

**DEMOGRAPHIC CHARACTERISTICS OF HOSPITALIZED CHILDREN WITH
FAVISM IN AL-FALLUJAH CITY: A CASE SERIES**Basim A. Alabdely*¹ and Ziad T. A. Al-Rubaie²¹MBChB, DCH, CABP, Head of pediatrics department at Al-Fallujah teaching hospital for maternity and Childhood.²MBChB, MPH, PhDc, Department of medical research, School of medicine, The University of Notre Dame Australia, Sydney, NSW, Australia.***Corresponding Author: Basim A. Alabdely**

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Article Received on 02/10/2018

Article Revised on 23/10/2018

Article Accepted on 13/11/2018

ABSTRACT

Background: Glucose-6-phosphatase dehydrogenase (G6PD) deficiency is one of the most common X-linked inherited pediatric disorder. Acute hemolytic anemia can be developed in children with G6PD deficiency after ingestion of Fava beans, which is called 'Favism'. **Objective:** The objectives of this study are to identify the demographic characteristics of hospitalized children with favism in Fallujah hospital; and to explore the challenges in addressing the research questions for future studies. **Methods:** This was a case series study design. The children admitted to the hospital suffering from acute hemolytic anemia after ingestion of fava bean from March to May 2012 were included in the study. The demographic characteristics and risk factors included: age, gender, consanguinity, residency, onset of hemolysis, onset of admission (in months), severity of illness, potential complications, received urgent blood transfusion or not, duration of stay in hospital and death toll. The primary outcome was acute hemolytic anemia following ingestion of fava bean 'Favism cases'. The distribution of the characteristics was presented in number and percentages. The continuous variables were presented as mean and standard deviation (SD) and range. **Results:** A total of 74 patients were admitted to the hospital suffering from acute hemolytic anemia after ingestion of fava bean. The rate of favism in Al-Falluja city was 6.7%. The mean age of patients was 3.6 years (SD 2.5). 60 (81%) were males and 14 (19%) were females. Most of patients (n=53, 71.62%) were from rural area. The peak month of admissions was during April 2012 (n= 68, 92%). About 80% of cases developed hemolysis within first 72 hours after ingestion of fava beans. Of them, 97% of cases experienced moderate to severe hemolysis. All cases have received urgent blood transfusion. No deaths were reported. **Conclusion:** Favism is a life-threatening and needs prompt intervention. The condition is predominant in males during fava bean season especially in rural areas. Education campaigns should be regularly performed to increase the awareness of the families about this serious condition. Further researches are needed to develop an optimal preventive strategy.

KEYWORDS: Favism, Fallujah, Glucose-6-phosphate-dehydrogenase, hemolysis.**INTRODUCTION**

Glucose-6-phosphatase dehydrogenase (G6PD) deficiency is one of the most common disease-producing enzymopathy in humans. It is inherited as an X-linked disorder. The disorder affects 400 million people worldwide. The disease is highly polymorphic, with more than 300 reported variants. It confers protection against malaria, which probably accounts for its high gene frequency.^[1,2]

Most individuals with G6PD deficiency are asymptomatic unless triggered by other factors such as infection, drugs, or ingestion of fava beans. The peak period of hemolysis is between 24 to 48 hours following ingestion of triggering substances.^[3,4]

In severe cases, the hemoglobin concentration may fall down very quickly and hemoglobinuria and jaundice might be developed. Acute hemolytic anemia that resulted from ingestion of Fava beans in a person with G6PD deficiency is called 'Favism'.^[5,6,7]

The objectives of this study are to identify the demographic characteristics of hospitalized children with favism in Fallujah hospital; and to explore the challenges in addressing the research questions for future studies.

METHODS

This pilot study was a case series design. The children admitted to the hospital suffering from acute hemolytic anemia after ingestion of fava bean from March to May 2012 were included in the study. We excluded mild or

asymptomatic cases.^[8,9] Ethics approval was obtained from Al-Falluja hospital ethics committee.

All patients have been deidentified and evaluated by obtaining history, physical examination, and proper investigations including complete blood count (CBC), blood film, total serum bilirubin (TSB), urinalysis (for urobilinogen) and other investigations (such as chest X-Ray and abdominal ultrasound if indicated). The G6PD enzyme level assay was not reported because the test is not available in the hospital.

The demographic characteristics and risk factors included: age, gender, consanguinity, residency, onset of hemolysis, severity of illness, potential complications, received urgent blood transfusion or not, duration of stay in hospital and death toll. The primary outcome was acute hemolytic anemia following ingestion of fava bean 'Favism cases'. The distribution of the characteristics was presented in number and percentages. The continuous variables were presented as mean and standard deviation (SD) and range. The distribution of the cases was assessed among different categorical groups including age, gender, residency, onset of admission (in months), onset of hemolysis and hemoglobin (Hb) level.

RESULTS

A total of 74 patients were admitted to the hospital suffering from acute hemolytic anemia after ingestion of fava bean. The rate of favism in Al-Falluja city was 6.7%. Sixty patients (81%) were males and 14 (19%) were females (figure 1).

15 patients (20.3%) were products of consanguineous marriages. Of them, eight were males and seven were females

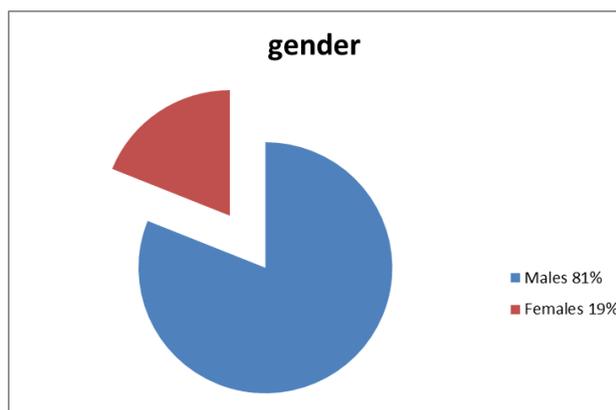


Figure 1: The distribution of Favism in gender.

The mean age of patients was 3.6 years, (SD 2.6). The minimum age of admission was eight months and the maximum were 12 years (table1).

Table 1: Distribution of Favism case among age groups.

Age	Numbers of case	Percentage
< 2 years	22	29.72%
2 – 4 years	26	35.13%
4 – 6 years	15	20.27%
6 – 8 years	5	6.75%
8 – 10 years	4	5.4%
10 – 12 years	2	2.7%

Majority of patients (n=53, 71.62%) were from rural areas around Al-Fallujah city while only 21 patients (28.38%) of the cases are resident of Al-Fallujah city (Urban area) (figure 2).

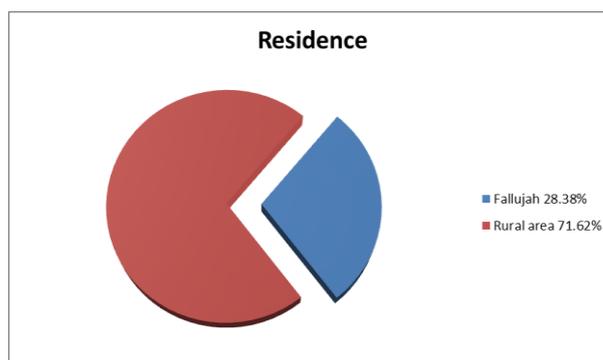


Figure 2: Geographical distribution of Favism cases.

The peak month of admissions was during April 2012 (n= 68, 92%). No admissions were reported after May 2012 (table 2).

Table 2: Distribution of the favism cases according to the onset of admission (in months).

Date of admission	Number of cases	Percentage
March 2012	4	5.4%
April 2012	68	91.9%
May 2012	2	2.7%

About 80% of cases developed hemolysis within first 72 hours after ingestion of fava beans (table 3). Of them, 97% of cases experienced moderate to severe hemolysis. All patients have received urgent blood transfusion. No deaths toll was reported.

Six patients (8.1%) give a history of inhalation of the odor of cooked fava beans. All of them developed hemolysis within 24 hours.

The duration of stay in hospital for all cases is from one to three days except one patient stay for one week due to severe hemolysis associated with complications.

Table 3: Distribution of Favism cases according to the onset of hemolysis after ingestion of fava beans or history of inhalation the odor of the cooked fava beans.

Onset of hemolysis	Number of cases	Percentage
First 24 hours.	40	54%
25 – 72 hours.	19	25.7%
73 – 120 hrs.	15	20.3%

Hemoglobin levels at time of admission were shown in table 4. The patients with Hb level below 4 gm/dl were critically ill and needed prompt resuscitation and life-threatening supportive measures with good outcome.

Table 4: Distribution of Hb levels at time of admission.

Hb levels	Number of cases	Percentage
< 4 gm/dl	4	5.4%
4 – 6 gm /dl	35	47.3%
6.1 – 8 gm/dl	32	43.34%
8.1 – 10gm/dl	3	4.05%

DISCUSSION

Seventy-four patients were identified to have acute hemolytic anemia after ingestion of fava bean. Of them, 60 (81%) were males and 14 (19%) were females. Majority of patients were from rural area (n=53, 71.62%). The disease most prevalent during April 2012 (n= 68, 92%). About 80% of cases developed hemolysis within first 72 hours and most of them experienced moderate to severe hemolysis that required urgent blood transfusion. No deaths were reported.

The main strength of our study is that enrolled all cases admitted to Al-Falluja city suffered from hemolysis due to ingestion of fava bean. The sample is representative of Al-Falluja city and its surrounding suburbs since the hospital is the only referral hospital that managing such cases. However, the main limitation of the study is that the sample was relatively low to allow us to estimate the predictors of favism in Al-Falluja population since the disease is seasonal and can only occur within short period of time (2-3 months) and during the fava bean season in spring.

The rate of the favism is nearly similar to the global prevalence of the disease (6.7% versus 7.1%).^[10] In Iraq, a screening study conducted by Amin-Zaki et al (1972), to compare G6PD deficiency among ethnic groups in Iraq, found that 8.4% of newborns had G6PD deficiency whom identified by blood sample examination. The authors also reported 8.9% G6PD deficiency in adult blood samples.^[11] While Hilmi et al (2002) reported lower prevalence of 6.1% among adults' male aged between 18 and 60 years old.^[12] Al-Mendalawi 2010 reported about 70% of patient experienced hemolysis within 1-3 days after exposure to noxious agents in the

north and middle of Iraq^[13] which is lower than our study estimates (80%).

The common symptoms are neonatal jaundice and acute hemolytic anemia. G6PD deficiency is an X-linked inherited disease that primarily affects males. However, homozygous females are found in populations in which the frequency of G6PD deficiency is relatively high. Therefore, the heterozygous females (carrier) can suffer hemolytic attacks,^[8,9] and this explain why we have identified 19% of our case were females.

The disease is mostly affecting the younger age group (first 6 years of age) and this might be related to the activity of the enzyme. However, this alteration in enzyme activity in relation with the age is not well clearly understood and need to be clearly explained.

Most of our cases (92%) were presented during April and only 2.7% of them were admitted during May despite that fava beans are still available in the markets during May. This reduction in the incidence of the disease during May might be explained either by the awareness of the people about the risk of fava beans (legumes) in precipitating acute hemolysis or the oxidant materials that present in this legume lose its oxidant activity at the end of season. This is also not clearly explained and need to be clarified in future studies. Furthermore, we have identified that the most admitted cases were from rural areas (71.62%) compared to 28.38% from Al-Fallujah city (as urban); and this is may be due to the availability of fava beans in farms in rural area, lack of awareness of the farmers due to low level of education and inadequate preventive measures including lack of control measures of the parents to their children.

Most (96%) of the cases were admitted to the hospital with moderate to severe hemolysis (the hemoglobin level ranges from 4-8 gm/dl) while three cases (4%) was developed progressive hemolysis within 24 hours. Most of the cases developed acute hemolysis within first 72 hours after ingestion of the fava beans (n=59, 80%). Of them 40 cases developed hemolysis within 24 hours. These results highlighted the importance of urgent intervention and provision of diagnostic tools, blood units for transfusion to avoid serious complications including deaths.

As we have highlighted above, we have demonstrated that 19% of the case were affected females despite it is a X- linked recessive inheritance disorder and 20% of cases were identified from consanguineous parents. This is might lead to arise some questions to be answered in the future including:

- Are the numbers of females identified in our results can be explained as homozygous one?
- Is there any role for autosomal recessive mode of inheritance of this disease?

In spite of severe hemolysis and critically ill patients when received in the pediatric emergency ward, no deaths were reported that reflects the good management and rapid intervention by the medical team in pediatric wards.

Our encouraging findings in this pilot study highlighted the need of future study to be conducted in wider samples and to estimate the factors that can be significantly predict acute hemolysis in children with G6PD deficiency. In addition, the current intervention measures and managements need to be weighed against some adverse outcomes such as (adverse effects arise from blood transfusion and duration of hospital stay) to improve these outcomes and prevent complications.

CONCLUSION

The early and acute onset of Favism might lead to severe hemolysis which is life-threatening and need prompt intervention with good follow up. The condition is predominant in males during fava bean season especially in rural areas. Education campaigns should be regularly performed to increase the aware of the families about this serious condition in order to avoid exposure of their children to the precipitating agents such as the fava beans and certain drugs and chemicals. Further researches are needed to develop an optimal preventive strategy.

We recommend conducting further researches to explore the underestimated epidemiological factors of the disease in order to explain the facts and evidences that we have reported in our study results.

ACKNOWLEDGMENT

We would like to thank Al-Fallujah hospital medical staff for their kind help in data collection and fill the questionnaire forms.

Author Contributions

BA and ZA contributed in development of research questions. BA led data collection and contributed in the writing and interpretation of the results. ZA led data analysis and contributed in the writing and interpretation of the results.

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