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The Prevalence of G6PD Deficiency and its Associated Factors Among the National University Students in the Middle Province (Ibb City), Yemen

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Abstract:-

- ***Background***

Glucose 6 phosphate dehydrogenase (G6PD) is a critical an enzyme for protecting erythrocytes from oxidative stress and hemolysis. G6PD deficiency is a significant public health problem in the world countries and it is associated with hemolytic complications in individuals exposed to internal and external oxidative stress. The present study aimed to determine the prevalence of G6PD deficiency and its associated factors among university students from different indigenous areas in Ibb city.

- ***Method***

A cross-sectional study recruited randomly on 200 students (150 males & 50 females) whose decedent from different areas in Ibb province. 3ml of blood samples were collected to quantify G6PD activity levels and complete cell count (CBC) and questionnaire apply to collected history symptoms of hemolytic anemia and socio-demographic information.

- ***Result***

Twenty three (19 males and 4 females) students were have G6PD deficiency with overall prevalence rate was 11.5% (9.5 % in males & 2.0% in females). G6PD deficient students having low significant ($p<0.05$) levels of Hb and RBCs count compared to normal G6PD students. 56% of G6PD deficiency students had been residing in Al-dihar place compared to 35% residing in AL-mashanah and 9% residing in other places with odd deficiency no significant (OR=1.7; 95%CI 0.8-5.0, p=0.44). 78 % of G6PD deficient students were having parents consanguineous marriage with a higher odd (OR=5.0; 95% CI 2-13, p=0.002). 70% (OR=11.0; 95% CI 4.4-30.9, p<0.0001) and 17% (OR=5.1; 95%CI 1.4-19, p= 0.015) of G6PD deficient students were having history of hemolytic episodes and favism, respectively, with a higher significant odd. 61% (OR=6.0; 95% CI 3-14, p <0.0001), 70% (OR= 9.0; 95% CI 3-23, p <0.0001), 61% (OR=10; 95% CI 4-27, p<0.0001) and 57% (OR= 6 ; 95% CI 2-14, p <0.0001) of G6PD deficient students were having a higher odd incidence of tea urine color, jaundice, pallor and yellowish eyes than normal students, respectively. 65% (OR=10.4; 95% CI 4-27, p<0.0001) and 17% (OR=4.0; 95% CI 1-14, p<0.035) of G6PD deficiency were having a higher odd incidence of treatment hemolytic anemia and blood transfusion than normal students, respectively. Whereas, 39% (OR=4.0; 95% CI 1.6- 11, p=0.003) and 30% (OR=3.1; 95% CI 1.2- 8, p=0.033) of G6PD deficient students were having a higher odd incidence of infections and drugs than normal students. However, 57% (OR=0.8; 95% CI 0.34-2.1, p=0.7) of G6PD deficient students were having a lower odd of history ingestion fava beans than normal.

- **Conclusion**

Generally, G6PD deficient individuals potentially having a higher susceptibility to development life-threatening hemolytic episodes (change urine color, skin pallor, jaundice, yellowish eyes) after exposure to internal or external oxidative stress agents. Low Hb, consanguinity between parents, susceptibility to ingestion fava beans, infections and medications, history of treatment and hemolytic episodes of anemia considered significant independent predictors of G6PD deficiency in our population.

Keywords:- *Glucose-6-Phosphate Dehydrogenase (G6PD), G6PD Deficiency, Episodes, Hemolytic Anemia, Risk factors, Students, University, Ibb, Yemen.*

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I. INTRODUCTION

G6PD is an enzyme present in all body cells where its plays an essential role in generation of nicotinamide adenine diphosphosphate-H (NADPH) that prevent accumulation of oxidative stress agents in red blood cells (RBCs) and hemolysis [1]. Therefore, G6PD deficiency becomes a harmful to all body cells especially RBCs that lead to impairment of intracellular antioxidant mechanism causing acute hemolytic crisis anemia as well as enhancing recurrent infections, atherosclerosis and cardiovascular disease [2,3]. Crisis of hemolytic anemia (dark urine, jaundice, skin pallor and favism) in G6PD deficient individuals can be triggered by exposure to infections and toxins, ingestions of fava beans and some drugs that induced oxidative stress accumulation in RBCs [2]. However, most of G6PD deficient people are usually asymptomatic (unexplained clinical manifestations) and they do not know their condition but some of them will be severe from hemolytic anemia during his life when exposed to extra-internal and external oxidant stress agents [4] especially in individuals whose frequently exposure to infection and consumption of fava beans and drugs.

G6PD deficiency is the most common human enzyme defect, among the world's population, there are more than 400 million individuals worldwide were affected [5,6]. It is still a major health problem in development countries where this disorder is a very common mainly in Africa, Mediterranean countries, East Asian ethnic origins and Northern Europe [7,8,9]. The rate of prevalence G6PD deficiency has been reported form various the Arab countries that ranging from 1-65 % [10] with the highest frequency in KSA 65% [10,11], in Bahrain up to 45% [10,12, 13,14,15], in Oman is reach 29% [10, 16, 17], in Unite Arab Emirate 6-32 % [10, 18, 19] and in Iraq 6-13 % [23, 24].

Yemen is one of the Arab countries with the highest prevalence rate of G6PD deficiency (12.0%) in Hodiedah city, the west region endemic with malaria [22] and 4.8 % among newborns [20] and 7.1% among male blood donors in Sana'a capital city, the north region of our country[21]. However, the previous studies were only demonstrated the prevalence rate of G6PD deficiency in the west and north borders in Yemen, while clinical complications correlated with G6PD deficiency were still essential needed to study and clarify in order to prevent the complications of the disease.

To date, no neonatal G6PD screening programme apply in our government or private hospitals or any study carried out on G6PD deficient individuals underlining hemolytic crisis among population related to G6PD deficiency. Therefore, lack of the awareness, the level of education and medical knowledge of healthcare workers as well as parents lack information about the nature of G6PD deficiency disease, complications and its predisposing factors, all of these are still need essential effort work to studies and clarify in order to reduce and prevent the recurrent infections, kernicterus, sepsis and episodes of hemolytic crisis in G6PD deficient individuals during their life, especially when exposed to infectious agents, fava beans and medications.

Therefore, our study will be focused on determining the prevalence of G6PD deficiency and its associated factors as the first essential step towards evaluating its impact on the health of our population especially among indigenous tribes whose residency restricted to agriculture region at the middle our country. So, this study will be conducted on university medical students whose only decedent from various indigenous areas in Ibb city.

II. METHODOLOGY

A. Study Design and Data Collection

This study was designed to determine the prevalence and the predisposing factors associated of G6PD deficiency among university students whose districted from different areas of Ibb city. The protocol of this study was approved by the ethical committee of the faculty medical health sciences, the National university, Ibb city. The questionnaire was designed to use as survey and informed consent for each involuntary student who agreed to participate in this study, the study was carried out between February and April 2022 using questionnaire to survey demographic information, consanguineous parents, history of favism, symptoms of hemolytic anemia (pallor, dark-tea urine, jaundice), consumption of fava beans and drugs, history of any infections (malaria, dengue virus, typhoid fever, respiratory infection), blood transfusion and heredity of hemolytic anemia.

B. Study Subjects and Samples Collections

A total 200 university students randomly selected from the different medical levels and excluded students from other cities. 3 millilitres of venous blood were collected into pre-labelled EDTA tubes and analyzed for hematological parameters such as complete blood count (CBC) and quantitative assays of G6PD activity levels.Prepare Your Paper Before Styling.

C. Hematological and Biochemical Parameters

Hemoglobin (Hb), red blood cells (RBCs) count, hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW) were measured using automated hematology analyzer Sysmex KX-21N (Sysmex Corp, Chuo-Ku, Kobe, Japan). Then each sample was analyzed spectrophotometric for determination of G6PD activity level using a quantitative assay kit (Spinreact G-6-PDH kit) according to the manufacturer's instructions. The cutoff values for G6PD activity levels was determined by Hb concentration (U/gHb) of RBC based on the World Health Organization (WHO) guidelines that considered any male and female who has RBCs G6PD activity level < 30% of the normal medium are G6PD deficient subjects [18]. According to WHO classification criteria of G6PD activity levels, student who has G6PD activity <10% of the normal activity was classified as severe deficiency, whereas student who has

G6PD activity between 10-60 % of the normal activity was classified as moderate deficiency [18].

D. Statistical Analysis

Data were analyzed using the IBM SPSS statistics version 20.0 (IBM Corp., Armonk, NY, USA). Quantitative variables were examined for normality before analysis and presented as the mean and standard deviations (SD), while non- normally distributed quantitative variables were expressed as median and interquartile range (IQR). Crosstabulation was used to tested non-quantitative (Categorical) variables and presented as proportions, and Pearson's Chi square was used to determine the significance of association between G6PD deficiency and its associated factors. These association will be presented as Odds ratio (OR) at 95 % confidence interval (CI) using multiple logistic regression analysis and the association was considered statistically significant at $p < 0.05$.

III. RESULTS

- *Demographic and Hematological Characteristics of the Study Population.*

Table I show sociodemographic characters, G6PD activity and hematological parameters for G6PD deficiency and normal males and females students. A total number 200 university students were conducted in this study, 150 (75%) males and 50 (25 %) females, the majority age of students (77%) were found in 18-24 years, however, it was not found significant differences(p=0.965) in age among G6PD deficient and normal students.

The average mean ± SD level of G6PD activity was calculated for both males and females students based on the manufacturer's cutoff value 6.97-20.5 U/gHb. The mean ± SD level of G6PD activity for males was calculated after excluded severe deficiency students and depend on the WHO guidelines for G6PD activity levels considered any male and female who has G6PD activity < 30% of the normal mean must be regarded as G6PD deficient. So, the average mean ± SD of G6PD activity level for males students had been found 6.8 ± 2.03 U/gHb was used to determine the cut-off point for G6PD deficiency that was considered any level <4.8 U/gHb of the normal male mean. 8/23 (34.8%) students having severe G6PD deficiency with activity level <0.5 U/gHb (<10%), while 15 (65.2%) students having G6PD activity <4.8 U/gHb (<60%) and 177 students had normal G6PD activity >4.8 U/gHb (>60%).

19 (9.5%) of males and 4 (2.0%) of 50 females were found to be have G6PD deficiency level, with overall prevalence was 11.5 % out of 200 students participants, G6PD deficient males showed higher prevalence rates than females students, however, there was no significant distribution of G6PD deficiency in male and females students (P= 0.375). The average mean ±SD levels of Hb (14.1±0.6 vs 12.9 ±1.0) for G6PD deficient males and females were be found significantly (p=0.006) lower compared to the mean levels of Hb (15.6 ±1.2 vs 13.5 ±1.4) for normal G6PD males and females students. Similarity, there were found significantly (p<0.041) lower the mean levels of RBCs count (5.0 ±0.5 vs. 4.7 ±0.8) for G6PD deficient males and females compared to the means of RBCs count (5.5 ±0.6 vs. 4.7 ±0.5) for normal G6PD males and females students. These finding might be reflected the association between levels of hemoglobin, RBCs count and G6PD deficiency in G6PD deficient individuals compared to normal G6PD students and in non-diagnosis individuals.

- *Factors Associated With G6PD Deficiency.*

The distribution of G6PD deficiency students according to risk associated factors summarized in table II based on the multivariate analysis**.** It was found that the G6PD deficient males showed higher prevalence rates than females students, however, there was no significant association between G6PD deficiency and gender students (*OR=1.7 ; 95% CI 0.5-5.2, P= 0.375*). The highest prevalence rates of G6PD deficiency was found among students residing in Al-dihar 56% followed by students residing in AL-mashanah 35% then resident in other place 9%, however, the odd of incidence of G6PD deficiency was 1.7 higher in Al-dihar with no significant association between G6PD deficiency and the resident area (*OR=1.7;* 95% CI *0.8-5.0, P=0.44*). In addition, there was found 78% of G6PD deficiency students their parents are consanguineous marriage with odds incidence of G6PD deficiency being 5.0 times a higher among G6PD deficient students (*OR=5.0; 95% CI 2-13, p=0.002)* compared to normal G6PD students whose parents are consanguineous, this is reflect the strong significant association between the prevalence of G6PD deficiency and relatives consanguineous marriage. The present study suggested consanguinity marriage between parents was showed a good predictor factor to prevalence of G6PD deficiency in our population depending on univarinte analysis.

Moreover, table II show predicators factors to evaluations the episodes of hemolytic anemia that associated with G6PD deficiency. In the present study, it was found 70% of G6PD deficiency had clinical significant episodes of hemolytic anemia with the odds of incidence symptoms being 11.0 times as higher in G6PD deficient students (*OR=11.0; 95% CI 4.4-31, p<0.0001*), these reflected a higher significant association of episodes hemolytic anemia and G6PD deficiency. However, only 4/23 (17 %) of G6PD deficiency were a known history of family favism (acute hemolytic anemia) with a higher significant incidence of odd (*OR=5.1; 95%CI 1.4-19, p= 0.015*). In addition, it was found that a higher incidence of change urine to tea color (61%), skin pallor (61%), yellowish eyes (57%), jaundice (70%), however, 65 % and 17% of G6PD deficient students were had pervious history of treatment of hemolytic anemia and blood transfusion.

Based on the multivariate analysis for clinical symptoms of hemolytic anemia as showed in table II, G6PD deficient individuals were more likely than normal students to develop of dark urine with odd incidence 6.0 times (*OR=6.0; 95% CI 3- 14, p <0.0001*), skin pallor with odd incidence 10.0 times (OR=10; *95% CI* 4-27, p<0.0001), yellowish eyes with odd incidence 6.0 times (*OR= 6 ; 95% CI 2-14, p <0.0001*) and jaundice with odd incidence 9.0

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times (*OR= 9.0; 95% CI 3-23, p <0.0001*) than normal individuals, these reflected the strong significant association between occurring episodes of hemolytic anemia and G6PD deficiency. Moreover, there were found 39% of G6PD deficient students having a higher prevalence of infections (typhoid fever, dengue virus and malaria) with 4.0 times of odd incidence (OR=4.0; *95% CI* 1.6- 11, p=0.003) and 30% of G6PD deficient having history drugs used (antibiotics and antimalarial) with 3.1 times of odd incidence (OR=3.1; *95% CI* 1.2- 8, p=0.033) than normal, respectively. In addition, 57% of G6PD deficient having ingestion of fava beans with 0.8 times of odd incidence (OR=0.8; *95% CI* 0.34-2.1, p=0.7) and with no significant association between ingestion of fava beans and hemolytic episodes in G6PD deficiency individuals. Therefore, our findings suggested that sever hemolytic episodes that appearing in some individuals considered the hall marker predictive values in detection of G6PD deficiency individuals.

Table 1 Demographic Characters, G6PD Activity and Hematological Parameters for G6PD Deficiency and Normal Students

Parameters	**Normal G6PD activity (N = 177)**				**G6PD Deficient students (N=23)**				**P value**
Gender	**Males No. 131**	**(%) (65.5)**	**Females No. 46**	**(%) (23)**	**Males No. 19**	**(%) (9.5)**	**Females No. 4**	**(%) (2)**	**0.375**
Age (years)									
18-24	105	(80)	41	(89)	17	(90)	2	(50)	
24-30	26	(20)	5	(11)	2	(10)	2	(50)	0.99
Mean ± SD	22.6 ±2.5		22.2 ±2.5		22.2 ±2.4		23.0 ±2.97		
G6PD activity(U/gHb) Mean ± SD	7.3 ±2.5		8.7±4.0		1.6 ±1.3		2.2 ±0.5		0.001
Hb (g/dL) Mean ± SD	15.6 ±1.2		13.5 ±1.4		14.1 ±0.6		12.9 ±1.0		0.006
RBCs (cells/10^6 µl) Mean ± SD	5.5 ±0.6		4.7 ±0.5		5.0 ±0.5		4.7 ±0.8		0.041

Table 2 The Distribution of G6PD Deficiency and its Associated Factors Among Students.

Parameters	**G6PD Deficiency(n=23)**			**OR (95% CI)**	**P Value**
		Total No.	**n(%)**		
Gender	Male	150	19 (12.7)		
	Female	50	04 (8)	1.7 (0.5-5.2)	0.375
Age (years)	18-24	165	19 (83)	0.001 (-0.12-0.12)	0.99
	24-30	35	4 (17)		
District of Residency	Al-dihar	88	13 (56)		
	AL-mashnah	88	08 (35)	1.7 (0.8-5.0)	0.44
	Other Place	24	02 (9)		
Consanguinity Parents	Yes	96	18 (78)		
	No	104	05 (22)	5.0 (2-13)	0.002
History of Heredity anemia	Yes	11	04 (17)		
	No	189	19 (83)	5.1 (1.4-19.1)	0.015
History of Hemolytic Anemia	Yes	45	16 (70)		
	No	155	07 (30)	11.0 (4.4-30.9)	<0.0001
History of Urine Tea color	Yes	32	14 (61)		
	No	168	9 (39)	6.0 (3- 14)	<0.0001
History of Pallor	Yes	48	14 (61)		
	No	152	09 (39)	9.0 (3-23)	<0.0001
History of Yellowish Eyes	Yes	46	13 (57)		
	No	154	10 (43)	6.0 (2-14)	<0.0001
History of Jaundice	Yes	45	16 (70)		
	No	155	07 (30)	10 (4-27)	<0.0001
History Ingestion Fava Beans	Yes	118	13 (57)		
	No	62	10 (45)	0.8 (0.34-2.1)	0.70
History Treatment of Anemia	Yes	42	15 (65)		
	No	158	08 (35)	10.4 (4-27)	<0.0001
History of Infections (Malaria, Dengue, Typhoid)	Yes	24	09 (39)		
	No	153	14 (61)	4.0 (1.6- 11)	0.003
History of Using Drugs	Yes	23	07 (30)		
	No	154	16 (70)	3.1(1.2-8)	0.033
History of Blood Transfusion	Yes	13	04 (17)		
	No	187	19 (83)	4.0 (1 -14)	0.035

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IV. DISCUSSION

This study represents the first attempt to evaluate the prevalence of G6PD deficiency and its associated risk factors in the indigenous of Yemeni population specially amongst people whose life in different areas in Ibb city. The prevalence rate of G6PD deficiency was found 11.5 % among university students (9.5 % males and 2.0% females) these finding in similarity with study recently reported by Abdul-Ghani et al [22] who reported the prevalence of G6PD deficiency 12% among children from a malaria-endemic area of Hodiedah city. The prevalence rate of G6PD deficiency in these study is higher than the rates that are findings by Al-Nood et al [20] on blood donors and by Nasser, et al [21] on newborns hospitals in Sana'a capital city, where the prevalence rates had been found 7.1% and 5%, respectively. However, the prevalence of G6PD deficiency is lower than that result reported at (2011) by Hussein et al in Thamar city (14.8%) [25] and in Saudi Arabia (17%) [26]. Moreover, the G6PD deficiency prevalence rate among our population study is lower than the rates reported from neighbor countries such as Saudi Arabia 2-45.9 % [27, 28], Oman 27% [27], Jordanian 7-17.1% [29,30], China 28 .1% in Wuhan [31], and in Southwest Nigeria 28.1% [32].

The majority of G6PD deficiency students (90% boys and 50% girls) have been found at aged 18-24 years. The mean age of males was 22.2±2.4 years lower than compared to 23.0 ±2.97 years females with G6PD deficiency students, whereas, there was no significant difference among male and female of G6PD deficient students, this is suggested no association between age and G6PD deficiency. The current results indicate to (12.7%) of males have a higher significant prevalence of G6PD deficiency than females (8.0 %), this is quit similar to studies reported by AbdulGhani et al [22] in Hodiedah, where the prevalence rate was 12.8 % in males vs. 5.5% in females and other study reported by Karadsheh et al [29] in Jordan in which the prevalence rate was 11.1% in males and 5.8% for females in Amman area. The significant association between gender and G6PD deficiency has been reported from different parts of the world in which demonstrated that the higher frequency of G6PD deficiency rate among males explained the fact of G6PD deficiency is an X-linked hereditary disorder [33].

When comparison the means levels of hemoglobin and RBCs counts between G6PD deficient and normal G6PD students males and females revealed higher significant difference ($p<0.05$) this is might be attributed to the fact that G6PD deficient RBCs have more prone to haemolysis and destruction due to accumulation of internal oxidative radicals resulting in lost effective ability to maintaining their integrity than normal RBCs, even without exposure to external oxidative stress that caused by fava beans, medications using and exposed to infections. Our findings indicate to 56% of G6PD deficient students residence in Al-dihar place were found having a higher prevalent enzyme deficiency than in Al-mashanh (35%) and other place (9%) with no significant difference, these results indicate to the residency place having no risk for enhancing the prevalence of G6PD deficiency among our population compared to study reported by AbdulGhani, et al [22].

The overall rate of consanguineous marriage among parents of participants students was 48%, however, 18/23 (78%) of G6PD deficient students (16 males and 2 females) were parents having consanguineous marriage with a higher odd incidence of G6PD deficiency (OR=5.0; 95% CI 2-13, $p=0.002$) than normal G6PD students. These result in the line with studies reported from different countries such as in Yemen [22,40], in Jordan [34], in Egypt [35], in Qatar [36], in Oman [10,16,17,25] and in Iran [37].

The consanguinity marriage between the first-cousin was a deeply root in our social culture reflected the higher frequency prevalence of x-linked genetic disorders such as G6PD deficiency. The highest prevalence of consanguineous marriage rates in Arabian communities reach to 70 % among first-cousin [7], this is considered the greatest problem challenged healthcare that lead to circulate of x-linked genetic disorders within population. Therefore, the present study indicate to high frequency rates of G6PD deficiency significantly correlate with consanguinity parents and considering a good independent predictor act as great risk factor to increasing the prevalence of G6PD deficiency among our population.

G6PD deficient individuals had been found more prone to develop episodes of haemolytic crisis occurs when exposed to internal external oxidative agents such as favism which is more frequent among the population of the Mediterranean countries [38] where high and widespread of human ingestion of green, fresh, dried or cooked fava beans, however, most cases of G6PD deficiency with hemolytic crisis were self-limiting once exposure to the trigger is stopped [41]. 4/23 (17.4%) of G6PD deficiency students were having past history of hemolytic episodes due to favism with a higher odd incidence (OR=5.1; 95%CI 1.4-19, $p= 0.015$) tis is in line with study reported in Saudi Arabia (15.2%) [26]. So far several studies indicate to the toxic glycosides, vicine and convicine, which are present in fava beans, have been implicated in inducing of hemolytic crisis in some subjects with G6PD deficiency erythrocytes[39]. 17% of G6PD deficiency students having history of blood transfusion with a higher odd incidence (OR=4.0; *95% CI* 1-14, $p<0.035$) than normal students.

The current results indicate to 16/23 (70%) of G6PD deficient students were found having history of hemolytic anemia with a higher odd incidence (OR=11.0; *95% CI* 4.4-30.9, $p<0.0001$) than normal, this is reflected strong association between occurring hemolytic episodes and G6PD deficiency in non-diagnosis individuals when exposed to infections, drugs and fava beans. 13/23 (57%) of G6PD deficient students were having history of ingestion fava beans when triggered by hemolytic episodes with a lower odd incidence (OR=0.8; *95% CI* 0.34-2.1, $p=0.7$) than normal, this is finding lower than that reported in Iran (93%) [45] and in Jordan (97%) [34], however, the result agree with many studies reported from different countries such as

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in Saudi Arabia (32.3%) [26]. However, ingestion of fava beans was considered an independent risk factor for G6PD deficiency in the current study with low incidence effecting might be contributed to the possible effect of other factors such as most of our population study are ingestion fava beans.

In fact, most G6PD deficient individuals were remain clinically asymptomatic, but when exposure to different external oxidative agents that evocated hemolytic episodes such as infections (respiratory, typhoid fever, dengue virus and malaria) or consuming drugs (antibiotics and antimalarial) without description from physician that are potentially dangerous to evocated and causing episodes of hemolytic anemia especially in individuals whose non-diagnosis or screening for G6PD deficiency. In addition, the finding in this study indicate to a higher prevalence of infections 39% with a higher odd incidence (OR=4.0; *95% CI* 1.6- 11, p=0.003) this is results a higher than reported in Saudi Arabia (12.9%) in Iran 7.6% [37], in Jordan 13.9 % [30], in Nigeria 22% [44]. While 30% of G6PD deficiency students having history using of antibiotic and antimalarial drugs with a higher odd incidence (OR=3.1; *95% CI* 1.2- 8, p=0.033) than normal, this is finding is a higher than reported from Saudi Arabia (9.7%) [26]. However, our findings with many studies reported from different countries were demonstrated a higher association between infections, drugs and occurring hemolytic episodes in G6PD deficiency individuals and suggesting them are the main independent risk factors responsible for hemolytic crisis in G6PD deficiency individuals and a hall marker predictive factors in detection of G6PD deficiency individuals.

A lot of studies highlighted the development and persistence of acute hemolytic anemia is a vital hall marker indicators for G6PD deficiency in individuals after exposed to oxidative agents such as fava beans, infections, and medications. Consequently harmful increased oxidant stress in G6PD deficient RBCs causing denaturation and precipitation of Hb as heinz bodies on RBCs membrane ended with destruction RBCs resulting in change color of urine to tea, jaundice and skin pallor [42,43]. Several reports from different countries where high G6PD deficiency frequency were highly provided the exposed to fava beans, infections and drugs are the main risk factors for the development of acute hemolytic anemia in G6PD deficient individuals. Significantly there was found 57% of students with G6PD deficiency having a higher odd incidence of change urine to tea color (OR=6.0; *95% CI* 3- 14, p <0.0001) than normal students, this is in similarity with studies reported in Saudi Arabia (38.7%) [26] and in Iran (49%) [45], whereas disagree with another study reported in Iran at 2018 by Honar et al. (97%) [46]. The odd incidence of skin pallor was a higher significantly (OR= 9.0; *95% CI* 3-23, p <0.0001) found in 70% of G6PD deficient students than normal, this is lower than study reported by Honar et al. in which 100% of cases with G6PD deficiency suffer from pallor and yellowish Sclera and nearly in similarity with study reported in Saudi Arabia (48.4%) [26], whereas, our result disagree with other study reported in Iran (25%) [45]. Also, there were found 57 % of G6PD deficiency students were suffering from yellowish eyes with a higher odd incidence (OR= 6 ; *95% CI* 2-14, p <0.0001). 70% of G6PD deficiency students having a higher odd incidence of jaundice (OR= 9.0; *95% CI* 3-23, p <0.0001) this is in agree with study reported in Eygpt (61.5%) [47] and disagree with reported in Saudi Arabia (19.4%) [26], whereas, 65% of G6PD deficiency having a higher odd incidence of treated hemolytic episodes (OR=10.4; *95% CI* 4-27, p<0.0001), this is finding agree with study reported in Iran (71%) [45]. These finding with pervious findings were reflected the strong significant association between occurring of hemolytic episodes (change urine color, skin pallor, jaundice, yellowish eyes), history treatment of hemolytic anemia and G6PD deficiency after triggering by infections, fava beans and drugs. The obtained results provided that G6PD deficient individual was likely prone to develop complications and symptoms of hemolytic anemia than normal students. Likewise, 17% of G6PD deficiency students were had significantly (p=0.035) blood transfusion, this is disagree with result reported by Kavehmansh et al in Iran (96%) of children admitted to hospital having receive blood transfusion [45].

Multivariate analysis for independent predictors for G6PD deficiency in our conducted students were found consanguinity between parents, history symptoms of hemolytic episodes (yellowish eyes, pallor, jaundice, tea urine), suffering from infections, ingestion fava beans and drugs, and history treatment of anemia and blood transfusion. The overall these independent predictors might be act as great risk factors as well as predictors for G6PD deficiency in our population whose lack any screening program for early detection and diagnosis of G6PD deficiency individuals. Interestingly, the current study suggest that G6PD deficiency could be represent a significant health problem for those undiagnosed and asymptomatic G6PD deficient individuals through the incidence of hemolytic crisis anemia when exposure to different oxidative stress especially in population whose not yet using screening program for detection enzyme deficiency.

V. CONCLUSION

The present study showed that the prevalence of G6PD deficiency among students whose original indigenous of Ibb city population is 11.5%. The most significant independent predictors of G6PD deficiency among population are clinical symptoms of hemolytic crisis episodes that might be appearing in individuals whose suffer from infections (typhoid fever, malaria and dengue virus) and ingestion of fava beans and medications as well as consanguinity between parents. The findings in these study are highlighted the need for the routine screening for G6PD deficiency in newborn, children and individuals whose non-suffering or suffering from hemolytic anemia in evidence-based management to minimize the complications risks of hemolytic episodes. The future studies should be pointed toward determine and identification of the G6PD variants that implicated in the severity of G6PD deficiency complications in our population.

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