Age of Spontaneous Regeneration of Glucose-6-Phosphate Dehydrogenase Among Children in Baghdad.

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ABSTRACT:

BACKGROUND:

Glugose-6- phosphate dehydrogenase deficiency is the most common human enzyme deficiency in the world andlead to hemolytic anemia as early sign.

OBJECTIVE :

To determine the age of the patient with G6PD deficiency in which can the enzyme return to normal activity indifferent areas of Baghdad and to study if there is sex predilection for spontaneous regeneration of the enzyme.

PATIENTS AND METHODS:

Case control study carried on patients at AL-kadhyimia teaching hospital and patientscollected from different areas of Baghdad city during period from 1st of April 2012 to 31st of December 2012, 159 patients of G6PD disease, the range of their age 2-17years old age and 121(76%) of them were male and 38(24%) were female. Another 100 normal children of different sex and age range from 6-17 years were regard as control group, they were collected from different schools in Baghdadcity ,all of them had normal enzyme activity.

RESULTS:

Age of spontaneous regeneration of G6PD wasstatistically significant becauseP value =<0.001(highly significant)i.e. as patient becomes older (>14year) he has a very good chance for the enzyme to return to normal activity.

CONCLUSION:

The age of spontaneous regeneration of G6PD enzyme in children was above 14 yearsandthere is no sex predilection.

KEY WORDS: Glugose-6- phosphate dehydrogenase deficiency,hemolytic anemia.Age.

INTRODUCTION:

Favism is an acute hemolytic anemia, usually in persons of Mediterranean area descent, occurring when an individual with G6PD deficiency of erythrocytes eats fava beans or inhales the pollen, of Viciafaba[1]. The term 'favism' ; however, is used rather broadly for symptoms caused by a reaction to a number of different substances including, but not limited to, favas[2]. G6PD deficiency is the most common human enzyme deficiency in the world[3] Individuals with the disease may exhibit nonimmune hemolytic anemia in response to a number of causes, most commonly infection or exposure to certain medications or chemicals. [3,4].

,It is considered to be the most important disease of what is known as hexos monophosphate pathway of RBC metabolism[5].

This X-linked inherited disorder most commonly affects persons of African, Asian, Mediterranean, or Middle-Eastern descent, but it can be found in virtually any population.[3,6,7]G6PD is the first enzyme in the pentose phosphate pathway; it converts glucose 6-phosphate to 6-phosphogluconate-d-lactone with the reduction of NADP+ to NADPH. The NADPH plays a vital role in protecting erythrocytes against oxidative damage.[9] G6PD deficiency affects primarily the erythrocytes, older cells being more severely affected than newly formed ones [7,8, 9].

The World Health Organization recommends screening all newborns in populations with a prevalence of 3 to 5 percent or more in males. [10,11].

AIMS OF STUDY:

To determine the age of the patients with G6PD deficiency in which can the enzyme return to normal activity in different areas of Baghdad,and tostudy if there is sex predilection for spontaneous regeneration of enzyme.

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PATIENTS AND METHODS:

Case control study carried on 159 patients at AL-kadhyimia teaching hospital and patients collected from different areas of Baghdad city during period from 1st of April 2012 to 31st of December 2012, selection criteria are include that the patients had documented enzyme deficiency by laboratory test and was receiving at least one blood transfusion for acute hemolytic attack in his life, with positive family history of enzyme deficiency,Another 100 normal children of different sex and age range from 6-17 years wear regard as control group, they were collected from different school s in Baghdad city ,for both two groups blood sample for enzyme assessment are taken after thepatient agreement and their families. Patients whose enzyme return to normal at different ages, undergo challenge test by ingestion of fava bean or given aspirin in a dose of 60-100mg/24h and another blood test were done for enzyme level assessment for double check and all of them had normal enzyme activity.

Data analysis were done by statistical package for social Science (SPSS) version 19, quantitative variables were using mean and standard deviation. P-value $\leq$ 0.05 were considered to be statistically significant.

RESULTS:

The mean age of the study group was (12.13$\pm$4.49) years with a range of (2-17) years, and the mean age of control group was (13.47 $\pm$ 3.79)years with range of (6-17) .

Out of 159 patient's there were 38 (23.9%) females, and 121 (76.1%) males; with a male to female ratio (3.18:1). As in figure (1)

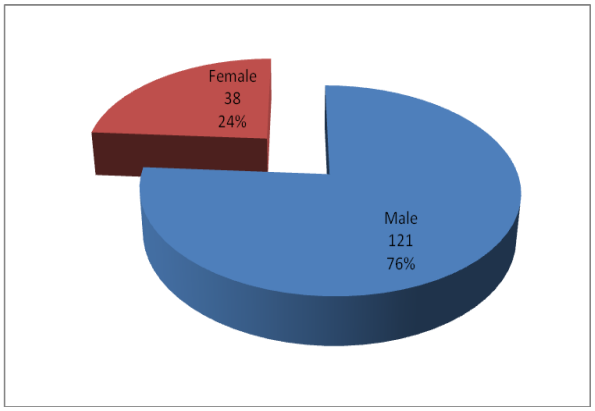

Figure 1: Distribution of cases according to gender.

Out of 159 patients , 79 (49.15%), who were previously diagnosed to have G6PD, are still having G6PD deficiency at time of sample collection and in 80 (50.85%) patients the enzyme activity return to normal. While 144 patients (90.6%) had positive family history of G6PD deficiency, and the number of patients presented with hemolysis at time of sample collection was (42) accounting for (26.4%) and all patient's (159) had previous hemolysis and received blood .as shown in table(1).

Table1: General characteristics of the study sample.

Age (year)	Total no.	Gender ratio male:female	Previous hemolysis	Receive blood	Positive Family history	Normal Enzyme assay		Healthy control group	p-value (gender)	p-value (enzyme)
						No.	%			
2	2	1:1	2	2	2	0	0.00	0	---	----
3	2	2:0	2	2	2	0	0.00	0	----	----
4	3	3:0	3	3	1	0	0.00	0	----	----
5	11	2.67:1	11	11	11	0	0.00	0	----	----
6	7	7:0	7	7	6	0	0.00	6	----	0.001*
7	8	8:0	8	8	8	0	0.00	6	---	<0.001*
8	10	2.33:1	10	10	7	0	0.00	7	1.000	<0.001*
9	12	1.4:1	12	12	10	0	0.00	9	1.000	<0.001*
10	7	7:0	7	7	7	0	0.00	6	----	0.001*
11	3	2:1	3	3	3	0	0.00	3	1.000	0.100
12	2	2:0	2	2	2	0	0.00	3	---	0.100
13	5	4:1	5	5	4	2	40.00	5	1.000	0.167
14	8	7:1	8	8	8	5	62.50	5	1.000	0.231
15	28	2.5:1	28	28	28	26	92.86	18	0.732	0.513
16	24	2.43:1	24	24	20	22	91.67	15	0.711	0.514
17	27	2.38:1	27	27	25	25	92.59	17	0.739	0.515
Total	159	3.18:1	159	159	144	80	50.85%	100	0.724	<0.001*

We subjected patients who developed normal enzyme level to challenge by administration of fava beam r aspirin tablets(60mg/kg/24hr) then after (3-5)days, we repeat enzyme level test, and all of them passed the test successfully .As in table(2)

Table 2: Relationship between age of patient and their enzyme level after challenge test

Age (years)	No. of patients	Patients with normal enzyme	Patients with normal enzyme after challenge (fava & Asprin)*	
			No.	%
13	5	2 (40%)	2	100
14	8	5 (62.5%)	5	100
15	28	26 (92.8)	26	100
16	24	22 (91.6%)	22	100
17	27	25 (92.5)	25	100
Total	92	80 (86.9)	80	100

The mean age of male patients whose enzyme return to normal was (11.88±4.52) years, which is not significantly different from the mean age of female patients (12.94±4.33),(P-value =0.204) i.e. there is no effect of gender on the mean age of patients enrolled in the present study, as in figure(2),

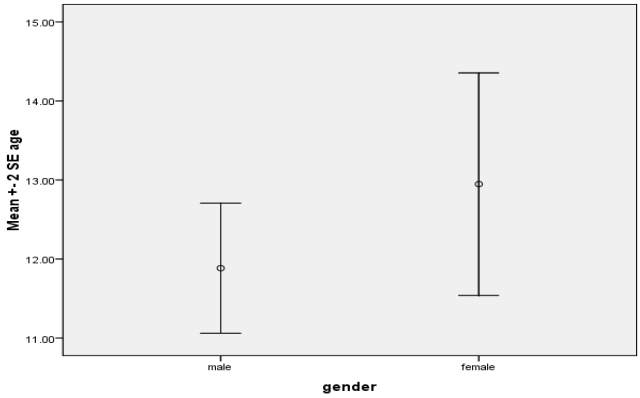

Figure 2:The (95% Confidence interval) mean age of male and female.

There was no significant association between gender and G6PD status which showed a p-value of (0.484). As shown in table (3) and figure (3)

Table 3: Association between gender and G6PD status.

G6PD	Male	Female	Total
Normal	59 (48.7%)	21 (55.2%)	80 (50.3)
Deficiency	62 (51.3)	17(44.8%)	79 (49.7)
Total	121	38	159

P. value =0.484 not significant

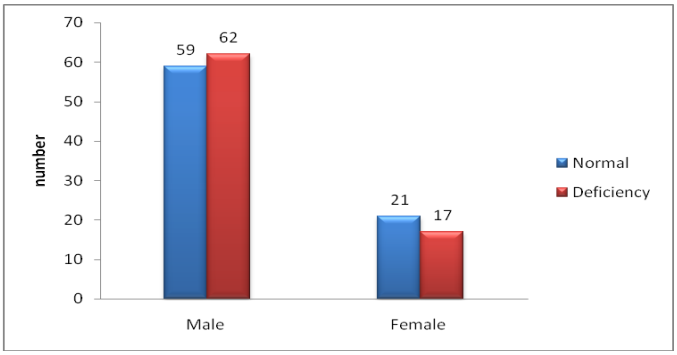

Figure 3 : Association between gender and G6PD status.

To study the correlation between a numeric variable, a Spearman rank test is used shows highly significant P<0.001, positive correlation between age and G6PD deficiency status, i.e. as patient becomes older he has a very good chance for the enzyme regeneration. As in Figure (4)

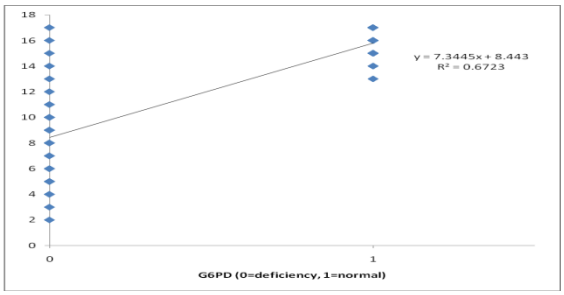

Figure 4: Correlation between age and G6PD status (r =0.796).

Out of 80 patients with age 14 years and more 78 patients had normal level of G6PD enzyme ,while only 9 patients had deficiency ,and the best age cutoff value to define enzyme regeneration is to perform ROC (receiver operator characteristic analysis), which showed that the best age was (14 years). At this age and above the sensitivity of (97.3%) and a specificity was (89.6 %). As in table (4) figure (5).

Table 4: Classification of cases according to 14 years and more cutoff age.

	G6PD		
Age	Normal	Deficiency	Total
≥14	78 (89.6%)	9 (10.4%)	87
<14	2 (2.7%)	70 (97.3)	72
Total	80 (50.3%)	79 (49.7%)	159

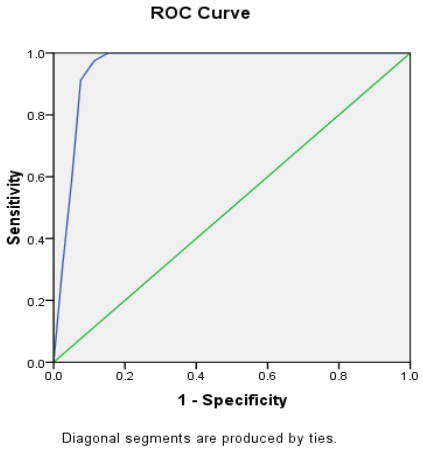

Figure 5: ROC curve to find the age cutoff value.

DISCUSSION:

The current study shows (24%) females were affected, this is similar to that observed by Al-Omran who reported female in 21%[12] ,The prevalence of G6PD deficiency in female may be due to the high rate of consanguinity in marriage among our society, leading to increased number of female homozygote and the high frequency of inactivation of the normal x-chromosomes in female heterozygote, by Lyon hypothesis[13],.. While (76%) males which is Similar to study carried out in Taiwan [14] reported (80%) in male , this minor difference because of the difference in study mass .

positive family history in (90.6%) patients, which higher than Lorraine Lica.[2]reported 80% because the selective criteria in current study were patients with positive family history, about 9.4% of our cases had no family history of G6PD deficiency which agree with Erbagcl A B[15] reported 10% with no family history of g6pd, which may be due to sporadic mutation .

Current study showed that the age of

regeneration was above 14 years, Which agree with other studies demonstrated that decreasing incidence of G6PD deficiency with advancing age **(** Beutler E, Vulliamy T, Luzzatto) [16] and (Petrakis NL, Wiesenfeld SL, Sams BJ) [17].

CONCLUSION:

1. G6PD enzyme may be regenerated with increasing age of the patients. The age of spontaneous regeneration in children(male and female) is above 14 years .i.e. the deficiency is not lifelong.
2. There is no sex predilection in mean age at which enzyme activity return to normal.

Recommendations:

Screening of all family members of affected patient's for enzyme status to prevent acute hemolysis and inform the families of affected patient's about the types of food and drugs that can causes hemolysis.

Great need for newborns screening for early diagnosis of enzyme deficiency

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