

Relationship between Mothers' Ingestion of Fava Beans and Occurrence of Favism Attack among Their Breastfed Infants

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Abstract

Background: Favism is genetic acute hemolytic anemia that results from the ingestion of fava beans and associated with Glucose-6-phosphate dehydrogenase (G6PD) deficiency. Thus, breastfed infants that have favism certain foods can potentially pass via the breast milk and cause hemolysis. **Aim:** to assess the relationship between mothers' ingestion of fava beans and occurrence of favism attack among their breastfed infants. **Design:** a correlational descriptive design was conducted. **Sample:** A purposive sample of 50 mothers and their breastfed infants suffered from favism were involved in the study. **Setting:** The study was carried out at outpatient clinic of hematology and emergency outpatient clinic at Pediatric University Hospital which affiliated to Cairo University Hospitals. **Tools:** The following tools were utilized for data collection: (1) Interviewing questionnaire that included demographic data for the studied infants and their mothers, and (2) A structured questionnaire used to assess the relationship between mothers' ingestion of fava beans and occurrence of favism attack. **Results:** the current study findings revealed that nearly two thirds of infants were between 6 to <12 months of age, most of mothers ingested fava beans before breastfeeding with mean duration 2.38 ± 1.52 hours and the mean duration of infants' occurrence of favism attack after their mothers ingested fava beans and give breastfeeding was 46.48 ± 10.91 hours. Also there were highly statistically significant differences between frequency of occurrence for favism attack and infants' age, family history of G6PD deficiency and a statistical significant difference was found with the male gender. **Conclusion:** The current study concluded that there were highly statistically significant differences between infants' frequency of occurrence of favism attack and infants' breastfeeding status, time and type of fava beans ingested by their mothers, a statistical significant difference was found between infants' occurrence of favism attack with mothers ingestion for large amount of fava beans, duration of mothers ingestion of fava beans before infants' breastfeeding while no statistical significant difference was found with names of fava beans. **Recommendations:** health education program should be designed and provided for mothers of children with G6PD deficiency particularly favism for prevention and management.

Key words: G6PD deficiency, Breastfed infants, Mothers, Fava beans.

Introduction

Favism is more life-threatening illness in children than in adults (Martínez et al., 2020). Favism is a common type of acute hemolytic anemia, especially among children that results from the ingestion of fava beans and associated with G6PD deficiency (Ravikumar & Greenfield, 2020). Favism is the most common form of G6PD deficiency (Steiner, Lüdemann & Kramer-Steiner, 2018). The prevalence of G6PD deficiency among Egyptian neonates is 8.9 % (Abo El Fotoh & Rizk, 2016). In Egypt, prevalence of favism had been estimated to be 26% of infants and children with acute hemolytic attack (Pulkkinen, Zhou, Lampi & Piironen,

2016). It is common among males between the ages 2 and 10 years (Ata, Muthanna, Javed, Uddin & Yassin, 2020). Although most affected children are asymptomatic, exposure to oxidative stressors such as fava beans, certain drugs or infection can elicit acute hemolysis (Valencia, Ocampo, Arce-Plata, Recht & Arévalo-Herrera, 2016).

Breastfed infants that have G6PD and favism certain foods and drugs can potentially cause hemolysis and pass via the breast milk so avoid certain foods and other substances in mothers' diet to avoid creating a G6PD crisis will improve health outcomes of infants with favism (Steiner et al., 2018). Favism severe reaction occurring within 6 to 24 hours of the fava bean

ingestion as a result of massive destruction of red blood cells (Siler et al., 2016). In affected children, favism is greatly influenced by the amount of beans ingested and probably by many other factors as infection (Luzzatto, Ally & Notaro, 2020). Fava beans are popular food with high protein content for human (Getachew, Vandenberg & Smits, 2018). Fava beans contain toxic glycosides namely vicine and convicine, these toxic glycosides are the factors responsible for favism for humans particularly young males that have a deficiency of G6PD activity (Zam & Belal, 2020).

Children presenting with an attack of favism who is brought to the emergency department with hemolytic attack of pallor, jaundice and often fever. Additionally, fava bean ingestion can cause methemoglobinemia, an abnormal variation in the hemoglobin in which the ferrous iron in heme is oxidized to the ferric state (Ata et al., 2020). Children with G6PD deficiency who exposed to certain foods, chemicals and medicines causing symptoms of hemolysis include pale skin, yellow skin, eyes and tongue, dark yellow/brown urine, tiredness, fast heartbeat and difficulty breathing, fever, neonates has G6PD deficiency develops neonatal jaundice need to be treated with phototherapy and in severe cases blood transfusion is needed to treat haemolytic crisis sometimes no treatment is necessary as the red cells repair themselves over time (Wetern Ministry of Health, 2018 & World Health Organization (WHO), 2018).

The pediatric and community health nurse play a vital role in primary prevention regarding health promotion and disease prevention through health education and the secondary prevention through early detection and early management of favism. The care of children suffering from favism depending on mothers' awareness by the triggering factors. Thus favism attack is easily controlled if the prohibited substances are avoided so, mothers should be checked anything provided to the affected infants to avoid certain foods, medications and other substances that can trigger an onset of hemolysis. In addition, a breastfeeding mother who is not G6PD deficient can have an infant who is G6PD deficient needs to avoid certain foods and other substances in mothers' diet to avoid creating a G6PD crisis in the infant (Akoijam et al., 2016).

Significance of the Study

Glucose-6-phosphate dehydrogenase deficiency is the most common enzymopathy, children with favism are always G6PD-deficient but not all G6PD-deficient individuals develop hemolysis when they ingest fava beans (Bancone & Chu, 2021). The vast majority of cases of favism occur in children with severely deficient variants of G6PD and the severe form occurs more often in the Mediterranean and African population (Antwi-Baffour, Adjei, Forson, Akakpo, Kyeremeh & Seidu, 2019). The prevalence was high 56.5% in males and 43.5% in females with mean age of 1.93 ± 3.98 years (Albagshi, Alomran, Sloma, Albagshi, Alsuweel & AlKhalaf, 2020).

In Egypt an overall prevalence of G6PD deficiency of 4.3% of neonates with a male:female ratio of 3.2:1 that under certain condition can cause hemolytic manifestations (Abo El Elella, Tawfik, Barseem & Abo El Fotoh, 2017). There were a total of 8.96 million people born with G6PD deficiency in 2019 and a total of 438 million living with G6PD deficiency. G6PD deficiency was responsible for 13000 all-ages deaths, 367 of which were in children under 5 (The Institute for Health Metrics and Evaluation (IHME), 2019).

There are serious complications that occur in neonates born with G6PD deficiency as jaundice and acute hemolytic anemia so those affected children need further treatment and care (Richardson & O'Malley, 2022). Jaundice and acute hemolytic anemia are a serious health problem which developed in infants with favism that raise the risk of morbidity and mortality (Ong et al., 2017). Consequently, Pal et al., (2019) recommended that those affected infants need for further assessment, early detection, care and treatment to prevent any hazards. Ahmed and Saad (2017) reported that the second most common cause of inpatient admissions in Pediatric Hospital Cairo University was acute haemolytic crisis in spite of blood transfusion 90% of those with acute haemolytic crises were due to G6PD deficiency, the prevalence of G6PD deficiency in Egypt is estimated to be 5.9% and the peaking of cases in Egypt reflects the coincidence of haemolysis with beans that grow best in spring season.

In the same line, Anderson (2018) reported that infant's exposure to maternal foods that might cause immediate adverse reactions in the infants

such as fava beans which cause hemolysis, subsequent pallor and jaundice in breastfed infants after maternal ingestion of fava beans. Additional medicinal herbs and foods that may trigger hemolysis include various types of beans (in addition to fava), camphor, naphthalene and henna (**Luzzatto & Areses, 2018**). Hemolytic anemia and resulting jaundice due to favism occur in newborns who breastfeed from mothers who ingest fava beans that used more commonly for food and feed (**Harcke, Rizzolo & Harcke, 2019**). **Luzzatto and Areses (2018)** concluded that the active agent in fava beans was transferred from mother to child through breast milk and found that toxic agent is capable on causing acute hemolytic anemia among their breastfed infants.

Favism via breast milk can be quite severe from hemolysis and complication as breastfed infant developed renal failure then death 10 days after maternal fava bean ingestion, affected 18 breastfed and 4 exclusively breastfed male Arab infants developed symptoms 2 to 6 days after maternal ingestion of fava beans (**El Sayed, Tantawi, Adly & Farouk, 2012**). Overall, the male to female ratio of the patients was 6-2 and the highest frequency of attacks was in May when fava beans ripened, so it is recommended that mothers nursing a G6PD deficient infant should not consume fava beans (**Sköld, Svendsen & Pedersen, 2017**).

In spite of favism is a serious disease a recent study by **Elgammal, Bahgat, El-Shanshory and Farag (2020)** found that the majority of the nurses showed poor knowledge and practice related to favism children and the majority of the infants with favism acquired the hemolysis attack because of lack knowledge of their mothers about the predisposing factors for the disease. So preparing the health care providers and primary care givers to manage and prevent factors that agitate occurrence of favism attack and assessment the relationship between mothers ingestion of fava beans and occurrence of favism attack among their breastfed infants are very important to enhance wellbeing of infants and minimize burden in the clinical setting and community (**Abo Elfotouh & Rizk, 2016**).

There are few studies conducted on the prevalence of G6PD deficiency from favism among Egyptian infants children as well as on the breastfed infants (**Ellella, Tawfik, Barseem & Moustafa, 2017**). There are no available studies in Egypt to assess the relationship between

mothers' ingestion of fava beans and occurrence of favism attack. Carrying out the current research will help spot the light on this significant silent health problem in Egypt. Moreover, conducting the research will add to the nursing body of knowledge, so the aim of the current study was to assess the relationship between mothers' ingestion of fava beans and occurrence of favism attack among their breastfed infants.

Aim of work:

The current study was aimed to assess the relationship between mothers' ingestion of fava beans and occurrence of favism attack among their breastfed infants.

Research questions:

To fulfill the aim of the study the following research questions were formulated:

1. Is there a relationship between occurrence of favism attack among breastfed infants and their mothers' ingestion for fava beans?
2. What are the most common factors that agitate occurrence of favism attack among breastfed infants of mothers' ingested fava beans?
3. What are the manifestations of favism attack among breastfed infants of mothers' ingested fava beans?

Materials and Methods

Design:

A correlational descriptive design was conducted to achieve the aim of the current study.

Research setting:

The study was conducted at the outpatient clinic of hematology at Pediatric University Hospital (Al-Monira) which affiliated to Cairo University Hospitals, the outpatient clinic of hematology receives children suffering from blood disorders mainly sickle cell anemia and thalassemia while children with favism attend with their parents only for follow up the laboratory investigation and checkup on children health condition after occurrence and recovery of favism attack in the hematology outpatient clinics, and the affected children attend to outpatient clinics three days per week.

Subjects:

A purposive sample was used to recruit 50 mothers and 50 their breastfed infants according to the study period for data collection, breastfed infants who attended for follow up after favism attack recovery in the

outpatient clinic of hematology also attended for management at the emergency outpatient clinic in the Pediatric University Hospital (Al-Monira) and agreed to participate in the current study and eligible for inclusion criteria.

Inclusion criteria:

- All breastfed infants and young children from birth until 2 years of age and diagnosed with favism.
- Infants taking breast feeding (exclusive and not exclusive).
- Infants who have last favism attack caused by their mothers ate fava beans.
- Mothers of infants diagnosed favism regardless mother's age, educational level and residence.

Exclusion criteria:

- Infants who had another blood disorders as sickle cell anemia or thalassemia caused the hemolytic attack as they diagnosed by the doctor at hematology clinic.
- Infants who have favism attack caused by another factors except their mothers ate fava beans such as infants directly ate fava beans, illness or administered oxidant drugs.

Tools of data collection:

The required data was collected through the following tools, tool 1 and 2 were designed in simple Arabic language and developed by the researchers after extensive review of related literature Ghali1 and Al Mamoori (2020), Hagag et al., (2018) and Ahmed and Saad (2017).

Tool (1) *An interviewing questionnaire*, It consisted of 10 multiple choice questions which included demographic data for the studied mothers as (age, educational level, job, place of residence, type of family and number of children) and demographic data for breastfed infants with favism as (age, gender, rank and family history of G6PD/favism).

Tool (2) *A Structured questionnaire used to assess the relationship between mothers' ingestion of fava beans and occurrence of favism attack*, it composed of three parts in form of 15 multiple choice questions and cleared as the following:

Part I: Infants' breastfeeding status included 3 multiple choice questions about feeding status for breastfed infants (type of breastfeeding, duration of exclusive

breastfeeding, type of introducing food beside breastfeeding).

Part II: Factors agitate occurrence favism attack after mothers ingested fava beans sheet included 5 multiple choice questions (amount of fava beans ingested by mothers, type and name of fava beans ingested, duration and frequency of occurrence favism attack after fava beans ingested).

Part III: Manifestations and managements of favism attack sheet among breastfed infants as reported by mothers included 7 questions about the manifestations of favism attack as pallor, yellowish discoloration, urine dark orange in color and enlarged lymph nodes, and also type of management the infants received, duration of recovery and discharge from hospital).

Validity and Reliability: tool two was tested and evaluated for their face and content validity by three experts in nursing and medical fields /Cairo University and also to ascertain relevance, clarity and completeness of the tools, experts elicited responses were either agree or disagree for the face and content validity was done. Testing reliability of proposed tools was done by using Cronbach alpha test, it was 0.78.

Ethical considerations: once a formal acceptance was taken from the director of the Pediatric University Hospital to collect the data from the outpatient hematology clinic, a meeting was scheduled with the director of outpatient clinics to present the current research study. Once all necessary consents were granted, a date was chosen to conduct the study according to the available time of the mothers and their infants with favism. A detailed description about the study and questionnaires was given to the mothers. Study participants were informed that they had the right to refrain from participating in the study at any time without experiencing any negative consequences. Informed consents were obtained from all eligible participants who agreed to participate in the study. Data confidentiality and patients' privacy were secured. Code numbers were created and kept by the researchers to keep patients' anonymity.

Pilot study: A pilot study was conducted on 10% of the study sample (5 mothers and

their infants with favism) who met the inclusion criteria of the study at Pediatric University Hospital in the outpatient clinic of hematology to assess the applicability and estimate the time required to fulfill the tools. Minor modifications were done in certain sentences as rephrasing, rearrangement of multiple choice questions in the structured questionnaire to assess the relationship between mothers' ingestion of fava beans and occurrence of favism attack, adding the question regarding duration to occur manifestations of favism attack after mother's ingestion of fava beans. The pilot study was excluded from the total sample size.

Procedure: An official permission was obtained from the director of the Pediatric University Hospital. A meeting was scheduled with the directors of the outpatient clinic of hematology to present the research study. The researchers were attending the outpatient of the previous mentioned setting, by using a time schedule, 3 days/week, from 8 to 1 pm and met the mothers and their infants diagnosed with favism and attending at the hematology clinic for follow up and checkup only after favism attack treated and recovered, the mothers attend once or twice with their infants after recovery of attack until their infants became stabilized. Data collection was carried out over a period of 12 months starting from January 2020 ended at December 2020.

A formal written consent obtained from mothers to get their acceptance. The researchers conducted visit to the outpatient clinic to explain the aim of the study to the studied mothers and to gain their cooperation and acceptance to share in the current study, tool one and two were filled by the studied mothers through an interview with the mothers have infants with favism and attended for follow up after recovery of favism attack, also the researchers collected the data from the mothers at the waiting room in the outpatient clinic, the researchers met each mother once to fill the tools during the time of follow up in hematology clinic, for mothers who could not read and write the researchers filled data after asking them and choose the choices based on mothers response for the questions. The time spent to fill the two tools was ranged between 30-45 minutes according to the needed

explanation, voluntary participation, confidentiality and anonymity were assured.

Statistical analysis: The collected data were coded and examined using Statistical Package for the Social Sciences (SPSS) version 20. The collected data were summarized and tabulated using descriptive statistics. Qualitative data were described using number and percent. Quantitative data were described using mean and standard deviation. The used tests were Chi-square test for categorical variables. Level of significance was set at $P < 0.05$.

Results

Table (1) reveals that nearly three quarters (72%) of the mothers their age were <25 years old with mean age of studied mothers were 24.16 ± 4.49 years old, the majority of them (80%) were housewife and two thirds of them (60%) had primary school education. More than three quarters (78%) had one child and (52%) were from urban areas.

Table (2) more than two thirds of infants (66%) were males, nearly two thirds (58%) of infants their age ranged between 6 to <12 months with mean age 8.05 ± 2.2 months, less than three quarters (70%) of them ranked the first and the majority of them (82%) had family history of G6PD deficiency.

Table (3) two thirds of infants (60%) took exclusive breastfeeding and (68%) their exclusive breastfeeding until 6 months of age with mean duration of 5.96 ± 2.69 months and (60%) of mothers introduced a Yogurt beside breastfeeding for their infants.

Table (4) reveals that, more than two thirds (68%) ingested raw and fresh type of fava beans, more than three quarters of mothers (76%) ingested large amount of fava beans before breastfeed their infants and most of them (92%) reported that they ate beans and falafel while the minority ate peas and chickpeas and nuts (4% & 4% respectively). Also most of mothers (90%) ingested fava beans before breastfeeding time with mean duration 2.38 ± 1.52 hours, and the mean duration of infants' occurrence of favism attack after their mothers' ingested fava beans and give breastfeeding was 46.48 ± 10.9 hours.

Table (5) reveals that more than two thirds of infants (64%) had twice favism attack; the mean time of the last attack since 7.68 ± 3.6

days. Concerning the clinical manifestations of favism attack, the highest percentages of infants had pallor, jaundice, urine dark orange color, lymph nodes enlargement and other as fever, irritability, and tachycardia (82%, 100%, 90%, 56% & 60% respectively). Most of the infants (88%) received management as blood transfusion and medications for the favism attack with mean duration of hospitalization and recovery 6.708 ± 4.026 days.

Table (6) shows that there were highly statistically significant differences between studied infants' frequency of occurrence of favism attack with infants' breastfeeding status, time and type of fava beans ingested by their

mothers when p value < 0.01 and a statistical significant difference was found with duration of mothers ingestion of fava beans before infants' breastfeeding and occurred favism attack and amount of fava beans at p value < 0.05 , while no statistical significant difference was found with names of fava beans ingested.

Table (7) reveals that there were highly statistically significant differences between frequency of occurrence for favism attack and studied infants' sociodemographic data regarding age and family history of G6PD deficiency when p value < 0.01 , also a statistical significant difference was found with the male gender at p value < 0.05 .

Table (1): Frequency distribution of demographic data of studied Mothers (n=50).

Mothers' data	No.	%
Age/ years		
• < 25	36	72
• 25-< 35	10	20
• ≥ 35	4	8
Mean\pmSD	24.16 \pm 4.49	
Job		
• Working	10	20
• Housewife	40	80
Educational level		
• Not read and write	3	6
• Read and write	3	6
• Primary school	30	60
• Intermediate education	9	10
• Higher education	5	18
Type of family		
• Nuclear	40	80
• Extended	10	20
Number of children		
• One	39	78
• Two	6	12
• Three and more	5	10
Place of residence		
• Urban	26	52
• Rural	24	48

Table (2) Frequency distribution of studied breastfed infants and young children demographic data (n=50).

Infants and toddlers' characteristics	No.	%
Gender		
• Male	33	66
• Female	17	34
Age/ months		
• < 6	2	4
• 6 - < 12	29	58
• 12 - < 18	18	36
• ≥18	1	2
Mean ±SD	8.05±2.2	
Rank		
• First	35	70
• Second	10	20
• Third	5	10
Family history of G6PD deficiency		
• Yes	41	82
• No	9	18

Table (3): Frequency distribution of infants' feeding status as reported by their mothers (n=50).

Items	No.	%
Infants' breastfeeding status		
• Exclusive	30	60
• Not exclusive	20	40
Duration of exclusive breastfeeding/months		
• 3	11	22
• 4	4	8
• 5	1	2
• 6	34	68
Mean ± SD	5.96 ± 2.69	
Type of introducing food beside breastfeeding		
• Yogurt	40	60
• Biscuits	16	32
• Boiled vegetables or fruits	4	8

Table (4): Frequency distribution for factors agitate occurrence of favism attack among breastfed infants as reported by their mothers in relation to ingestion of fava beans (n=50).

Items	No.	%
Types of fava beans		
• Raw and fresh	34	68
• Coked	11	12
• Dried	5	10
Amount of fava beans		
• Small	8	16
• Enough	4	8
• Large	38	76
Names of fava beans ingested		
• Beans and falafel	46	92
• Peas	2	4
• Chickpeas and nuts	2	4
Time of fava beans ingested by mothers in relation to infants breast feeding		
• Before breastfeeding	45	90
• During breastfeeding	5	10
Duration of mothers ingestion of fava beans before infants breastfeeding/hours		
Mean ± SD	2.38 ± 1.52	
Duration of infants' occurrence of favism attack after their mothers ingested fava beans and infants take breastfeeding/ hours		
• 12-<24	12	24
• 24-<48	48	96
• ≥ 48	10	20
Mean ± SD	46.48 ± 10.91	

Table (5): Frequency distribution of last favism attack's characteristics, manifestations, management and duration of recovery among breastfed infants as reported by their mothers (n=50).

Favism attack's characteristics		No.	%
Frequency of occurrence			
• Once		13	26
• Twice		32	64
• Three times		3	6
• Four times		2	4
Last attack since /days (Mean ± SD)		7.68 ± 3.6	
Last favism attack's manifestations:			
-Pallor			
• Yes		41	82
• No		9	18
-Jaundice			
• Yes		50	100
• No		0	0
-Urine dark orange color			
• Yes		45	90
• No		5	10
-Lymph nodes enlargement			
• Yes		28	56
• No		22	44
-Other as complications:			
• Fever, irritability, and tachycardia		30	60
• Fatigue		4	8
• Kidney failure		1	2
Received management as blood transfusion and medications			
• Yes		44	88
• No		6	12
Duration of hospitalization and recovery/ days (Mean ± SD)		6.708 ± 4.026	

Table (6): Relation between mothers' ingestion for fava beans and their breastfed infants' occurrence for favism attack (n=50).

Items	No.	Frequency of occurrence for favism attack								X ²	P-value	
		Once (n=13)		Twice (n=32)		Three (n=3)		Four (n=2)				
		No.	%	No.	%	No.	%	No.	%			
Infants' breastfeeding status	Exclusive	30	9	69.2	21	65.6	0	0.0	0	0.0	18.14	.000**
	Not exclusive	20	4	30.8	11	34.4	3	100	2	100		
Time of fava beans ingested by mothers in relation to infants breast feeding	Before breast-feeding	45	13	100	28	87.5	2	66.7	2	100	29.16	.000**
	During breast-feeding	5	0	0.0	4	12.5	1	33.3	0	0.0		
Duration of mothers ingestion of fava beans before infants breastfeeding and occurred favism attack on their infants/hours	12-<24	12	4	30.8	8	25	0	0.0	0	0.0	9.263	.045*
	24-<48	28	6	46.1	22	68.8	1	33.3	0	0.0		
	≥ 48	10	3	23.1	2	6.2	2	66.7	2	100		
Types of fava beans	Raw and fresh	34	5	38.4	29	90.6	0	0.0	0	0.0	44.11	.000**
	Coked	11	4	30.8	2	6.3	3	100	2	100		
	Dried	5	4	30.8	1	3.1	0	0.0	0	0.0		
Amount of fava beans	Small	8	5	38.4	3	9.4	0	0.0	0	0.0	10.63	.036*
	Enough	4	2	15.4	2	6.2	0	0.0	0	0.0		
	Large	38	6	46.2	27	84.4	3	100	2	100		
Names of fava beans ingested	Beans and falafel	46	10	76.9	31	96.9	3	100	2	100	6.835	.336
	Peas	2	2	15.4	0	0.0	0	0.0	0	0.0		
	Chickpeas	2	1	7.7	1	3.1	0	0.0	0	0.0		

No significant at p > 0.05. *Significant at p < 0.05. **highly significant at p < 0.01.

Table (7): Relation between infants' sociodemographic data and their frequency of occurrence for favism attack (n=50).

Items	No.	Frequency of occurrence for favism attack								X ²	P-Value	
		Once (n=13)		Twice (n=32)		Three (n=3)		Four (n=2)				
		No.	%	No.	%	No.	%	No.	%			
Age (months)	< 6	2	2	15.4	0	0.0	0	0.0	0	0.0	38.03	.000**
	6 - <12	29	3	23.1	26	81.3	0	0.0	0	0.0		
	12 -<18	18	8	61.5	6	18.7	2	66.7	2	100		
	≥18	1	0	0.0	0	0.0	1	33.3	0	0.0		
Gender	Male	33	11	84.6	17	53.1	3	100	2	100	6.947	.044*
	Female	17	2	15.4	15	46.9	0	0.0	0	0.0		
Family history of G6PD deficiency	Yes	41	9	69.2	32	100	0	0.0	0	0.0	31.20	.000**
	No	9	4	30.8	0	0.0	3	100	2	100		

No significant at $p > 0.05$. *Significant at $p < 0.05$. **highly significant at $p < 0.01$.

Discussion:

In spite of the vast nutritional and environmental benefits provided by fava bean, its ingestion provokes an acute hemolytic anemia called favism in children with a G6PD deficiency (Zam & Belal, 2020). Favism is potentially life threatening illness and its precipitating factor is commonly ingestion of fava beans, infection and exposure to some medications or chemicals (Elgammal et al., 2020). Favism occurs after the ingestion of raw fresh beans, cooked beans (rare cases), or through breastfeeding (Luzzatto & Arese, 2018). Thus, breastfeeding provides protection against infections in infants that reduce morbidity and mortality; while breastfed infants that have G6PD certain drugs and foods can potentially cause hemolysis and pass via the breast milk so avoid certain foods and other substances in mothers' diet to avoid creating a G6PD crisis will improve health outcomes of infants with favism (Al Jurdi, 2020). So the aim of the current study was to assess the relationship between mothers' ingestion of fava beans and occurrence of favism attack among their breastfed infants.

Regarding to the characteristics of the studied infants, the study findings revealed that nearly two thirds of infants were between 6 to <12 months of age, more than two thirds of infants were males, less than three quarters ranked the first and the majority of them had family history of G6PD. These results were supported by Ghali & Al Mamoori (2020) who studied "Hemolysis in children with Glucose-6-Phosphate Dehydrogenase Deficiency after ingestion of fava beans; facts predicting severity" and found that younger age group children (infants and toddlers) tend to present

with the severe form of hemolysis and family history of G6PD was significant in 88.2% of children with the severe form. Also Kasemy, Bahbah, El Hefnawy & Alkalash (2020) found that most of infants with favism were males.

The study in accordance with Tang et al. (2018) who studied "evaluations of newborn screening program performance and enzymatic diagnosis of glucose-6-phosphate dehydrogenase deficiency" and found that newborns with G6PD males to females ratio was 6.4% : 1.7%. In addition to Hagag, Badraia, Elfarargy, AbdElmageed & Abo-Ali (2018) who studied *Glucose-6-Phosphate Dehydrogenase Deficiency in 5 Years Retrospective Egyptian Study* and found males were more commonly affected than females (932 males versus 68 females) and the highest prevalence of hemolytic crisis in G6PD deficiency children was found within the age group of 1-3 years old.

From the researcher point of view a higher risk of having G6PD deficiency and favism are male infants and a family history of the favism, in addition the culture of the parents in Egypt give more concern for male children than female to seek care when they are ill in highly specialized hospital as in hematologic clinic in pediatric university hospitals to seek the appropriate care and management for the favism attack.

The current study finding revealed that, nearly three quarters of the mothers their age were <25 years with mean age 24.16 ± 4.49 years old, and more than three quarters had one child and more than half were from urban areas. This finding contradicted with findings of Kasemy et al. (2020) who studied "Prevalence of and

mothers' knowledge, attitude and practice towards glucose-6-phosphate dehydrogenase deficiency among neonates with jaundice: a cross-sectional study" and reported that the mean age of the studied mothers were 31.45 ± 4.77 years and less than half of mothers with parity >2 . The urban area based living individuals tend to present with mild hemolysis while those from rural areas tends to present with more severe episodes of hemolysis.

The current study found that two thirds of infants took exclusive breastfeeding until 6 months of age with mean duration of exclusive breastfeeding was 5.96 ± 2.69 months and two thirds of mothers introduced Yougart beside breastfeeding after six months of age. That study supported with **Nieuwoudt, Ngandu, Manderson & Norris (2019)** who mentioned that the current public health consensus is that exclusive breastfeeding for the first six months is the best start for health and development and continued breastfeeding for two years with the introduction of safe complementary foods from six months. **In addition, World Health Organization & Regional Office for Europe (2019)** established appropriate infant and young child feeding practices include the initiation of feeding solid/semi-solid foods from 6 months.

The current study contradicted with **Farag, Ammar and El-Awady (2020)** who concluded that exclusive breastfeeding is not universal in Egypt. The minority of children aged 4-5 months are exclusively breastfed. Also **Kamel, Sabry, Ismail & Nasr (2020)** who studied *"Pattern of infants' feeding and weaning in Suez Governorate, Egypt"* and found that most infants were ever breastfed, exclusive breastfeeding was not widely practiced, among 92 infants aged <6 months, only minority were exclusively breastfed. The complementary feeding period (6–24 months) is a window of opportunity for preventing malnutrition and improving long term development and health (**Michaelsen, Grummer & Bégin, 2017; WHO, 2016**). From the researchers' point of view support breastfeeding even after introducing foods until 2 years of child age should be one of the overarching goals in the protection of children's health.

The current study supported with **Handayani & Yulaikah (2020)** who found that there were significant relations between consumption of green beans on the lactating mothers and increase the hormone of prolactin and milk production, the protein needed by breastfeeding mothers can be supplied from green beans. Beans and peas are sources of protein nutritional requirements for mothers and transferred in breast milk to the infants (**Kominiarek & Rajan, 2016**). From the researchers' point of view beans are popular food in Egypt in addition it has many nutritional value and cheap type of food so different social standards, most of mothers and their infants eat fava beans.

Concerning ingestion of fava beans and occurrence of favism in breastfed infants as reported by mothers, the current study finding revealed that most of mothers ingested fava beans before starting breastfeed their infants with mean duration 2.38 ± 1.52 hours, and the mean duration of infants' occurrence of favism attack after their mothers ingested fava beans and give breastfeeding was 46.48 ± 10.91 hours. All exclusively breastfed and all their mothers had eaten fava beans in the preceding days, the conclusion that the active agent was transferred from mother to child through breast milk is almost inescapable and acute hemolytic anemia may develop (**Luzzatto & Areses, 2018**). The study supported by **Ventura (2017)** who found that compounds in mother's diet are transmitted from mother to child through breast milk at around 2 hours post ingestion in analysis of milk samples. There is strong evidence that maternal diet during lactation shapes food preferences during infancy (**Alison, Phelan & Silva, 2021**).

National Center of Biotechnology (2018) reported that four exclusively breastfed male Arab infants developed favism after their mothers ingested fava beans, they ranged in age from 2 to 4 months and developed excessive pallor 2 to 3 days after maternal ingestion of fava beans, their urine was deep orange in color, severe acute hemolytic anemia was diagnosed and all were shown to be G6PD deficient. In the same context (**Kattamis, 1971 in Wisnumurti et al., 2019**) found that breastfed infants less than 12 months old appears hemolysis from 2 to 6 days after the ingestion of fava beans by the mother who was clinically free of any symptom. From the

researchers' point of view lactating mothers consumption to fava beans and any other nutrients are transferred to their infants after breastfeeding and fava beans triggered the hemolytic attack among those affected infants who carry of the gene defect and can be severe with young infants and affected by the consumed amount and type of fava beans.

The current study finding proved that, more than three quarters of mothers ingested large amount of fava beans before breastfeed their infants in relation to the last favism attack and more than two thirds ate row fresh fava beans, most of them reported eating beans and falafel while the minority ate peas, nuts and chickpeas. This finding was supported by **Ghali and Al Mamoori, (2020)** who studied "*Hemolysis in children with Glucose-6-Phosphate Dehydrogenase Deficiency after ingestion of fava beans; facts predicting severity*" and found that two thirds of the younger children have recorded ingestion of fresh row type of fava beans while one third ingested dried type and more severe hemolysis usually had a history of ingestion of fresh row type of fava bean also most common precipitating factor of hemolysis is fava beans and falafel followed by low incidence of chick pea. Moreover, **National Center For Biochemistry (2018) about drugs and lactation data base with fava beans**, stated that favism attack caused by eating the fava beans plant and transmitted in breastfeeding.

The current study finding revealed that, more than two thirds of infants had twice frequency for occurrence of favism manifestations, mean time of the last attack since 7.68 ± 3.6 days, the highest percentages of infants had pallor, jaundice, urine deep orange color, lymph nodes enlargement and other manifestation as fever, irritability, and tachycardia. Most of the infants received management as blood transfusion and medications for the favism attack with mean duration of recovery and discharge from hospital 6.708 ± 4.026 days. The finding agreed with **Hagag et al. (2018) who studied "Glucose-6-Phosphate Dehydrogenase Deficiency: 5 Years Retrospective Egyptian Study"** and reported that infants with favism attack presented mainly with the majority of infants had pallor, dark red urine and jaundice

after 24-72 hours of exposure directly to the precipitating factors of fava beans with mean 36 ± 17.73 hours and the mean age of the first presentation was 12.8 ± 5.54 months.

Most infants with favism are asymptomatic unless triggered by ingestion of fava beans, hemolysis ensues in about 24-48 hours after fava beans ingestion. In severe cases, hemoglobinuria and jaundice result (**Kliegman, Geme, Blum, Shah & Tasker, 2020**). In addition, **Kavehmansh, Arab, Abolghasemi & Torabi (2016)** found that hemolytic crises were significantly more common in spring which is the peak time for fava bean consumption, its most common initial symptoms were jaundice, dark color urine, fever and pallor, the first etiological agent triggering hemolysis was fava bean intake followed by infections and drug consumption and the interval between fava bean ingestion and onset of hemolysis was 12 hours.

In addition, **Khazaei et al., (2019) and Arnaout, El-Gharbawy, Shaheen, Afifi & Abd EL-Dayem (2011)** studied 50 G6PD-deficient pediatric patients in Egypt, their ages ranged between 7 months to 10 years, their clinical presentations included acute hemolytic attack following ingestion of fava beans only favism was encountered the majority while minority was drug intake and infection. The rate of jaundice in G6PD deficiency neonates was significantly higher than non G6PD deficiency (**Xu et al., 2021**). From the researchers point of view and related literature infant with favism when exposed to fava beans and its compound as divicine through breast milk, it triggers hemolysis of red blood cells that increase blood bilirubin level, loss of hemoglobin to cause the manifestation of anemia as pallor and the information given from hospitals and health workers regarding favism cause is not enough.

The current study proved that there were highly statistically significant differences between studied infants' frequency of occurrence of favism attack with infants' breastfeeding status, time and type of fava beans ingested by their mothers and a statistical significant difference was found with duration of mothers ingestion of fava beans before infants' breastfeeding and occurred favism attack and amount of fava beans, while no statistical significant difference

was found with names of fava beans ingested. The study supported with **Ghali and Al Mamoori (2020)** who found that severity of hemolysis highly significant with younger age group children tend to present with the severe form of hemolysis, a significant correlation found between the type of fava bean ingestion (fresh, raw), family history of G6PD and the severity of hemolysis which need initial hospitalization and management by blood transfusion. There are provoking factors in favism children that needed to be avoided, management of symptoms and any complications are essential to ensure that children can remain as healthy as possible (**Sumathepala, 2020**).

The current study findings in accordance with **Hagag et al. (2018)** who found that the highest prevalence of hemolytic crisis caused by favism in Egyptian children at age 1-3 years and received blood transfusion as a management. Also **Kavehmansh et al., (2017)** found that hemoglobin level was significantly lower in male children in hemolytic crises caused by favism and the majority of the admitted children received blood transfusion during their hospital admission.

Favism is a consequence of the ingestion of fresh, frozen, cooked, raw, or dried fava beans (**Almuhaini, Alruzayhi & Alwassel, 2018**). Favism also has been reported in breastfed infants whose mothers had eaten fava beans. Managing favism involves avoiding foods and medications that can trigger the condition, reducing stress levels can also help in controlling symptoms (**Bichali et al., 2017**). In case of favism attack that progressed to hemolytic anemia, more aggressive treatment is required including oxygen therapy and blood transfusion consequently affected infants need to stay in the hospital while receiving these treatments, as close monitoring of severe hemolytic anemia is critical for ensuring a full recovery without complications (**Martínez et al., 2020**). From researchers point of view regular investigation, genetic testing in those affected children with G6PD deficiency needs to be made routinely within the health system and educating all breastfed mothers had infants with favism or family history to prevent eating fava beans while breastfeeding to

prevent agitation of favism crisis in their infants.

Conclusion:

The current study concluded that nearly two thirds of infants were between 6 to <12 months of age, the mean duration of the mothers ingestion for fava beans before breastfeeding was 2.38 ± 1.52 hours and the mean duration of infants' occurrence of favism attack after their mothers ingested fava beans and give breastfeeding was 46.48 ± 10.91 hours. Also there were highly statistically significant differences between frequency of occurrence for favism attack and infants' age, family history of G6PD deficiency and a statistical significant difference was found with the male gender.

Also there were highly statistically significant differences between infants' frequency of occurrence of favism attack and infants' breastfeeding status, time and type of fava beans ingested by their mothers, a statistical significant difference was found between infants' occurrence of favism attack with mothers ingestion for large amount of fava beans, duration of mothers ingestion of fava beans before infants' breastfeeding while no statistical significant difference was found with names of fava beans. In addition the study concluded that the highest percentages of infants their favism attack's manifestations were pallor, jaundice, urine dark orange color, lymph nodes enlargement. So infants with favism are susceptible to potentially severe and life-threatening hemolysis after mothers ingestion for fava beans while breastfeeding their infants, avoid exposure to precipitating factors of hemolysis is important.

Recommendations:

- Health education program should be designed and provided for mothers of children with G6PD deficiency particularly favism for prevention and management.
- Design handouts containing all necessary information about nursing care provided for favism children and a pamphlets distributed by the nurses to advise the breastfed mothers about diet as this cause hemolysis.
- Further repetition of such study on a large sample to generalize the study finding.

- Further studies for analysis of milk samples to assess vicine and convicine level compounds in fava beans that are transmitted from mother's diet to breast milk and detect the reservoir hours post ingestion in milk samples.

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