The Egyptian Journal of Hospital Medicine (January 2018) Vol. 70 (5), Page 713-717

Glucose-6-phosphate dehydrogenase deficiency (G6PD) (Favism) in Dammam, Eastern Province of Saudi Arabia

Almutairi, Meshael Kareem O[1], Alsayyid, Amnah Abdulrahman H[1], Nagah Mohamed Abo el-Fetoh[2], Abdulelah Aziz Eissa Alenzi[3]

[1]Imam Abdulrahman bin Faisal University, Dammam, [2]Family and Community Medicine Department, Faculty of Medicine, Northern Border University, [3]Northern Border University, Arar, KSA

ABSTRACT

Background: Glucose-6-phosphate dehydrogenase deficiency is an X linked recessive disorder expressed mostly in males. It is the most common enzyme deficiency worldwide, causes a spectrum of disease including neonatal hyperbilirubinemia, acute hemolysis, and chronic hemolysis.

The aim of the study was to determine prevalence, risk factors of G6FD deficiency and its symptoms among general population of Dammam, Eastern Province of Saudi Arabia.

Methods: A cross-sectional study was conducted during the period from 1 March 2016 to 30 July 2017. Data was collected from 182 individuals. Systematic random sampling technique was followed. Data was collected by using predesigned online questionnaire. **Results:** The overall prevalence of favism was 17%, of them, 67.7% were females and 32.3% were males. 15.2% of cases and 26.9% of the total sample had family history of the disease. Among the studied cases, 48.4% complained of pallor, 45.2% headache, 45.2% drowsiness, 12.9% nausea, 32.3% back pain, 64.5% tiredness, 25.8% abdominal pain, 38.7% discoloration of urine, 29% foot pain, 16.1% low grade fever and 19.4% complained of jaundice. Regarding risk factors of favism; 32.3% reported excess beans intake, 12.9% antibiotic intake and only 9.7% reported bacterial or viral infection. **Conclusions:** Glucose-6-Phosphate Dehydrogenase deficiency is a common disorder as it affects 17% of the study population of Dammam, Eastern Province of Saudi Arabia. It was more common in females than males. Health education sessions and further epidemiological studies are required because early detection and prevention is the key strategy for successful management and control of this genetic disease.

Keywords: Glucose-6-phosphate dehydrogenase (G6PD), Prevalence, Risk factors, Favism, Dammam, Eastern Province of Saudi Arabia.

INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) is a highly conserved housekeeping enzyme and rate-limiting enzyme of the pentose phosphate pathway in all cells [1]. G6PD is a ubiquitous enzyme that must be quite ancient in evolution because it has been found in all organisms, from prokaryotes to yeasts, to protozoa, to plants, and animals [2, 3]. Glucose-6-phosphate dehydrogenase deficiency is the most common enzyme deficiency worldwide. It causes a spectrum of diseases including neonatal hyperbilirubinemia, acute hemolysis, and chronic hemolysis. Persons with this condition also may be asymptomatic [4].

G6PD deficiency results from mutations in the G6PD gene and is well-known common cause of hemolytic anemia in human [5]. Because acute hemolysis is caused by exposure to an oxidative stressor in the form of an infection, oxidative drug, or fava beans, treatment is geared toward avoidance of these and other stressors. Acute hemolysis is self-limited, but in rare instances it can be severe enough to warrant a blood transfusion [4]. Glucose 6-phosphate dehydrogenase (G6PD) deficiency was discovered more than half a century ago and is still the most common inherited enzymopathy [6]. Clinically, this deficiency affects as many as 400 million individuals worldwide [2] and predisposes affected individuals to neonatal jaundice, drug- or infection-mediated hemolytic crisis, favism, and, less commonly, to chronic nonspherocytic hemolytic anemia [7].

The aim of the study is to determine prevalence, risk factors of G6PD deficiency and its symptoms among general population of Dammam, Eastern Province of Saudi Arabia

PATIENTS AND METHODS

Study design and setting: A cross-sectional study was carried out on population of Dammam, Eastern Province of Saudi Arabia, KSA.

Study period and target population: This study was conducted during the period from 1 March 2016 to 30 July 2017.

Sampling: The sample size was calculated using the sample size equation: $n=z^2p\ (1-p)/e^2$. Data was collected from 182 individuals aged between <20 to 60 years old. Systematic random sampling technique was followed.

Received: 6/11/2017 DOI: 10.12816/0043971
Accepted: 16/11/2017

Data collection

Data was collected by using pre designed online questionnaire which include questions designed to fulfill the study objectives.

- Socio-demographic characteristics including age, sex, educational level, marital status and occupational status.
- Questions about manifestations of favism and it's family history
- If the case were diagnosed and how it was diagnosed.

Statistical Analysis

All the data were analyzed using statistical package for social sciences (SPSS Inc.) version 20. Descriptive statistics for the prevalence and quantitative variables were used. Risk factors were determined using logistic regression. A 2-sided p-value of less than 0.05 was considered statistically significant.

Ethical considerations

Permission to conduct the study was obtained from the Research and Ethics Committee at the College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam, Eastern Province of Saudi Arabia. The questionnaire had a brief introduction explaining the aims and significance of the study.

The study was done after approval of ethical board of King Abdulrahman bin Faisal university.

RESULTS

Table (1): shows the socio-demographic characteristics, prevalence of favism and family history of favism among the studied population. The majority of participants were females (76.4%), almost one third aged between 20 to 30 years and another third aged between 30 to 40 years old, (65.4%) were married and (66.5%) had high educational level (university). About (48.4%) of participants were employed. 22.5% of participants had chronic diseases. 26.9% of participants had family history of favism but only 17% had favism.

Table (2): illustrate the relationship between favism and sociodemographic characters, chronic diseases and family history of favism in the studied population. There was no significant effect of sex, age, educational level or marital status but there was a significant correlation of family history ($P<0.001$) and chronic diseases ($P< 0.001$).

Table (3): illustrate manifestations of favism in the studied cases. 48.4% complained of pallor, 45.2% headache, 45.2% drowsiness, 12.9% nausea, 32.3% back pain, , 64.5% tiredness, 25.8% abdominal pain, 38.7% discoloration of urine, 29% foot pain, 16.1% low grade fever and 19.4% jaundice.

Regarding risk factors of favism; 32.3% reported excess beans intake, 12.9% antibiotic intake and only 9.7% reported bacterial or viral infection.

Table (4): discuss diagnosis and method of diagnosis of studied cases. 74.2% of the cases sought out for medical care. 77.4% were diagnosed to have favism. 29% were diagnosed by a complete blood culture, 12.9% by lactate hydrogenase dioxide and 45.2% others.

Table (1): Sociodemographic character, prevalence of favism and family history of favism among the studied population, Dammam, KSA

Sex	Frequency (n=182)	Percent
Female	139	76.4
Male	43	23.6
Age		
<20	21	11.5
20 -	59	32.4
30 -	50	27.5
40 -	35	19.2
50-60	17	9.3
Marital status		
Single	63	34.6
Married	119	65.4
Occupation		
Not working	94	51.6
Employed	88	48.4
Education		
Primary	5	2.7
Secondary	40	22.0
University	121	66.5
Preparatory	16	8.8
Chronic diseases	41	22.5
Favism	31	17.0
Family history of favism	49	26.9

Table (2): The relationship between favism and sociodemographic characters, chronic diseases and family history of favism in the studied population, Dammam, KSA

Variable	Favism		Total	value
Sex	**(n=151)**	**Yes (n=31)**	**(n=182)**	
Female	118	21	139	0.156
	78.1%	67.7%	76.4%	
Male	33	10	43	
	21.9%	32.3%	23.6%	
Age				
< 20	14	7	21	0.174
	9.3%	22.6%	11.5%	
20-	48	11	59	
	31.8%	35.5%	32.4%	
30-	41	9	50	
	27.2%	29.0%	27.5%	
40-	33	2	35	
	21.9%	6.5%	19.2%	
50-60	15	2	17	
	10.0%	6.5%	9.3%	
Marital status				
Single	48	15	63	0.061
	31.8%	48.4%	34.6%	
Married	103	16	119	
	68.2%	51.6%	65.4%	
Occupation				
Not working	78	16	94	0.576
	51.7%	51.6%	51.6%	
Employed	73	15	88	
	48.3%	48.4%	48.4%	
Education				
Primary	3	2	5	0.070
	2.0%	6.5%	2.7%	
Preparatory	15	1	16	
	9.9%	3.2%	8.8%	
Secondary	29	11	40	
	19.2%	35.5%	22.0%	
University	104	17	121	
	68.9%	54.8%	66.5%	
Chronic diseases				
Yes	20	21	41	<0.001
	13.2%	67.7%	22.5%	
No	131	10	141	
	86.8%	32.3%	77.5%	
Family history of favism				
Yes	23	26	49	<0.001
	15.2%	83.9%	26.9%	
No	128	5	133	
	84.8%	16.1%	73.1%	

Table (3): Manifestations and risk factors of favism in the studied cases, Dammam, KSA

Variable	Frequency (n=31)	Percent
Pallor	15	48.4
Headache	14	45.2
Drowsiness	14	45.2
Nausea	4	12.9
back pain	10	32.3
Tiredness	20	64.5
Abdominal pain	8	25.8
Discoloration of urine	12	38.7
Foot pain	9	29.0
Low grade fever	5	16.1
Jaundice	6	19.4
Excess beans intake	10	32.3
Antibiotic intake	4	12.9
Bacterial or viral infection	3	9.7

Table (4): Diagnosis and method of diagnosis of studied cases, Dammam, KSA

Variable	No. (n=31)	%
Seeking medical care	23	74.2
Reaching to diagnosis	24	77.4
Method of diagnosis		
Liver enzymes	2	6.5
Finding Heinz bodies	2	6.5
Complete blood picture	9	29.0
Lactate Hydrogen Dioxide	4	12.9
Others	14	45.2

DISCUSSION

Glucose-6-phosphate dehydrogenase deficiency is the most common enzyme deficiency worldwide, causes a spectrum of disease including neonatal hyperbilirubinemia, acute hemolysis, and chronic hemolysis. Persons with this condition also may be asymptomatic [4]. This is A cross-sectional study was carried out randomly on population of Dammam, Eastern Province of Saudi Arabia,during the period from 1 March 2016 to 30 July 2017, among 182 individuals aged between <20 to 60 years old . The aim of the study is to determine prevalence regarding risk factors of G6PD deficiency and its symptoms among general population of Dammam, Eastern Province of

Saudi Arabia. This study showed that only 17% of participants had favism and 26.9% of participants had family history of favism. In Indians prevalence of G6PD deficiency is generally 0−10%, although some communities may have higher prevalence: 27.5% for the Vataliya Prajapati community in Western India [8] and 27.1% for the Angami Nagas, a tribal group in Northeastern India [9]. G6PD deficiency in scheduled caste population was 10% which was comparable with the earlier reports in the same caste group[10]. The deficiency of G6PD is found in a belt extending from the Mediterranean area through Southwest Asia and India to Southeast Asia. Several epidemiological studies have identified pockets in Asia and the Middle East with prevalence of the disease as high as 62% in Kurdish Jews [11] and 31% in Northern Vietnam [12]. Frequency of G6PD deficiency varies worldwide among different ethnic groups ranging from 20 to 30% in Greece, 6% in Saudi Arabia, and 5.5% in South China [13]. In Africa, the prevalence of G6PD deficiency has been reported as high as 28.1% in Southwest Nigeria [14], 22.5% in Congo (Brazzaville) [15], 15.7% in Mali (Bamako) [16], 13.0% in Uganda [17], and 9.0−15.5% in Gabon [18]. In Southeast Asia, the prevalence of G6PD deficiency differs greatly by region and ethnic group. For example, in Myanmar, Iwai et al. [19] found prevalence of G6PD deficiency as high as 10.8% for the Shan people, 7.3% in the dominant ethnic group the Burma, and absent in the Akha, despite a regional proximity to the Shan. Regarding risk factors of favism; our study reported 32.3% excess beans intake, 12.9% antibiotic intake and only 9.7% bacterial or viral infection. In another study that explored the association of NEC (necrotizing enterocolitis) and G6PD deficiency; G6PD deficiency was significantly higher (27.8%) in infants with NEC compared with the 5.3% prevalence among NICU (neonatal intensive care unit) admissions [20].

Our study reported symptoms of favism in the studied cases. 48.4% complained of pallor, 45.2% headache, 45.2% drowsiness, 12.9% nausea, 32.3% back pain, , 64.5% tiredness, 25.8% abdominal pain, 38.7% discoloration of urine, 29% foot pain, 16.1% low grade fever and 19.4% jaundice. Many people with G6PD deficiency are asymptomatic. However, case reports of acute massive hemolysis with jaundice have been reported especially in the neonatal period, leading to kernicterus and fatality [21,22,23,24,25]. Massive hemolysis complicating G6PD deficiency has also been reported in patients with hepatitis infections, specifically hepatitis A and E in the Indian subcontinent [26]. A literature review by Lai et al., suggested that G6PD deficiency is a risk factor for diabetes, with the risk being greater in men than in women (odds ratio of 2.22 vs 1.87, respectively) [27]. A study by Rostami-Far et al., indicated that G6PD deficiency increases the likelihood of neonatal sepsis. The study involved 76 neonates with sepsis and 1214 without sepsis, with the prevalence of G6PD deficiency being significantly greater in the sepsis group than in the controls [28].

Conclusion and recommendations: Glucose-6-Phosphate Dehydrogenase deficiency is a common type of the inherited red blood cell enzymopathy as it affects 17% of the study population of Dammam, Eastern Province of Saudi Arabia. It was more common in females than males. Laboratory evidence of G6PD deficiency requires particular attention of the public. Health education sessions and further epidemiological studies are required because early detection and prevention is the key strategy for successful management and control of this genetic disease.

Declaration of conflicting interest: The authors declare that there are no conflicts of interest.

ACKNOWLEDGMENT

The success and outcome of this work required support and assistance of many people and we are fortunate to have this all along the completion of the work. Our thanks go to Afaf Shuaib Albaqawi and Hala Mohammed Alanazi (Intern, Faculty of Medicine, Northern Border University) and Islam Ahmed Mohamed Azab for their help in different steps of the research.

REFERENCES

1. **Kletzien R, Harris P, and Foellmi L (1994):** Glucose-6-phosphate dehydrogenase: a 'housekeeping' enzyme subject to tissue-specific regulation by hormones, nutrients, and oxidant stress. The FASEB Journal, 8 (2): 174–181.
2. **Luzzatto L and Battistuzzi G (1985):** Glucose-6-phosphate dehydrogenase. Advances in Human Genetics, 14 (5): 217–386.
3. **Notaro R, Afolayan A, and Luzzatto L (2000):** Human mutations in glucose 6-phosphate dehydrogenase reflect evolutionary history. The FASEB Journal, 14 (3): 485–494.
4. **Jennifer E and Frank M (2005):** USA, Martin Army Community Hospital, Fort Benning, Georgia. Am Fam Physician, 72 (7):1277-1282.
5. **Vulliamy T, Beutler E, and Luzzatto L (1993):** Variants of glucose-6-phosphate dehydrogenase are

due to missense mutations spread throughout the coding region of the gene. Human Mutation, 2 (3):159–167.

6. **Luzzatto L and Battistuzzi G (1985):** Glucose 6-phosphate dehydrogenase. Adv Hum Genet., 14 (19): 217-329.
7. **Spolarics Z, Siddiqi M, Siegel J *et al.* (2001):** Increased incidence of sepsis and altered monocyte functions in severely injured type A- glucose-6-phosphate dehydrogenase-deficient African American trauma patients. Critical Care Medicine, 29 (4): 728–736.
8. **Gupte S, Shaw A, and Shah A (2005):** Hematological findings and severity of G6PD deficiency in Vataliya Prajapati subjects. Journal of Association of Physicians of India, 53 (10):1027–1030.
9. **Seth P and Seth S (1971):** Biogenetical studies of Nagas: glucose-6-phosphate dehydrogenase deficiency in Angami Nagas. Human Biology, 43 (4): 557–56.
10. **Rai V and Kumar P (2012):** Epidemiological Study of Glucose-6-phosphate Dehydrogenase Deficiency in Scheduled Caste Population of India. Journal of Anthropology, 12 (1):1-5.
11. **Steensma D, Hoyer J, and Fairbanks V (2001):** Hereditary red blood cell disorders in Middle Eastern patients. Mayo Clinic Proceedings, 76 (3):285–293.
12. **Verlé P, Nhan D, Tinh T *et al.* (2000):** Glucose-6-phosphate dehydrogenase deficiency in northern Vietnam. Tropical Medicine and International Health, 5 (3):203–206·
13. **Gandapur A, Qureshi F, Mustafa G *et al.* (2002):** Frequency of glucose 6 phosphate dehydrogenase deficiency and related hemolytic anemia in Riyadh, Saudi Arabia. Journal of Ayub Medical College, 14 (3): 24–26.
14. **May J, Meyer C, Großterlinden L *et al.* (2000):** Red cell glucose-6-phosphate dehydrogenase status and pyruvate kinase activity in a Nigerian population. Tropical Medicine and International Health, 5 (2):119–123.
15. **Bouanga J, Mouélé R, Préhu C *et al.* (1998):** Glucose-6-phosphate dehydrogenase deficiency and homozygous sickle cell disease in Congo. Human Heredity, 48 (4):192–197.
16. **Duflo B, Diallo A, Toure K *et al.* (1979):** Glucose-6-phosphate dehydrogenase deficiency in Mali. Epidemiology and pathological role. Bulletin de la Societe de Pathologie Exotique et de ses Filiales, 72 (3):258–264.
17. **Davis J, Clark T, Kemble S *et al.* (2006):** Longitudinal study of urban malaria in a cohort of Ugandan children: description of study site, census and recruitment. Malaria Journal, 5 (18):332-338.
18. **Migot-Nabias F, Mombo L, Luty A *et al.* (2000):** Human genetic factors related to susceptibility to mild malaria in Gabon. Genes and Immunity, 1 (7): 435–441.
19. **Iwai K, Hirono A, Matsuoka H *et al.* (2001):** Distribution of glucose-6-phosphate dehydrogenase mutations in Southeast Asia. Human Genetics, 108 (6):445–449.
20. **Schutzman D and Porat R (2007):** Glucose-6-phosphate dehydrogenase deficiency: another risk factor for necrotizing enterocolitis. J Pediatr., 151 (4):435-7.
21. **Weng Y and Chiu Y (2010):** Clinical characteristics of G6PD deficiency in infants with marked hyperbilirubinemia. J Pediatr Hematol Oncol., 32 (1):11-4.
22. **Dhillon A, Darbyshire P, Williams M *et al.* (2003):** Massive acute hemolysis in neonates with glucose-6-phosphate dehydrogenase deficiency. Arch Dis Child Fetal Neonatal , 1 (88):534-536.
23. **Valaes T (1994):** Severe neonatal jaundice associated with glucose-6-phosphate dehydrogenase deficiency: pathogenesis and global epidemiology. Acta Paediatr Suppl., 1 (394):58-76.
24. **Kaplan M and Hammerman C (1998):** Severe neonatal hyperbilirubinemia. A potential complication of glucose-6-phosphate dehydrogenase deficiency. Clin Perinatol., 25 (3):575-90.
25. **Kaplan M and Hammerman C (2004):** Glucose-6-phosphate dehydrogenase deficiency: a hidden risk for kernicterus. Semin Perinatol., 28 (5):356-64.
26. **Abid S and Khan A (2002):** Severe hemolysis and renal failure in glucose-6-phosphate dehydrogenase deficient patients with hepatitis E. Am J Gastroenterol., 97 (6):1544-7.
27. **Lai Y, Lai N and Lee S (2017):** Glucose-6-phosphate dehydrogenase deficiency and risk of diabetes: a systematic review and meta-analysis. Ann Hematol., 96 (5):839-45.
28. **Rostami-Far Z, Ghadiri K, Rostami-Far M *et al.* (2016):** Glucose-6-phosphate dehydrogenase deficiency (G6PD) as a risk factor of male neonatal sepsis. J Med Life, 9 (1):34-8.