Benghazi University – Faculty of medicine

Department of pediatrics

Accuracy of diagnosis of glucose-6-phosphate dehydrogenase deficiency depending on clinical manifestations of favism.

دقة تشخيص مرض نقص انزيم جلوكوز 6 فوسفات ديهيدروجينيز اعتمادا على العلامات السريرية لمرض الفوال.

Thesis submitted in partial fulfillment of the requirement of master degree in pediatrics.

BY

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Contents

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I am also deeply thankful to **Mr. Hosam Almugasabi**. The lab technician in Children Hospital–Benghazi, who did the entire lab work in the study for his continuous guidance, devoted effort, and unique cooperation, will always be deeply remembered.

Dedication

To the soul of my father,

My role model who taught me the value of learning.

To the person I admire most, my mother

who offered me unconditioned support throughout the course of my life.

To my brother Mohamed, my sisters; Fayrouz, Fadia, Manal and Nesrin,

for their continuous encouragement, help and advice.

List of tables

List of figures

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Abbreviations

G6PD	Glucose-6-phosphate dehydrogenase**.**
WHO	World health organization.
U	Unit.
gm	gram.
mg	milligram.
dl	deciliter.
RBCs	Red blood cells.
NADP	Nicotinamide Adenine Dinucleotide Phosphate.
NADPH	Reduced NADP.
GSSG	Oxidized glutathione.
GSH	Reduced glutathione.
HK	Hexokinase.
6PGD	6-Phosphogluconic dehydrogenase.
EDTA	Ethylene Diamine Tetraacetic Acid.

Summary

Aim: to evaluate the accuracy of diagnosis of glucose 6 phosphate dehydrogenase deficiency depending on clinical manifestations of favism. **Patients and methods:** it is a prospective study including 22 patients who were admitted to Children Hospital–Benghazi from 1st of January 2012 to 31st of December 2013 with manifestations of favism. Some demographic features of patients were evaluated. After hemolysis recovery and return of reticulocytes count to normal level (after 8 weeks), Blood samples from these 22 favic patients were tested for G6PD deficiency in RBCs by quantitative rate reduction test and the enzyme activity was estimated by WHO method. G6PD assay was measured by the number of erythrocytes expressing G6PD activity as $U/10^{12}$ RBCs. **Results:** Twenty two patients were studied, twenty out of 22 were males and the other two were females. All of them were presented with favism including the triad of pallor, yellow discoloration of sclera and skin, and dark colour of urine after ingestion of fava beans. Male to female ratio was 10:1 and 19 patients (86.4%) were below 4 years of age. Twenty patients (90.9%) were Libyan and two patients were Egyptian, nationality of mothers was Libyan in 20 Libyan patients (90.9%), and Egyptian in 2 Egyptian patients (9.1%), nationality of grandmothers was Libyan in 18 Libyan patients (81.82%) and Egyptian in 4 patients (two of them were Libyan and two of them were Egyptian). Time elapsed between ingestion of fava beans and onset of symptoms was 1 day in 7 patients (31.8%), 2 days in 11 patients (50%) and 3 days in 4 patients (18.2%). Type of ingested fava beans was raw in 14 patients (63.6%) and cooked in 8 patients (36.4%). Only 2 patients (9.1%) had a previous history of favism and

only 4 patients (18.2%) had a history of neonatal jaundice. Positive family history of G6PD deficiency was found in 7 patients (31.8%). Hepatomegaly was found in 3 patients (13.6%), splenomegaly and heart failure were not detected in any patient. Hemoglobin levels at admission were ranged from 4.5 g/dl to 7.8 g/dl and serum unconjugated bilirubin ranged from 3.5 mg/dl to 9.8 mg/dl. Reticulocytes were counted in only 18 patients (81.8%) and all of them had reticulocytosis. Coombs test was done in only 11 patients (50%) and was negative in all of them. All 22 patients were treated with packed cell transfusion. G6PD level was low in all patients ranged from 12.6 to 213 $U/10^{12}$ RBCs. **Conclusion:** With review of literature the diagnosis of G6PD deficiency depending on clinical manifestations of favism is almost accurate.

Introduction

Glucose-6-phosphate dehydrogenase deficiency is the most common inherited enzyme deficiency in human, the pattern of inheritance is X-linked and it is evaluated to affect 400 million people throughout the world.[1] The highest prevalence rates are found in tropical Africa, the Middle East, tropical and sub-tropical Asia, some areas of the Mediterranean, and in Papua New Guinea.[2,3,4,5]

G6PD is a cytoplasmic enzyme that is found in all cells including red blood cells (RBCs). It catalyzes the first step reaction in the hexose monophosphate pathway to generate NADPH which is needed for reactions of many biosynthetic pathways, for catalase enzyme stability, as well as regeneration of the reduced form of glutathione (GSH). Catalase and GSH are important for detoxification of hydrogen peroxide and protection of cells against it. This is mainly true in RBCs which are characterized by sensitivity to oxidative damage and by lacking other NADPH producing enzymes,[6,7] in which the absence of mitochondria restricts the production of NADPH to hexose monophosphate shunt only.[8,9] G6PD deficiency is genetically heterogeneous in which about 500 different variant enzymes have been estimated.[9,10] The best known G6PD deficient variants that occur at a high frequency are the African variant G6PD A^-, which results in a deficiency of RBCs G6PD activity (5-15% of normal), and the Mediterranean variant B^- that results in a deficiency of RBCs G6PD activity (< 5% of normal).[11]

They have been classified depending on criteria established by the World Health Organization (WHO), and are divided into five classes according to enzyme activity:[7]

Class I: Severely deficient associated with chronic non-spherocytic hemolytic anemia.

Class II: Severely deficient (1-10% enzyme activity), associated with acute hemolytic anemia.

Class III: mildly to moderately deficient (10 - 60% enzyme activity).

Class IV: normal enzyme activity (60- 150%).

Class V: Increased enzyme activity (> 150%), not associated with the disease.

Most G6PD-deficient people are asymptomatic and the remainders only develop symptoms in response to oxidant stress. The commonest oxidant stressful causes are drugs, infection, and fava beans (favism).[12,13]

The ancient Greek knew favism, as the advice attributed to Pythagoras to avoid fava beans.[14] Favism is an acute hemolytic anemia that occurs usually within 24 -72 hours in G6PD deficient person after ingestion of fava beans. The compounds divicine and isouramil that found in fava beans have a causal role in irreversible oxidation of GSH and subsequent hemolysis.[15] Not all G6PD deficient individuals develop hemolysis after ingestion of fava beans,[16] and hemolysis will not reoccur in all G6PD deficient patients with subsequent ingestion of fava beans.[17]

The triad of pallor, jaundice and dark urine are the commonest symptoms.[18] Hematological and biochemical laboratory results including low hemoglobin, high unconjugated bilirubin, reticulocytosis, characteristic red cell changes (bite cells and Heinz bodies) and hemoglobinuria are the hallmarks. The main treatment for G6PD deficiency is avoidance of

oxidative agents like infection, fava beans, and oxidative drugs that induce hemolysis,[19] hemolysis may be so severe that it may require blood transfusion. Screening of newborns for early diagnosis of G6PD deficiency and proper education can reduce the incidence of clinical symptoms.[20] Assays of G6PD activity depend on measuring the rate of production of NADPH from NADP in RBCs is used to confirm the diagnosis of G6PD deficiency.[21,22,23]

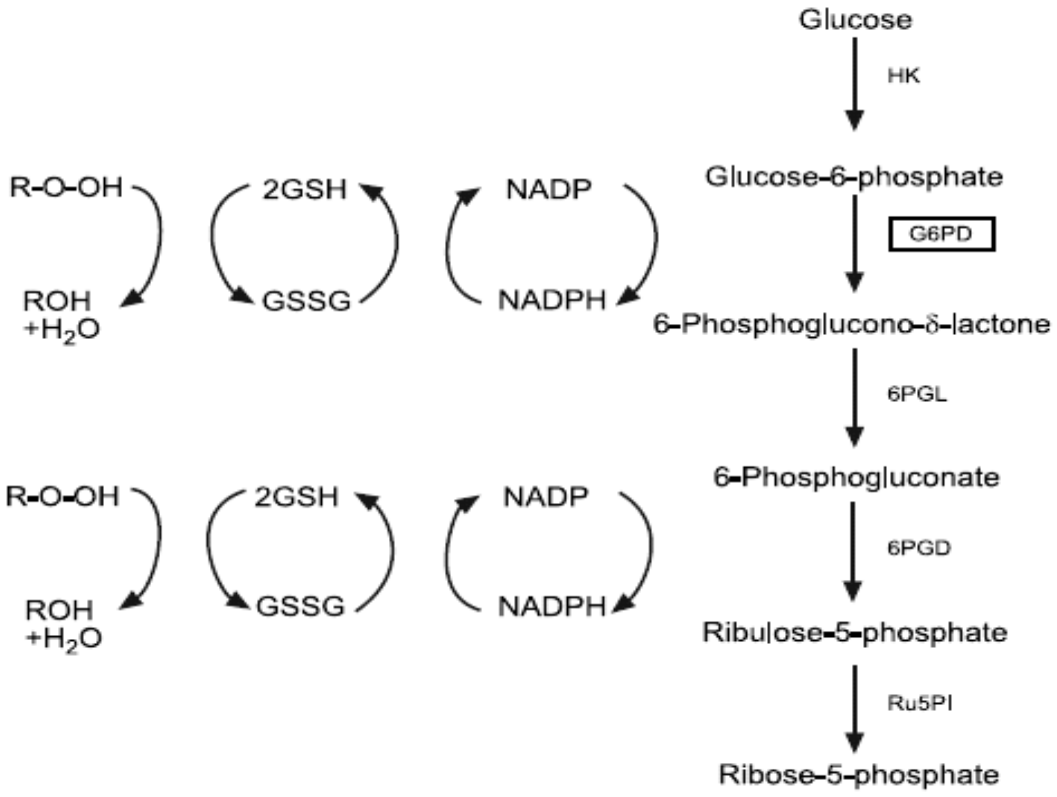

Figure 1.1: The action of G6PD in the pentose phosphate pathway.[16]

G6PD catalyzes $NADP^+$ to its reduced form NADPH.

(G6PD: Glucose-6-phosphate dehydrogenase, **NADP:** Nicotinamide Adenine Dinucleotide Phosphate, **NADPH:** Reduced NADP, **GSSG:** Oxidized glutathione**, GSH:** Reduced glutathione, **HK:** Hexokinase, **6PGD:** 6 Phosphogluconic dehydrogenase).

Review of literature

A cross sectional study was conducted by Sawsan S. in 2005, in the pediatric ward, Al Kadhiymia teaching hospital in Iraq, during the season of fava beans ingestion. Iraqi children that presented with favism were collected, 97 patients were studied, males were affected more than females with a ratio of 3.85:1. The peak age was between 1-5 years (78.36%). Previous history of neonatal jaundice was found in 24 patients (24.74%). The acute hemolytic attack was precipitated by fava beans ingestion in all patients (100%) and pallor was the main presenting feature. History of recurrence was found in 11 patients (11.34%). Family history of G6PD deficiency was found in 22 patients (22.68%). G6PD level was estimated two months later in 31 patients only (31.95%) and they were found to be deficient.[24]

A cross sectional descriptive study was conducted in the period from April 2010 to March 2011 by Sirdah M. and his colleagues in Al-Nasser Pediatric Hospital of Gaza, Palestine. It included 80 children aged between 2-8 years who were admitted due to hemolytic attacks. The results showed that 65 (60 males & 5 females) out of 80 children were found to be G6PD deficient. In most G6PD deficient patients (67.7%) hemolytic crisis occurred in early Childhood (≤ 40 months) and it was totally (100%) due to ingestion of fava beans, either green (96.9%) or dried (3.1%). Sixty four of G6PD deficient patients (98.5%) went through neonatal jaundice.[25]

A study was done in the University Department of Pediatrics, St. Sophie's Children's Hospital, Athens, Greece by Kattamis C. and his colleagues. It included 506 patients who were admitted to the hospital between the years of 1955 and 1966 due to hemolysis after fava beans ingestion. The age group was between 45 days -15 years. The highest incidence was seen in children aged between 2-5 years, only 36 patients (7.2%) were 10-15 years old. Twenty eight patients (5.5%) were less than 12 months of age, the youngest being 45 days old. Eighteen out of 28 infants were breast-fed and here the hemolytic attacks appeared 2-6 days after the ingestion of fava beans by the mother who was free of symptoms. Male to female ratio was 6.2:1. Hemolytic episode occurred due to fresh beans in 68% of patients, 31% with dry beans. The onset of symptoms varied from 24 hours to 9 days after eating the beans. Patients were admitted to the hospital because of change in urine colour, severe anemia and jaundice. About 80% of the patients were admitted between the third and the sixth day after ingestion of the beans, all patients admitted before the sixth days were transfused. G6PD activity was measured for only 41 males, it was completely absent in 28 males (70%), the remaining 13 patients had a low activity not exceeding 10% of the normal mean.[26]

A study was conducted by Meloni T. and his colleagues in Children Hospital of Sassari, Naples, Italy. The study reported 948 patients with acute hemolytic anemia following ingestion of fava beans, certain drugs and during infection. The highest percentage of hemolytic crises was due to fresh fava beans in 895 patients (94.4 %), while dried beans were the cause in only 28 patients, hemolytic anemia due to frozen beans were seen in only

3 children. No patients of favism were observed in breast fed babies whose mothers had eaten fava beans. The male sex proved to be the commonest hit. Hemoglobin values were lower than or equal to 7 gm/dl in about 75% of males and 50 % of females. Total bilirubin values were lower than 6 mg/dl in about 75% of males and 85 % of females.[27]

Four male infants from Iraq were reported by Taj-Eldin S. during the period from 1962 to 1968, only one patient was described in details; a four months male infant was exclusively breast fed, his mother had eaten boiled, dried fava beans. After two days he became pale, drowsy, and passed dark urine. He was ill, apathetic, and icteric. The spleen was not palpable, and the liver was 2 cm below costal margin. Hemoglobin was 3.8 g/dl, reticulocyte count was 7%, total bilirubin was 4.2 mg/dl (indirect reacting 3.6 mg/dl), and direct Coombs test was negative. Blood transfusion was given and the patient made a complete recovery. The other three patients were all exclusively breast fed male infants. In each infant, the symptoms noticed were pallor, icterus and change in urine colour. Their previous history and family history were not significant. All patients had negative coombs test, deficiency of the enzyme G6PD was proved by estimation of enzyme level in all infants. One of them his mother showed deficiency of the enzyme, but the father's enzyme level was normal. As the patients were all exclusively breast fed and their mothers had eaten fava beans in the preceding days, the conclusion that the active substance in fava beans was transmitted from the mother to the infant through breast milk.[28]

A prospective study was conducted by Darbandi B. and his colleagues at the 17th Shahrivar

Hospital in Iran. It included 101 patients who were admitted in the period from October 2011 to September 2012 with favism, 72 males and 29 females were studied, male to female ratio was 2.4:1. The peak age was between 2-4 years. The most referral to hospital occurred in spring 79.2%.[29]

A retrospective and descriptive study was conducted by Laosombat V. and his colleagues at Songklanagarind Hospital in Thailand, It was done in the period from January 1982 to December 2003. The study reported 225 patients (210 boys and 15 girls) with acute hemolysis following ingestion of fava beans, drugs, and during infection. Favism was found in only 8 patients (3.6%) patients, all of them were boys, one half of these patients were younger than 2 years, and three patients were between 2-5 years old. Sudden onset of anemia was found 1 to 3 days after ingestion of dried fava beans, the classic features of favism including pallor, hemoglobinuria, and jaundice were detected in all patients. At admission the hemoglobin concentrations in these children were ranged from 3.3 to 7.8 gm/dl, and unconjugated bilirubin levels were elevated in all patients, The G6PD level was low in all favic patients.[30]

A retrospective descriptive study was conducted by Alavi S. and his colleagues in the period from March 1995 to March 2001**,** data were collected from Mofid University Hospital of Children in Tahran. Patients with acute hemolysis after fava beans ingestion were included, the total number of patients was 523, 75.7% were males, the mean age of

Patients were 27.7 months ± 46.4. Dark urine, pallor, and jaundice were common manifestations of favism (96.6%, 75.3% and 70% respectively).[31]

A retrospective study was conducted by Nourz A. and Suliman M. in the period from 1st of December 2001 to 31st of May 2002. Data were collected from Children Hospital– Benghazi. Eighteen patients with acute hemolysis following exposure to fava beans were included. The peak age was from 1 to 3 years, male to female ratio was 2.6:1, family history of favism was found in 50% of patients. Five out of 18 patients (27.8%) had history of neonatal jaundice. Type of fava beans was mainly cooked in 10 patients (55.55%), raw in (33.33%), inhalation of fava beans pollen and breast milk each were the cause of hemolysis in 5.56% of patients. The time elapsed between exposure to fava beans and onset of symptoms ranged from 24 to 72 hours. Change colour of urine was seen in (88.89%) of patients, pallor and jaundice were found in all patients, hepatomegaly and splenomegaly were found in 22.2% and 16.67% of patients respectively, signs of heart failure and shock were not seen in any patient. Hemoglobin values were ranged between 3 and 9 gm/dl, and bilirubin values were ranged between 2.5 to 16.5 mg/dl. Fourteen out of 18 patients (77.8%) followed 2 to 3 weeks after recovery from hemolysis for G6PD enzyme level, which found to be normal in all of them, which is explained by the fact that the older more enzyme deficient RBCs are removed from the circulation and replaced by young cells which are rich in G6PD. An extension of this study was done on 26 favic patients. G6PD levels were estimated for all of them 8 weeks after recovery from hemolysis by spectrophotometer assay, and all of them found to be deficient.[32]

Aim of the study

To find out the accuracy of diagnosis of G6PD deficiency depending on clinical manifestations of favism.

Patients and methods

It is a prospective study including 22 patients who were admitted to Children Hospital– Benghazi from 1st of January 2012 to 31st of December 2013 with manifestations of favism. After hemolysis recovery and return of reticulocytes count to normal level (after 8 weeks), Blood samples from these 22 favic patients were tested for G6PD deficiency in RBCs by quantitative rate reduction test and the enzyme activity was estimated by WHO method. G6PD assay was measured by the number of erythrocytes expressing G6PD activity as $U/10^{12}$ RBCs.

Principle

In our work, the activity of G6PD enzyme was measured spectrophotometrically at 340 nm. The G6PD activity assay is based on the principle of measurement the rate of absorbance of reduced NADP+ (NADPH) in red blood cells hemolysate at 340 nm and 37°C, as described in the following reaction:

$G\text{-}6\text{-}P + 2NADP^{+} + H_2O \rightarrow 5P + 2NADPH + 2H^{+} + CO_2$.[16]

The following reagents were provided with the kit:

Reagent 1 (R1): NADP, buffer, lysing agent.

Reagent 2 (R2): G-6-P, buffer.

Assay procedure

Pipette into EDTA tube (1 ml) of working reagent 1, add (0.01 ml) of blood sample, mix well and incubate for (5-10 minutes) at 37°c then add (2 ml) of reagent 2. Mix well and after two minutes read initial absorbance (A1) by spectrophotometer, repeat the reading five minutes later for A2.

Determine the absorbance/ min (ΔAs/min) = Second reading (A2) – First reading (A1).

G6PD level in ($U/10^{12}$) = (ΔAs /min) x (47778/ N).

(N = Red blood cell count divided by 10^{6}).

Results:

Twenty two patients were studied, twenty out of 22 were males and the other two were females. All of them were presented with favism including the triad of pallor, yellow discoloration of sclera and skin, and dark colour of urine after ingestion of fava beans. Male to female ratio was 10:1 and 19 patients (86.4%) were below 4 years of age. Twenty patients (90.9%) were Libyan and two patients were Egyptian, nationality of mothers was Libyan in 20 Libyan patients (90.9%), and Egyptian in 2 Egyptian patients (9.1%), nationality of grandmothers was Libyan in 18 Libyan patients (81.82%) and Egyptian in 4 patients (two of them were Libyan and two of them were Egyptian). Time elapsed between ingestion of fava beans and onset of symptoms was 1 day in 7 patients (31.8%), 2 days in 11 patients (50%) and 3 days in 4 patients (18.2%). Type of ingested fava beans was raw in 14 patients (63.6%) and cooked in 8 patients (36.4%). Only 2 patients (9.1%) had a previous history of favism and only 4 patients (18.2%) had a history of neonatal jaundice. Positive family history of G6PD deficiency was found in 7 patients (31.8%). Hepatomegaly was found in 3 patients (13.6%), splenomegaly and heart failure were not detected in any patient. Hemoglobin levels at admission were ranged from 4.5 g/dl to 7.8 g/dl and serum unconjugated bilirubin ranged from 3.5 mg/dl to 9.8 mg/dl. Reticulocytes were counted in only 18 patients (81.8%) and all of them had reticulocytosis. Coombs test was done in only 11 patients (50%) and was negative in all of them. All 22 patients were treated with packed cell transfusion. G6PD level was low in all patients ranged from 12.6 to 213 $U/10^{12}$ RBCs.

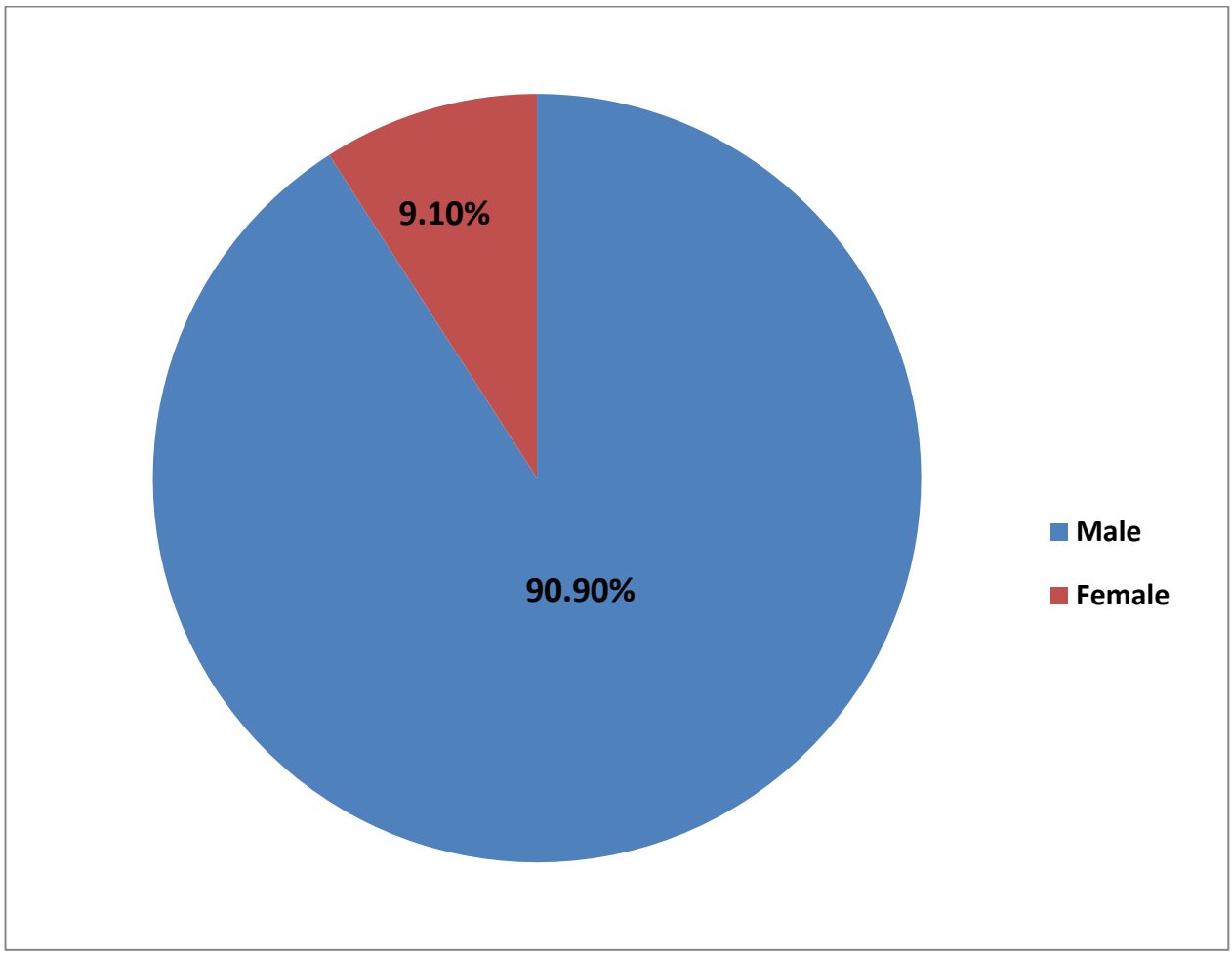

Figure 5.2: Patients distribution according to Sex.

Twenty out of 22 were males and the other two were females, male to female ratio was 10:1.

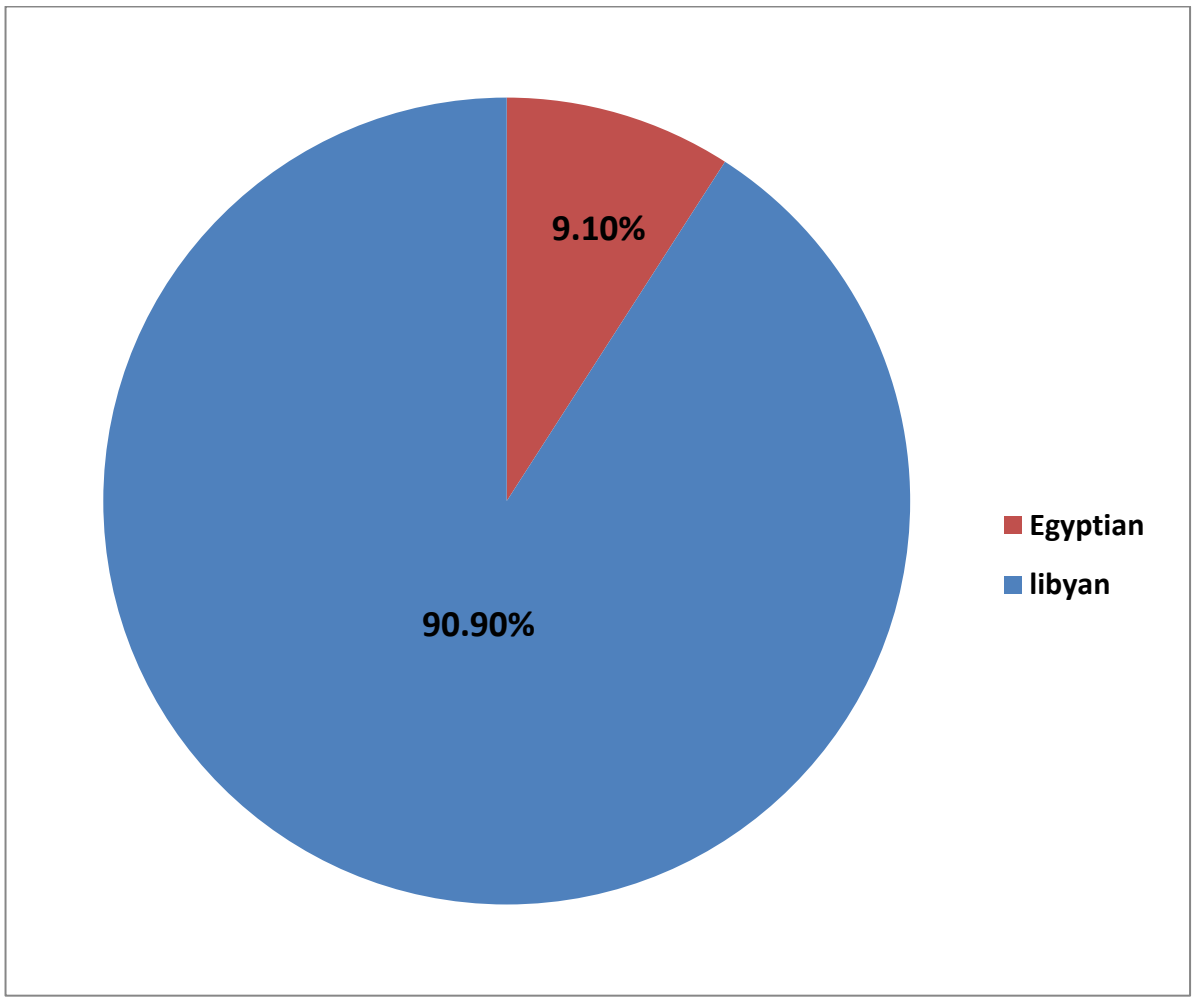

Figure 5.3: Patients distribution according to nationality.

Twenty patients were Libyan (90.9 %) and two patients were Egyptian (9.1 %).

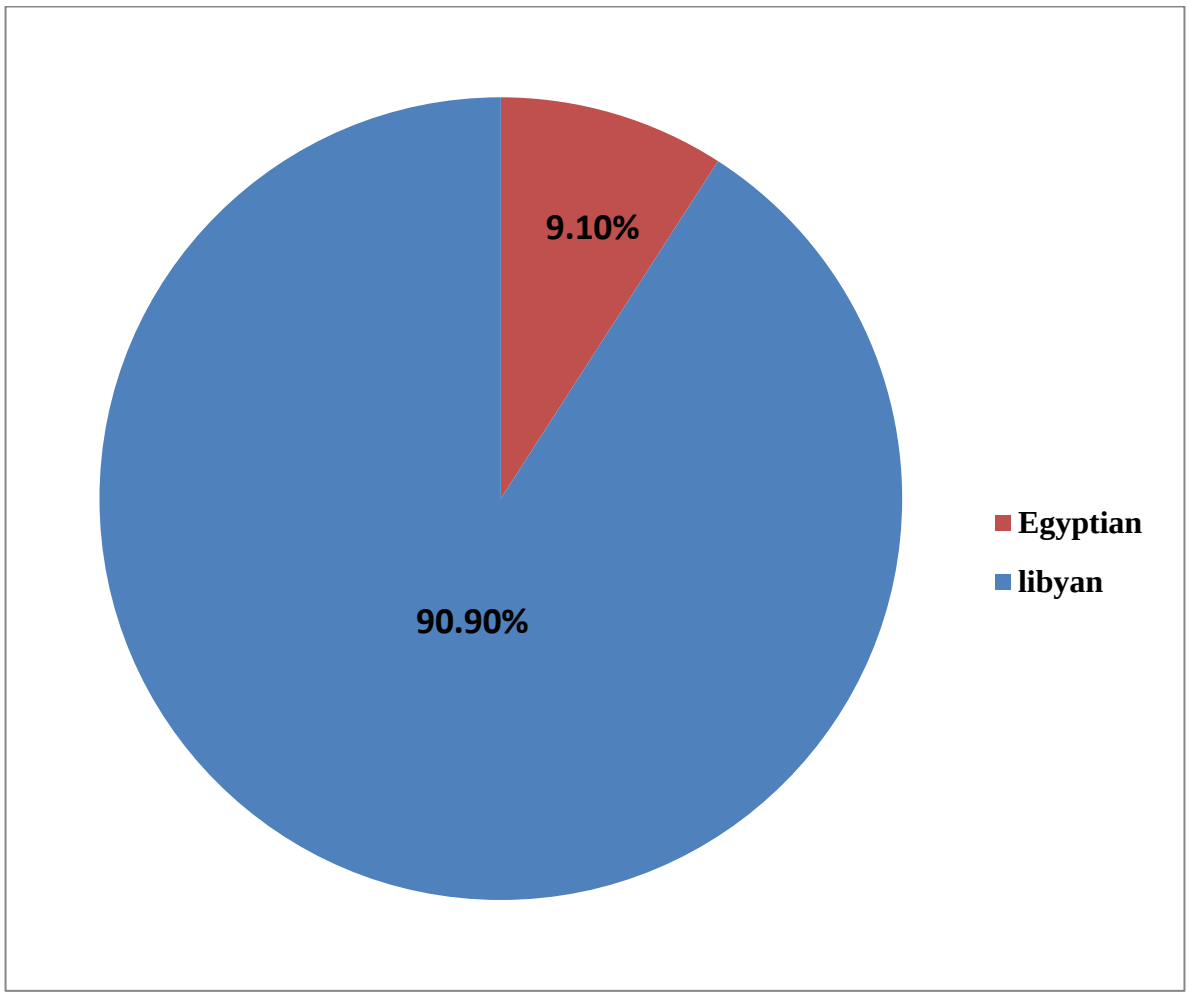

Figure 5.4: Nationality of mothers of 22 favic patients.

Nationality of mothers was Libyan in 20 Libyan patients (90.9%) and Egyptian in 2 Egyptian patients (9.1%).

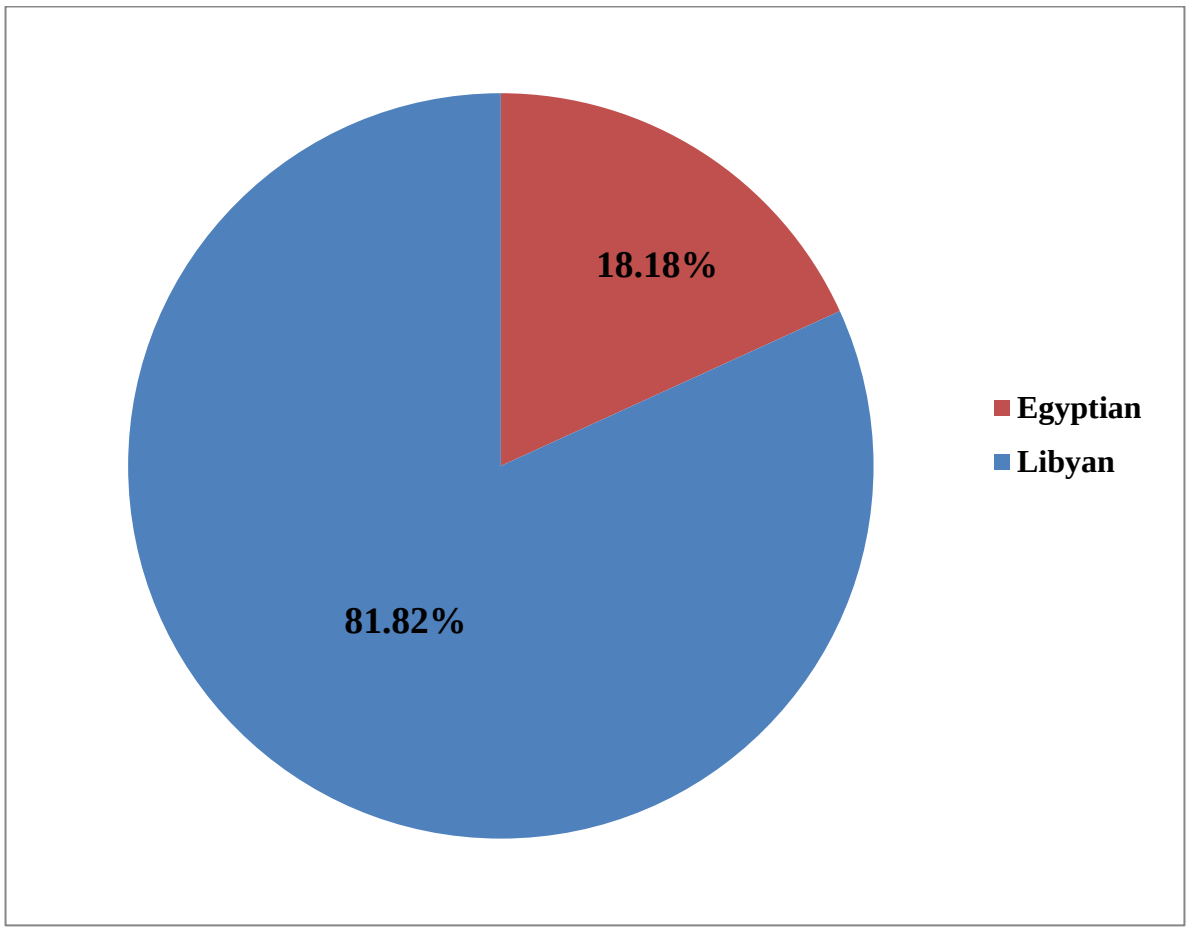

Figure 5.5: Nationality of grandmothers of 22 favic patients.

Nationality of grandmother was Libyan in 18 Libyan patients (81.82%) and Egyptian in 4 patients (two of them were Libyan and two of them were Egyptian).

Table 5.1: Distribution of patient's age and sex during infancy.

Age in months	Male	Female	%
1-4	**0**	**0**	**0**
5-8	**1**	**0**	**4.5%**
9-12	**1**	**0**	**4.5%**

Only two patients were presented with favism during infancy.

Table 5.2: **Distribution of patient's age and sex after infancy.**

Age in years	Male	Female	%
>1-4	15	2	77.3%
5-8	1	0	4.5%
9-12	1	0	4.5%
13-16	1	0	4.5%

Most of patients were below 4 years of age.

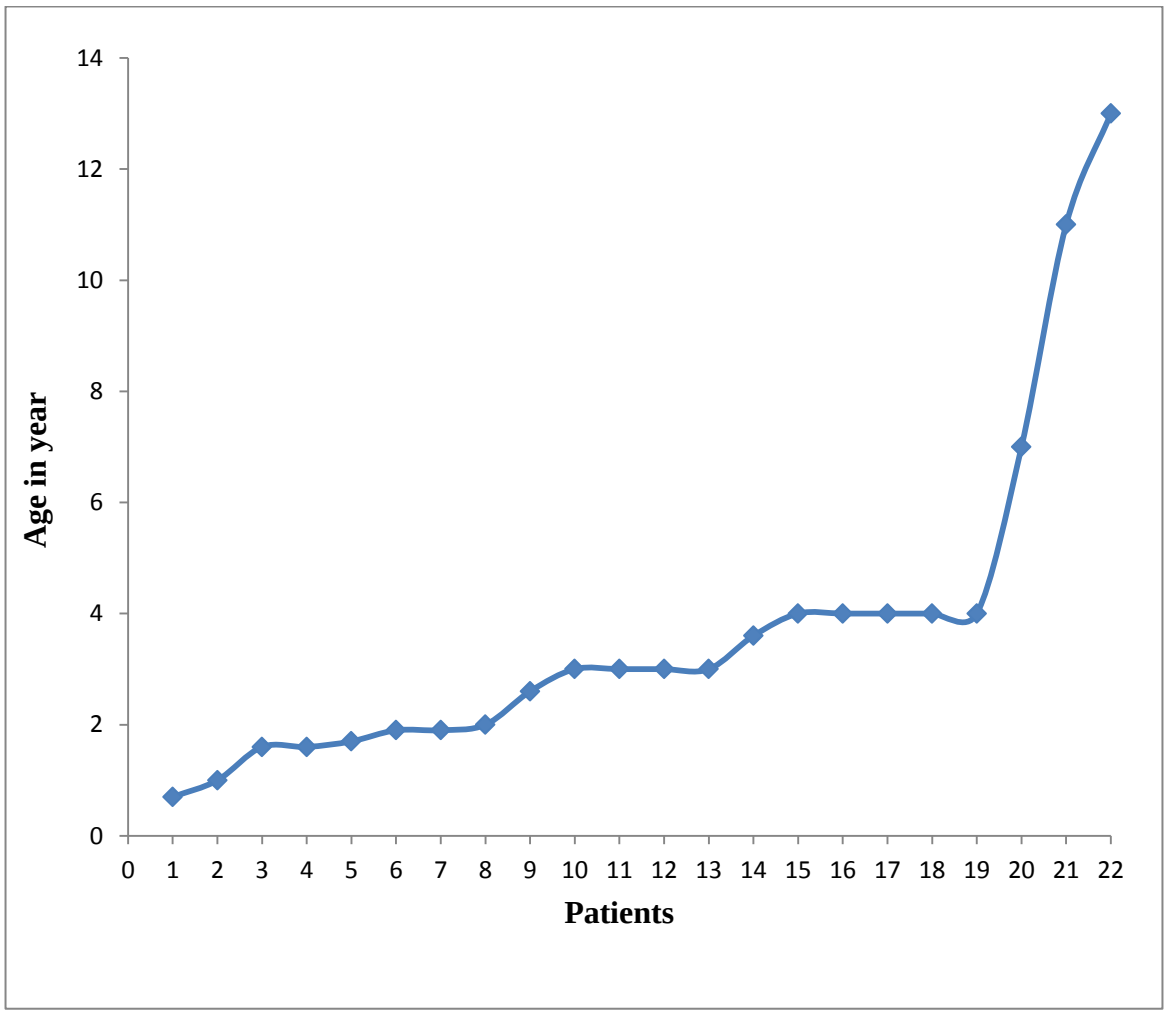

Figure 5.6: Age distribution in 22 favic patients.

*Numbering of patients was according to age from the youngest to the oldest.

Table 5.3: Clinical presentation of patients

Clinical presentation	Number of patients	%
History of fava beans ingestion.	22	100%
Pallor	22	100%
Jaundice	22	100%
Change in urine colour	22	100%
Hepatomegaly	3	13.6%
Splenomegaly	0	0%
Heart failure	0	0%

History of fava beans ingestion, Pallor, jaundice, and change in urine color were found in all patients, hepatomegaly was found in only 13.6% of patients.

Table 5.4: Time elapsed between ingestion of fava beans and onset of symptoms.

Time in days	Number of patients	%
1 day	7	31.8%
2 days	11	50%
3 days	4	18.2%

Onset of symptoms was within 3 days of fava beans ingestion.

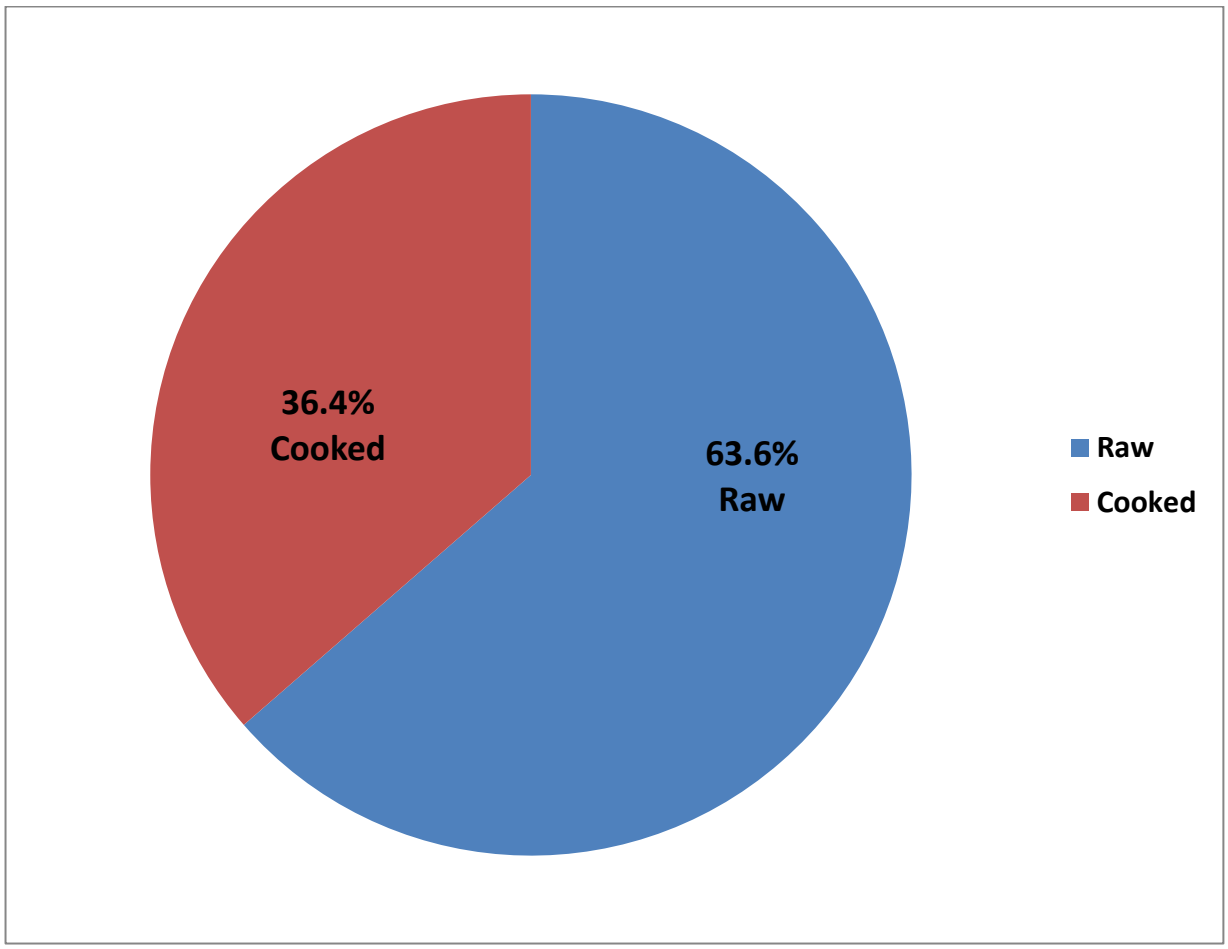

Figure 5.7: Types of ingested fava beans

Type of ingested fava beans was mostly raw in 14 patients (63.6%) and cooked in 8 patients (36.4%). No canned, frozen or dried fava beans.

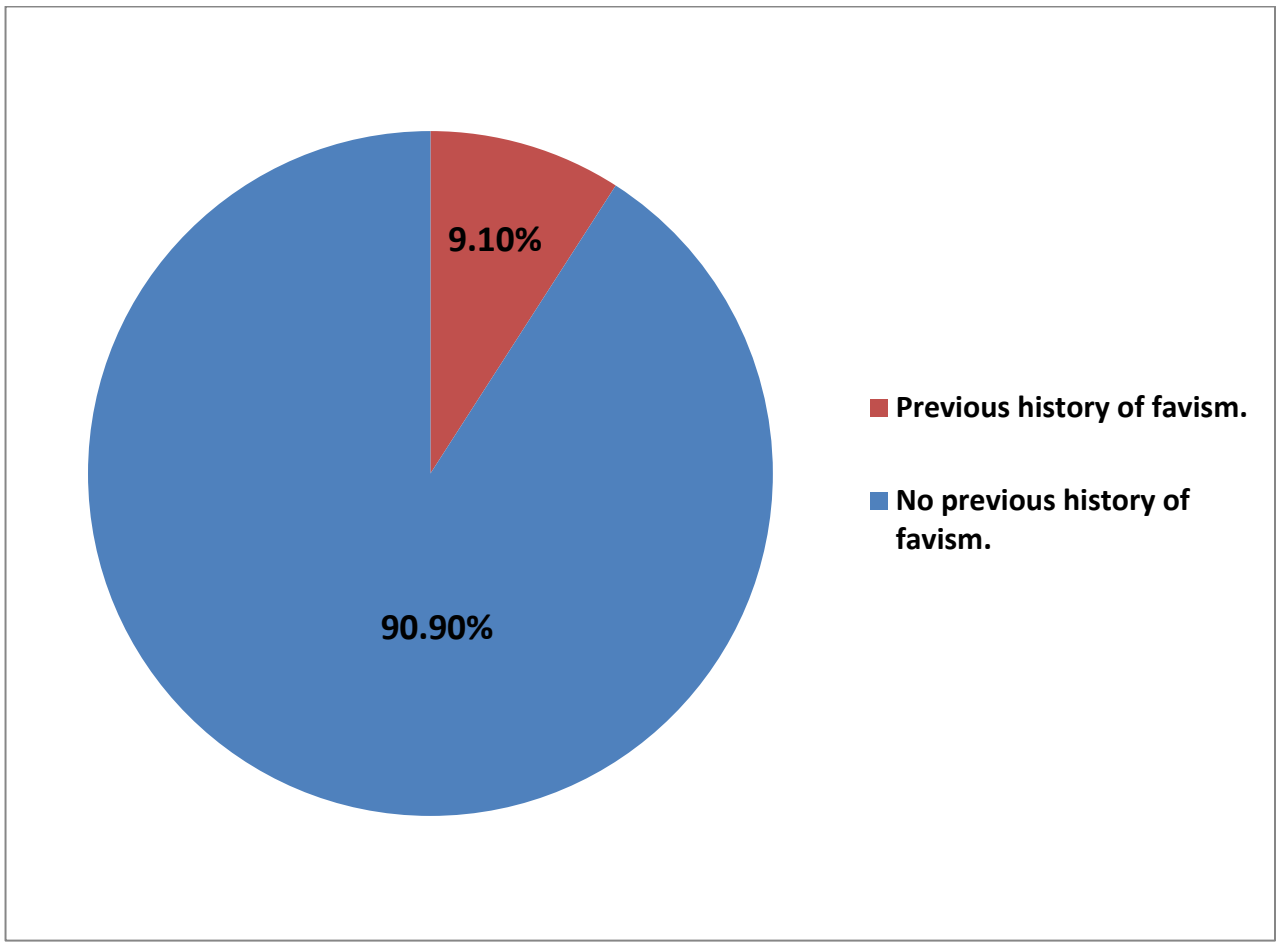

Figure 5.8: Patients with previous history of favism.

Previous history of favism was found in only 2 patients (9.10%).

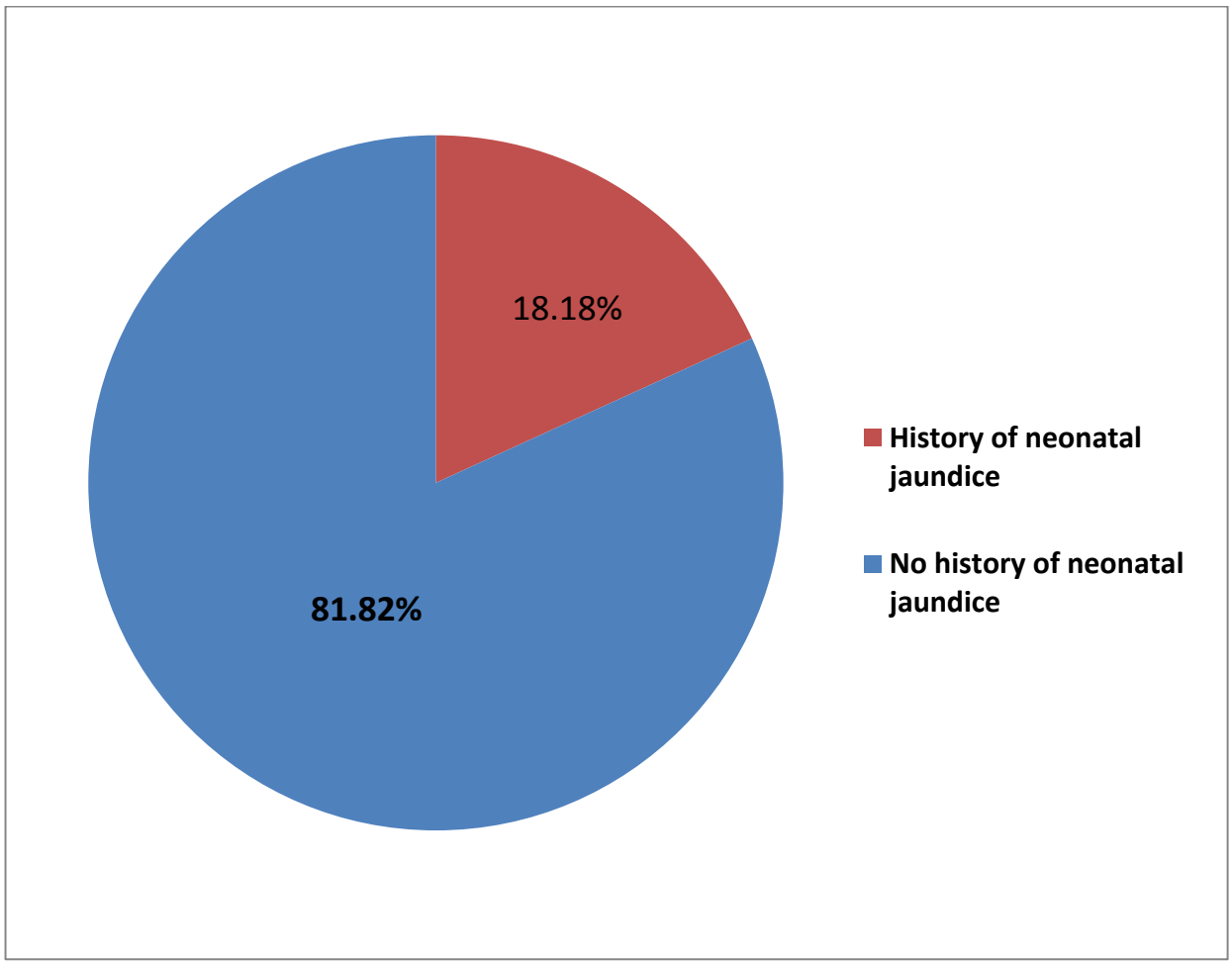

Figure 5.9: Patients with history of neonatal jaundice.

History of neonatal jaundice was found in only 4 patients (18.18%). Two of them were treated with phototherapy and the other two were treated with double volume exchange transfusion.

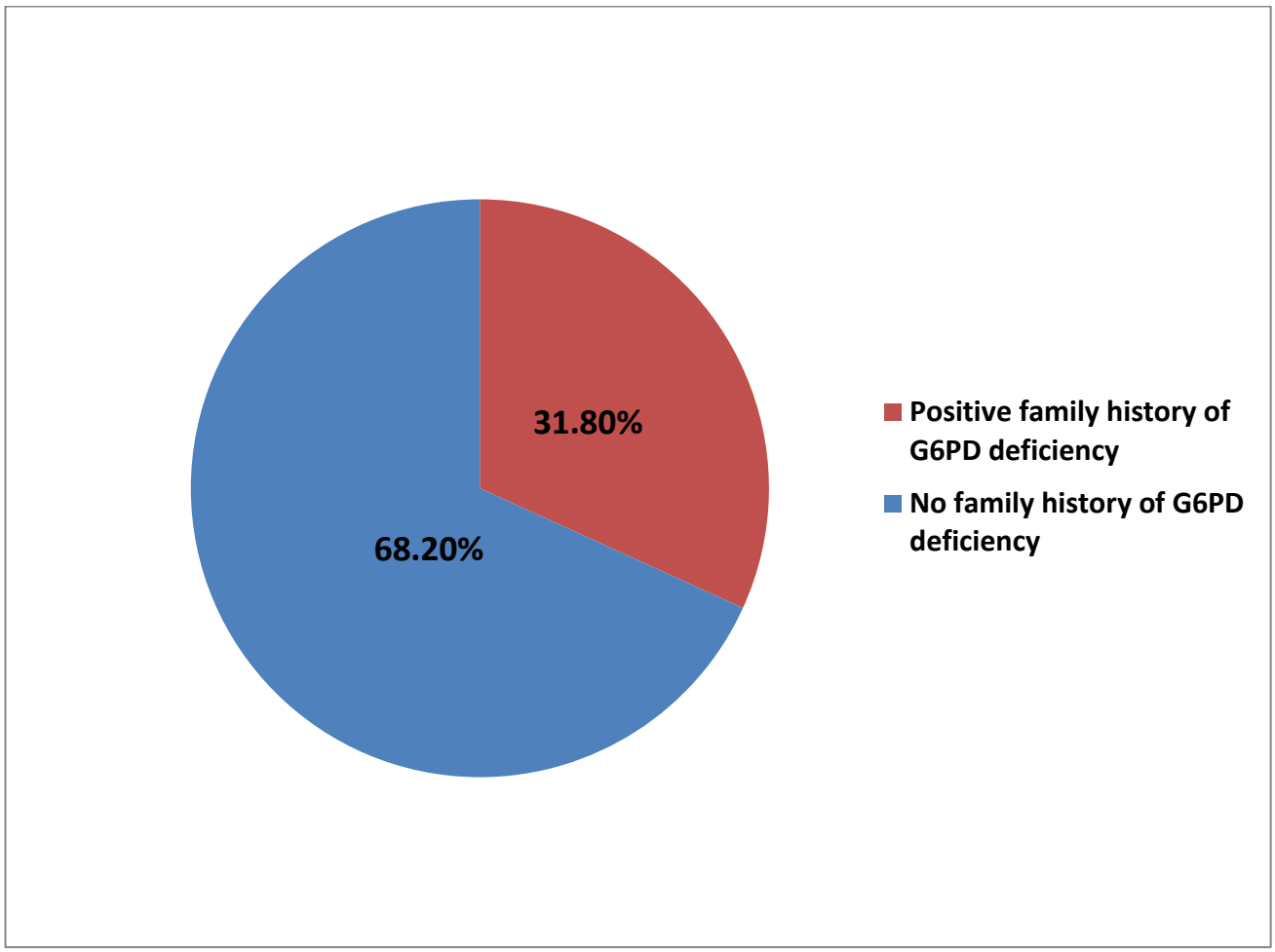

Figure 5.10: Patients with family history of G6PD deficiency.

Positive family history of G6PD deficiency was found in 7 (31.80%) patients.

Table 5.5: The Lowest and highest hemoglobin level at admission.

The lowest hemoglobin	4.5 gm/dl
The highest hemoglobin	7.8 gm/dl

Low hemoglobin levels were found in all patients ranged from 4.5 g/dl to7.8 g/dl.

Table 5.6: The Lowest and highest unconjugated bilirubin level at admission.

The lowest unconjugated bilirubin	3.5 mg/dl
The highest unconjugated bilirubin	9.8 mg/dl

High levels of unconjugated bilirubin were found in all patients ranged from 3.5 mg/dl to 9.8 mg/dl.

Table 5.7: WHO Classification of G6PD deficiency by the number of erythrocytes expressing G6PD activity as U/10^{12} RBCs.

Classes	Patients No.	%	G6PD level in U/10^{12} RBCs.
Class 1	0	0%	< 4.8
Class 2	6	27.3%	4.8-48.3
Class 3	16	72.7%	48.3-290
Class 4	0	0%	290-412
Class 5	0	0%	>412

G6PD levels were low in all patients ranged from (12.6 - 213 U/10^{12} RBCs).

Normal G6PD level is (290 – 412 U/10^{12} RBCs).

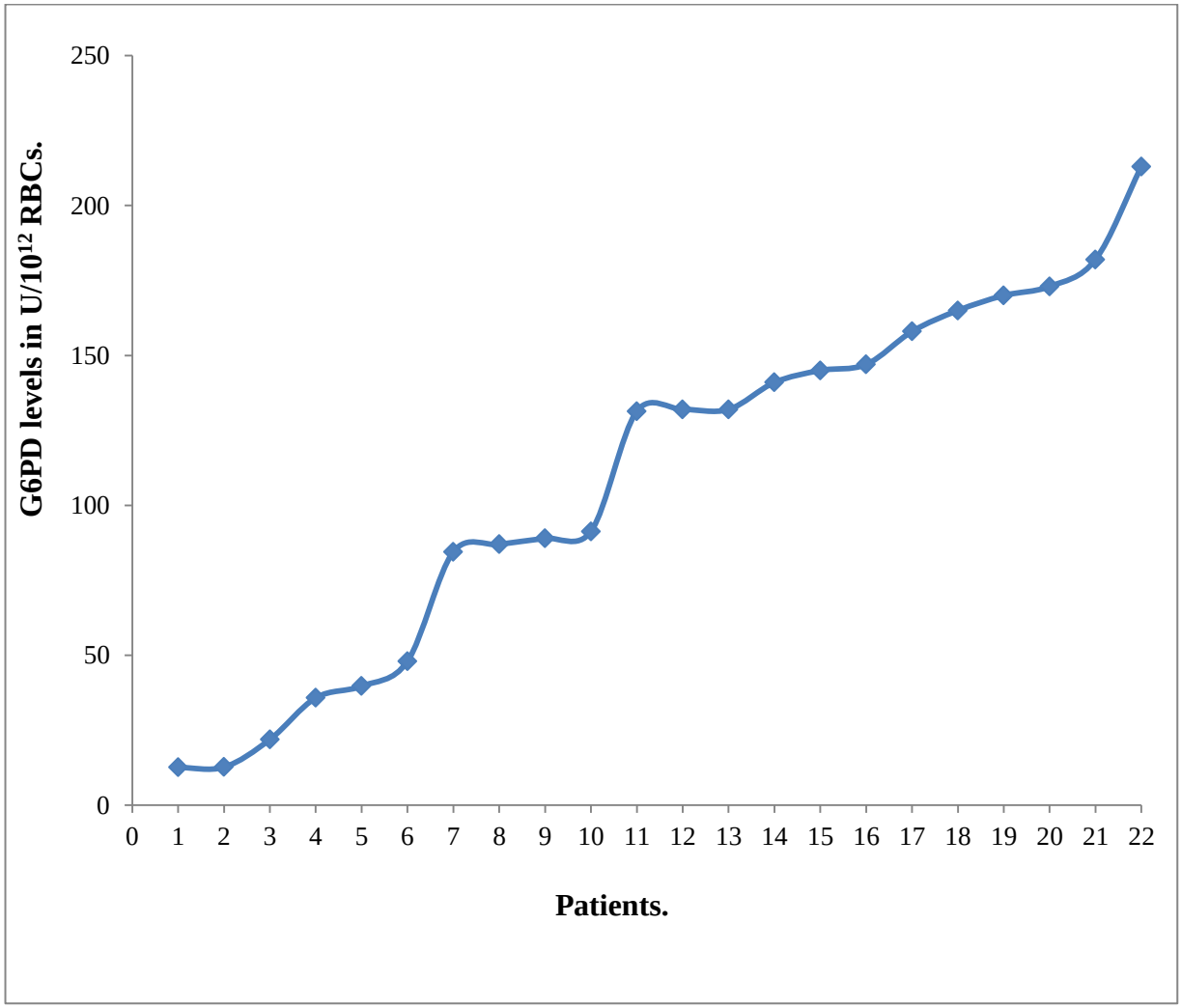

Figure 5.11: G6PD levels in U/10^{12} RBCs in 22 favic patients.

Most of patients (72.7%) were classified as class III (48.3-290 U/10^{12} RBCs).

*Numbering of patients was according to G6PD level from the lowest to the highest.

Discussion

In this study males to females ratio was 10:1, which is in agreement with other studies conducted by Sirdah M.[25] and Alavi S.[31] The G6PD deficiency gene is inherited as a sex linked. Although, male patients are more prone to the disease than females,[33] an increase in the number of female patients is noted in many studies,[33,34] they explained that by failure of screening methods to find out many heterozygote females.[34]

The highest incidence was between 1 and 4 years of age, which is similar to another study conducted by Darbandi B,[29] the decrease in the prevalence of the disease with age could be explained by the avoidance of eating fava beans.[35]

In the present study fresh beans were the main cause of hemolysis in 63.6% of patients, this is in agreement with another study conducted by Luzzatto L,[33] and different from those described by Kattamis C,[26] who described a higher incidence from dried fava beans, this difference may be due to the type of fava beans that commonly used in each community.[26] In agreement with with Kattamis C,[26] and unlike Schiliro,[36] we did not observe favism due to pollen inhalation in our study.

Hemolysis in breast fed babies whose mothers had eaten fava beans has been explained by many authors.[26,28,36] In our study, we did not observe favism in neonatal period, which is extremely rare condition but had been reported by Corchia C,[37] in a G6PD deficient newborn whose mother had eaten fava beans 5 days before delivery.

Our study showed that the time elapsed between ingestion of fava beans and appearance of symptoms was 24 to 72 hours, this is in agreement with the finding of Meloni T,[22] Nourz A,[32] and Luzzatto L.[33] However, the onset of symptoms after 72 hours from ingestion of beans had been described.[33]

History of neonatal jaundice was found in only 4 patients (18.18%), two of them were treated with phototherapy, and the other two were treated with double volume exchange transfusion. On the other hand, a higher incidence of neonatal jaundice (98.5%) was found by Sirdah M.[25] Many authors found that G6PD deficient newborns have a higher level of unconjugated bilirubin comparing to normal newborns with significant exaggeration of physiological jaundice,[38,39] this finding is a different entity from favism and it is of hepatic origin, this is explained by many authors by the fact that the liver of favic patients had impaired capacity for glucuronization with variable degrees.[40,41,42,43,44]

68.2% of patients had negative family history of favism, the parents of the only two female patients in the study did not have history of favism, several causes for this negative family history have been described, among these is the fact that in adults the ingestion of fava beans does not trigger hemolysis in more than 25% of patients,[18,45] another factor may be involved in the pathogenesis of favism is the amount of fava beans ingested in relation to body mass.[33] for these two female patients estimation of G6PD level of their parents is advised.

Regarding the clinical presentation of favism in our study, pallor, jaundice and change in urine colour were evident in all patients (100%), which is in agreement with another study conducted by Laosombat V.[30] Heart failure and hypovolemic shock were not detected in any patient as described by Luzzatto L.[33] At time of admission all patients had low level of hemoglobin and high level of unconjugated bilirubin which is in agreement with the result described by Kattamis C.[26] and Laosombat V.[30] Eighteen patients (81.8%) out of 22 had hemoglobin level < 7gm/dl. All patients were treated by packed cell transfusion, similar to finding of Kattamis C.[26] The guide lines of blood transfusion was described by Luzzatto L.[46] as following, any patient with hemoglobin level less than 7 gm/dl, and any patient with hemoglobin value less than 9 gm/dl in the presence of persistent hemolysis (change in urine colour and hemoglobinuria) must receive packed cell transfusion.

Quantitative estimation of G6PD level was performed for 22 favic patients in RBCs by quantitative rate reduction test, after hemolysis recovery, and return of reticulocytes count to normal level, all patients found to be deficient, which is similar to the result described by Abbas S,[24] Laosombat V,[30] and Nourz A.[32] Most of our patients were classified as class III, this is different from the results described by Shibuya A.[47] and Nafa K[48] in which class II was the commonest.

Conclusion

We can almost diagnose G6PD deficiency depending on full clinical manifestations of favism which includes; ingestion of fava beans followed by change colour of urine then pallor and jaundice, in presence of laboratory evidence of intravascular hemolysis.

Since the G6PD level sometimes is not available, avoidance of fava beans can be adviced to favic patient confidently until diagnosis confirmation by estimation of G6PD level is available.

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الملخص العربي

مرض نقص انزيم جلوكوز 6 الفوسفات ديهيدروجينيز هو مرض متنحي مرتبط بالصبغي الجنسي X , يعتبر هذا المرض اكثر امراض الانزيمات انتشارا في العالم , حيث يؤدي عوز هذا الانزيم الى فقر الدم الانحلالي عقب تناول الفول او الاطعمة المحتوية عليه والذي يعرف بمرض الفوال, و كذلك عقب التعرض لادوية و كيماويات معينة, و عند التعرض للعدوى و الالتهابات.

الهدف من الدراسة

هو معرفة دقة تشخيص مرض نقص انزيم جلوكوز 6 الفوسفات ديهيدروجينيز اعتمادا على العلامات السريرية لمرض الفوال.

الطرق و الادوات

تشمل الدراسة اثنين و عشرين طفلا ممن دخلوا مستشفى الاطفال بنغازي, في الفترة ما بين 1.1.2012 الى 31.12.2013 نتيجة لاعراض مرض الفوال, حيث تمت دراسة بعض الخصائص الاحصائية للمرضى, و من ثم قياس معدل انزيم جلوكوز جلوكوز 6 الفوسفات ديهيدروجينيز بعد انتهاء فترة تكسر خلايا الدم الحمراء.

النتائج

اظهرت النتائج ان اصابة الاطفال الذكور بالمرض تفوق الاناث بنسبة (10:1) , معظم الاطفال كان عمرهم اقل من اربع سنوات, نسبة اصابة الاطفال من الجنسية الليبية كانت (90.9%), الفترة الزمنية بين اكل الفول و ظهور اعراض مرض الفوال تراوحت ما بين يوم الى ثلاثة ايام, طفلان فقط (9.1%) كان لهم دخول سابق للمستشفى نتيجة لاعراض مرض الفوال, اربعة اطفال (18.2%) اصيبوا بمرض اليرقان خلال الشهر الاول من العمر , التاريخ العائلي للمرض كان ايجابيا لدى سبعة اطفال (31.8%), اعراض مرض الفوال من يرقان و شحوب و تغير في لون البول وجدت في كل الاطفال قيد الدراسة, تم قياس معدل انزيم جلوكوز 6 الفوسفات ديهيدروجينيز والذي وجد منخفضا لدى جميع المرضى.

الاستنتاج

علي الاغلب يمكن تشخيص مرض نقص انزيم جلوكوز 6 الفوسفات ديهيدروجينيز اعتمادا على العلامات السريرية لمرض الفوال.