

Knowledge and Attitude of Families of Children with G6PD Deficiency: A Cross-sectional Retrospective Study

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Keywords

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Abstract

Glucose-6-phosphate dehydrogenase (G6PD), deficiency is considered the most common enzyme deficiency worldwide. Several studies have reported the frequency of G6PD deficiency in different regions of Saudi Arabia. This retrospective descriptive cross-sectional study was conducted at the International Medical Center Hospital in Jeddah, Saudi Arabia, which included families of children who had been diagnosed with G6PD deficiency between August 2016 and June 2021 at the pediatric hematology clinic. The data was collected by a developed questionnaire through the online platform. The study included 233 respondents. Results showed that most respondents responded that G6PD develops due to a genetic defect (98.7%). Knowledge scores did not differ significantly based on the child's age and gender. However, mothers had a significantly higher median knowledge score than other relationship categories (p = 0.011). Additionally, younger age groups had significantly higher knowledge scores than older groups (p < 0.0001). Furthermore, the scores of relatives with a high school diploma and university degree were significantly lower than those with other educational levels (p = 0.046). The most reported perception of the causes and triggers of symptoms was eating legumes (91.0%). G6PD is a prevalent red blood cell disorder. Family and community awareness of the modes of inheritance, disease mechanisms, signs and symptoms, and management is critical to the overall well-being of children affected by this condition. Therefore, public education about this common condition is needed, especially in Middle Eastern communities.

ABBREVIATIONS

G6PD: Glucose-6-phosphate dehydrogenase; NNJ: Neonatal Jaundice; IQRs: Interquartile ranges; CIs: Confidence Intervals

INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) is an enzyme found in the cytoplasm of all cells in the body. It plays a vital role in preventing cellular damage from reactive oxygen species. It provides substrates to prevent oxidative damage [1]. Mutations in the G6PD gene cause G6PD deficiency, a well-known cause of hemolytic anemia in humans [2]. Furthermore, G6PD deficiency can result in acute hemolytic anemia during increased reactive oxygen species production [1]. Affected people are often

asymptomatic and unaware of their deficiency. However, they are at risk of developing acute hemolytic crises as a result of infection, fava bean consumption, and the use of drugs with a high oxidation potential [3].

In addition, this condition is inherited as an X-linked recessive trait and is one of the most common red-cell enzymopathies [4]. Homozygotes and heterozygotes can be symptomatic. The disease is typically more severe in persons who are homozygous for the deficiency and causes a variety of diseases, including neonatal hyperbilirubinemia, acute hemolysis, and chronic hemolysis [5]. G6PD deficiency is considered the most common enzyme deficiency worldwide [2].

Around 400 million people are affected. It most commonly

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affects persons of African, Asian, Mediterranean, or Middle Eastern descent [5]. The prevalence of G6PD deficiency and associated enzyme variants has been documented in the Kingdom of Saudi Arabia, with G6PD Mediterranean being most common among those of Mediterranean descent [3]. G6PD deficiency is prevalent in various ethnic groups around the world, ranging from 20% to 30% in Greece, 6% in Saudi Arabia, and 5.5% in South China [2].

Several studies reported the frequency of G6PD deficiency in different regions in Saudi Arabia, where G6PD deficiency was found to be 1.13% in blood donors in the capital city of Riyadh and 1.9% in the rural town of Al-Kharj. In comparison, it ranged in frequency from 3.5% to 6.7% in major cities like Najran, Riyadh, Bisha, Al-Ula and Makkah, frequencies in Jaizan, Al Hafouf, and Khaiber, as well as Al Baha and Al Qunfoda, have been recorded to be 11.6% to 18%, G6PD deficiency was found in the highest percentages in Al Qatif (45.9%) and Al Hassa (36.5%) [6].

A cross-sectional study that evaluated mothers' perceptions of G6PD deficiency and neonatal jaundice (NNJ) showed that mothers' perceptions of both were low [7]. In addition, there is an association between parental-child G6PD deficiency self-care discussions and improved child health; a cross-sectional study found that parental involvement in these discussions was aided by the clarity and thoroughness of patient information given by physicians [8]. This study revealed that there was a vast knowledge and awareness gap among families of children with G6PD deficiency.

Therefore, our primary objective of this cross-sectional retrospective study is to assess the awareness and understanding among families of children with G6PD deficiency regarding accurate information on the disease and assess the most common myths and wrong information about G6PD deficiency. Our secondary objective is to determine the most common trigger of G6PD deficiency symptoms in Jeddah, Saudi Arabia, and assess the timing of seeking medical help after the onset of symptoms.

MATERIALS AND METHODS

Study Design and Study Population

A retrospective descriptive cross-sectional study was conducted at the International Medical Center Hospital in Jeddah, Saudi Arabia. It included families of children presented to the pediatric hematology clinic who were diagnosed with G6PD deficiency between August 2016 and June 2021. Families of children older than 18 years of age diagnosed with G6PD deficiency and families of children with hemolytic anemia not due to G6PD deficiency were excluded.

Sampling Strategy

Study participants who fulfilled the inclusion criteria were enrolled using a convenience sampling technique. A validated survey tool was delivered through telephone conversations. The final analysis only included participants who fulfilled the inclusion criteria and completed the questionnaires.

Questionnaire Tool

A questionnaire was developed by an expert consultant in the pediatric hematology oncology field. The validity was assessed by delivering the questionnaire to 10 patients before distributing it to all patients. The first questionnaire domain includes questions about the demographic characteristic data of parents and children, which consists of the age and gender of the child, as well as the age and educational level of the parents. The second questionnaire domain includes two sections. The first section contains 17 true or false questions, which we used to assess parents' awareness and knowledge of G6PD deficiency. The second section included two questions to determine understanding regarding the disease and evaluate the most common myths and wrong information about G6PD deficiency. The third domain included two multiplechoice questions to determine the most common trigger of G6PD deficiency symptoms and assess the timing of seeking medical help after the onset of symptoms.

Sample Size

The sample size was estimated using the Raosoft calculator. To achieve a 95% confidence interval and a 5% margin of error, the target sample size was 385 participants.

Statistical Analysis

Data analysis was performed using RStudio (R version 4.1.1). Categorical data was expressed as frequencies and percentages, and numerical data was presented as median and interquartile ranges (IQRs). A multiple-response analysis was performed on variables with multiple available responses. Factors associated with participants' knowledge were assessed using a Kruskal-Wallis rank sum test or a Wilcoxon rank sum test whenever applicable. The predictors of participants' knowledge were explored by conducting a multivariate linear regression analysis. The knowledge score was used as a dependent variable, and the significantly associated variables from the univariate analysis were used as independent variables. The regression analysis results were expressed as beta coefficients and 95% confidence intervals (95%CIs). A p-value of 0.05 indicated statistical significance.

Ethical Statement

The Biomedical Ethics Committee approved the study at the Research Center of International Medical Center Hospital. Data were collected through telephone conversations, then entered and extracted from an online-based questionnaire. Participants obtained full enrollment consent at the beginning of the telephone conversations by being asked to answer if they agreed to participate in the study after explaining the objectives. The confidentiality of the study data was adequately ensured.

RESULTS

Demographic characteristics of participants and their children who had G6PD

The responses of 233 participants were received on the



online platform. More than half of the respondents were aged 31 to 40 (51.9%), and the majority had attained a university degree (82.8%). Out of the sample under study, mothers represented 52.4%, fathers represented 47.2%, and other relatives represented 0.4%. Approximately three-quarters of children were aged \geq 5 years old (73.0%) and were males (76.4%, Table 1).

Participants knowledge regarding G6PD

Focusing on the items with true, false, or do not know responses (Figure 1), the most frequent correct answers were reported for the fact that legumes can be replaced with other

Table 1: Demographic characteristics of participants and their children

Parameter	Category	N (%)	
Child's age	≥5 y	170 (73.0%)	
	6-12 y	56 (24.0%)	
	13-18 y	7 (3.0%)	
Child's gender	Male	178 (76.4%)	
	Female	55 (23.6%)	
Relationship to the child	Father	110 (47.2%)	
	Mother	122 (52.4%)	
	Other	1 (0.4%)	
Relative's age	20-30 years old	35 (15.0%)	
	31-40 years old	121 (51.9%)	
	41-50 years old	70 (30.0%)	
	>50 years old	7 (3.0%)	
Relative's educational level	< High school	0 (0.0%)	
	High school or diploma	38 (16.3%)	
	University	193 (82.8%)	
	Other	2 (0.9%)	

Abbreviations: N: Number

types of food (93.6%), patients with the G6PD disease cannot eat falafel (93.1%), and patients should not consume peanut butter (92.7%). Conversely, the most common incorrect answers were related to participants' perceptions that there is nothing wrong with a patient with G6PD taking painkillers such as aspirin and Panadol (60.5%), it is acceptable to take vitamin C from pharmacies (47.2%), and it is safe to drink green or black tea (46.8%). These results are depicted in Figure 1 and detailed in Table 2. Regarding the items with other available answers, the majority of respondents provided correct responses to the fact that G6PD developed as a result of a genetic defect (98.7%) and stressed the importance of consulting a physician if a child with G6PD gets an infection and the physician did not know about their original G6PD condition (Table 2).

Knowledge score and the factors associated with knowledge

The median knowledge score was 10.0 (IQR = 9.0 to 12.0). Knowledge scores did not differ significantly based on the child's age and gender. However, mothers had a significantly higher median knowledge score than other relationship categories (median = 11.0, IQR = 9.0 to 13.0 among mothers vs median = 10.0, IQR = 8.0 to 12.0 among fathers and median = 10.0, IQR = 10.0 to 10.0 among other relatives, p = 10.0 to 10.0 among participants from the 10.0 among participants

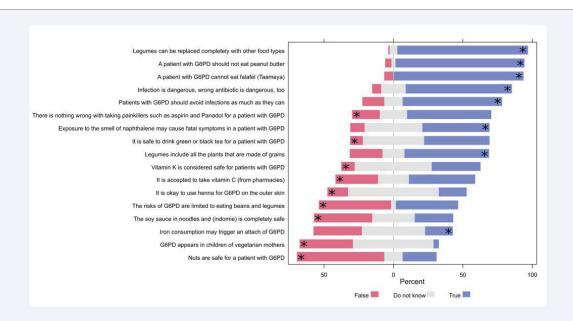


Figure 1 The percentages of participants' responses to knowledge items with the following responses: "No," "Yes," or "Do not know." An asterisk indicates a correct answer.



Table 2: Participants' responses to knowledge items

Parameter	Category	N (%)
A nationt with CADD cannot cat f-1-f-1 (T	True*	217 (93.1%)
A patient with G6PD cannot eat falafel (Taameya)	False	14 (6.0%)
	Do not know	2 (0.9%)
The risks of G6PD are limited to eating beans and	True	104 (44.6%)
legumes	False*	120 (51.5%)
legumes	Do not know	9 (3.9%)
	True*	166 (71.2%)
Patients with G6PD should avoid infections as	False	36 (15.5%)
much as they can	Do not know	31 (13.3%)
	True	56 (24.0%)
Nuts are sefe for a nationt with CADD	False*	145 (62.2%)
Nuts are safe for a patient with G6PD		
	Do not know	32 (13.7%)
There is nothing wrong with taking painkillers	True	141 (60.5%)
such as aspirin and Panadol for a patient with	False*	46 (19.7%)
G6PD.	Do not know	46 (19.7%)
m 16.1.3.	True	64 (27.5%)
The soy sauce in noodles and (indomie) is	False*	97 (41.6%)
completely safe	Do not know	72 (30.9%)
	True	109 (46.8%)
It is safe to drink green or black tea for a patient	False*	20 (8.6%)
with G6PD	Do not know	
		104 (44.6%)
	True	110 (47.2%)
t is accepted to take vitamin C (from pharmacies)	False*	70 (30.0%)
	Do not know	53 (22.7%)
n	True*	112 (48.1%)
Exposure to the smell of naphthalene may cause	False	23 (9.9%)
fatal symptoms in a patient with G6PD.	Do not know	98 (42.1%)
	True*	177 (76.0%)
Infection is dangerous, and the wrong antibiotic is	False	14 (6.0%)
dangerous, too		
	Do not know	42 (18.0%)
	True*	46 (19.7%)
Iron consumption may trigger an attack of G6PD	False	80 (34.3%)
	Do not know	107 (45.9%)
Vitania Via anni dana dan Carantina da sita	True	81 (34.8%)
Vitamin K is considered safe for patients with	False*	22 (9.4%)
G6PD	Do not know	130 (55.8%)
	True	8 (3.4%)
G6PD appears in children of vegetarian mothers	False*	89 (38.2%)
doi b appears in children of vegetarian mothers	Do not know	136 (58.4%)
	True	46 (19.7%)
It is okay to use henna for G6PD on the outer skin	False*	34 (14.6%)
	Do not know	153 (65.7%)
	True*	216 (92.7%)
A patient with G6PD should not eat peanut butter	False	10 (4.3%)
	Do not know	7 (3.0%)
	True*	218 (93.6%)
Legumes can be replaced completely with other	False	1 (0.4%)
food types	Do not know	
		14 (6.0%)
Legumes include all the plants that are made of	True*	141 (60.5%)
grains	False	54 (23.2%)
5 -	Do not know	38 (16.3%)
	Malnutrition	1 (0.4%)
G6PD develops as a result of	Genetic defect*	230 (98.7%)
	Do not know	2 (0.9%)
	Use the treatment	9 (3.9%)
A child with G6PD became infected, and when they visited the doctor for the first time, the	the doctor	
parents forgot to tell the doctor about the type of anemia he had. Should they	Return to the doctor* before using the	220 (94.4%)
	treatment	4 (1.7%)
	Do not know	

Abbreviations: G6PD: Glucose-6-phosphate dehydrogenase; N: Number

Table 3: Factors associated with participants' knowledge

Parameter	Category	Median (IQR)	p-value
Child's age	≥5 years old	10.0 (9.0, 12.0)	0.837
	6-12 years old	10.0 (9.0, 12.0)	
	13-18 years old	11.0 (9.0, 11.0)	
Child's gender	Male	10.0 (9.0, 12.0)	0.913
	Female	10.0 (8.0, 12.0)	
Relation	Father	10.0 (8.0, 11.0)	0.011
	Mother	11.0 (9.0, 13.0)	
	Other	10.0 (10.0, 10.0)	
Relative's age	20-30 years old	11.0 (9.0, 12.0)	<0.0001
	31-40 years old	11.0 (9.0, 12.0)	
	41-50 years old	9.5 (8.0, 10.0)	
	>50 years old	9.0 (8.5, 9.5)	
Relative's educational level	High school or diploma	10.0 (8.0, 11.0)	0.046
	University	10.0 (9.0, 12.0)	
	Other	12.5 (11.8, 13.2)	

Abbreviations: IQR: interquartile range

 $\textbf{Table 4:} \ Results \ of \ the \ regression \ analysis \ to \ assess \ the \ predictors \ of \ participants' \ knowledge \ regarding \ G6PD$

Parameter	Category	Beta	95% CI	p-value
Relation	Father	Ref	Ref	
	Mother	0.69	0.02, 1.36	0.044
	Other	0.88	-3.84, 5.60	0.714
Relative's age	>50 years old	Ref	Ref	
	20-30 years old	0.92	-1.12, 2.95	0.375
	31-40 years old	1.33	-0.59, 3.24	0.174
	41-50 years old	-0.05	-1.96, 1.87	0.963
Relative's educational level	High school or diploma	Ref	Ref	
	University	0.71	-0.17, 1.59	0.112
	Other	2.03	-1.40, 5.46	0.245

Abbreviations: CI: confidence interval

from the > 50-year-old group, p < 0.0001). Furthermore, the scores of relatives with a high school diploma (median = 10.0, IQR = 8.0 to 11.0) and a university degree (median = 10.0, IQR = 8.0 to 12.0) were significantly lower than those with other educational levels (median = 12.5, IQR = 11.8 to 13.2, p = 0.046, Table 3). Based on the outcomes of the regression analysis, being a mother was independently associated with higher knowledge scores than other participants' groups (β = 0.69, 95%CI, 0.02 to 1.36, p = 0.044, Table 4).

Participants' perceptions towards the triggers of symptoms and the best time to seek help for children with ${\tt G6PD}$

The most reported perceptions of the causes and triggers of symptoms were eating legumes (91.0%), eating peanut butter (81.5%), and eating nuts (61.8%). In contrast, the least common triggers were having tea (7.3%) and usage of painkillers (18.5%, Figure 2). Participants stated that the best time to seek help for a child with G6PD is as soon as the urine color has changed (72.1%), pallor and jaundice have developed (68.7%), and there is shortness of breath (64.8%, Figure 3).



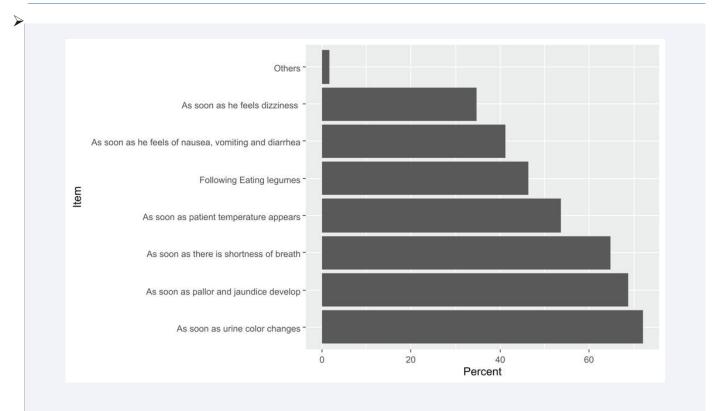


Figure 2 The percentages of participants' responses regarding the common causes/triggers of symptoms among children with G6PD.

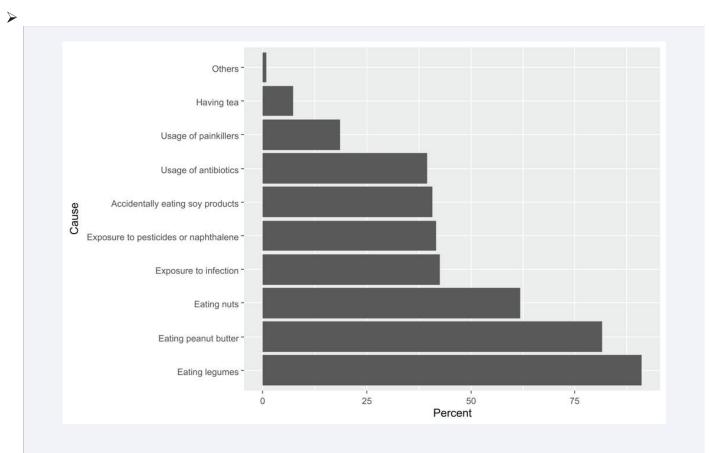


Figure 3 The percentages of participants' responses regarding the best time to seek help for a child with G6PD.



DISCUSSION

G6PD is the most common red blood cell enzymopathy [9]. G6PD plays a crucial role in generating the reduced form of nicotinamide adenine dinucleotide phosphate, which prevents oxidative in red blood cells. Deficiency of this enzyme makes affected individuals prone to oxidative stress in the form of hemolysis. There are three distinct forms of hemolysis in individuals with G6PD: NNJ due to excessive hemolysis, acute hemolytic anemia, and chronic nonspherocytic hemolytic anemia [10]. G6PD is inherited as an X-linked recessive condition. Therefore, it affects mainly males [11]. The prevalence of G6PD in Saudi Arabia is about 8.4% among the male population [12].

Parental awareness about this condition is essential for the well-being of the affected children. Therefore, we aimed to measure parental knowledge about and aptitudes towards G6PD. We are looking at their perceived information about this condition and the implications of having a child affected. This work will give insight into the public knowledge of this relatively common disease.

In our cohort, we found that most of the respondents were highly educated. Most of them have a university degree. Mothers were more than fathers. They were relatively young parents and caregivers, with an average age of 30-40. When it came to knowledge regarding G6PD, most of our respondents recognized that legumes could lead to hemolysis and are not allowed for children affected with G6PD. Specifically, more than 90% of them recognized that these children should not be given falafel and peanut butter. This is similar to prior published studies [13,14]. The fact that mothers knew precisely the types of food that could precipitate hemolysis is due to a good health education program.

Regarding medication safety, most respondents in our cohort did not recognize common drugs that can cause hemolysis in children with G6PD. We already know that it is difficult for parents and caregivers of children with G6PD to be fully aware of all the medications that can cause complications. This is partly because of the many drugs that can precipitate such a complication. In practice, most physicians tell families they can tell their primary physician or pharmacist that their child has G6PD, and the medical provider should know which medication(s) to avoid. In our cohort, most parents and caregivers did not see anything wrong with common drugs that can precipitate G6PD-induced hemolysis, such as painkillers and, specifically, aspirin. Although aspirin has been historically linked to hemolysis in G6PD patients, a review of the literature on its use in patients who have G6PD and acute coronary syndrome showed no reports of hemolysis in such patients [10].

As is known, G6PD is an inherited disorder. Understanding this is key for families of children with G6PD to understand both the mode of transmission and the particular risk for boys to be affected by this disorder [11]. In our cohort, most responders identified that G6PD is an inherited disorder due to a genetic defect. This is important because they will seek genetic counseling and advice. A 2011 study in Bahrain also showed a

good knowledge of G6PD inheritance. Interestingly, they found females to be more aware of G6PD and its inheritance [15].

Regarding the overall knowledge score, the median knowledge score in our cohort was 10 (IQR = 9.0 to 12.0). However, mothers have significantly higher median knowledge scores than other caregivers. Younger parents also have more knowledge than older parents. Prior studies have found mothers to be more knowledgeable about G6PD and its complications than other caregivers. In addition, many studies found an association between gender, family income, level of education, and overall knowledge and awareness of G6PD deficiency [16].

The perception of triggers of G6PD symptoms is considered necessary for taking immediate and timely action to seek help. As we know, Acute Hemolytic Anemia with Hemoglobin drop is the most common complication in which G6PD manifests. Thus, it is always considered a medical emergency. Therefore, families must identify triggers and causes to recognize symptoms that suggest such a complication. In our cohort, the most commonly perceived and reported trigger cause was eating Legumes. Almost 91% of our respondents identified consuming Legumes, 81% identified eating peanut butter, and 62% recognized that nuts could precipitate the G6PD crisis. This is even better than some published studies on parental awareness of G6PD triggers, especially in communities where it is not that common [17].

Recognition of symptoms of G6PD plays a vital role in timely management. The first symptom our respondents acknowledged that medical help should be sought when found is a change in urine color, then pallor, jaundice, and shortness of breath. Prior studies have shown intermediate knowledge of G6PD symptoms. Parents and caregivers are more aware of G6PD triggers than know symptoms when they occur. This is attributed in part to confusion and inexperience. Families who have more than one child with G6PD and a child who had developed symptoms in the past were more able to recognize symptoms when they occur again in the same child or for the first time in another child with G6PD [17].

CONCLUSION

G6PD is a pervasive red blood cell disorder. Family and community awareness of the modes of inheritance, disease mechanisms, signs and symptoms, and management is critical to the overall well-being of children affected by this condition. We need more education for the public about this relatively common condition, especially in Middle Eastern communities. Awareness about G6PD and manifestations, as well as timely actions when children have complications, can affect immediate and long-term outcomes.

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