Frequency of G6PD Deficiency among Bahraini students: A Ten Years Study

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Background: G6PD deficiency is a genetic disease, common in Bahrain, and has high frequency world wide. The majority of affected individuals are asymptomatic. The disease can cause hemolytic anemia, which could be drug-induced or following infection, neonatal jaundice, chronic non-spherocytic hemolytic anemia and favism. The aim of the study is to report on the frequency of G6PD among the students in Bahrain, during 1999-2008.

Setting: Hematology Laboratory at Salmaniya Medical Complex.

Design: A cross sectional interval study, performed annually for a period of ten years.

Method: All the students of the 11th grade (2nd grade in secondary schools) were screened annually, this program continued for ten years 1999-2008. Samples were collected from the school children and tested for G6PD level. Blood samples were analyzed in the hematology laboratory at SMC. Students were issued cards showing their status and their results were recorded in the computer for data analysis. Informed consent was taken from the parents.

Result: 60,424 students were screened from 1999-2008. The ratio between males and females was 2:3. The mean prevalence of G6PD was 22.3% for homozygous. High prevalence rate was seen in Sitra 197/433 (45%), and Western area 90/250 (36%). No significant difference was observed during this period.

Conclusion: The mean prevalence rate of G6PD Deficiency among Bahraini students was 22.3%, for homozygous, which is comparable with the prevalence in other Gulf countries. No significant change in the prevalence rate during the 10 years was observed. More studies are needed to explore the clinical effect of this condition.

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Glucose 6 phosphate dehydrogenase deficiency is the most common enzymopathy in man. It is estimated to affect over 400 million people worldwide[1]. It was discovered by Alving and coworkers, while investigating unusual hemolytic reaction that occurred in ethnic black individuals following the administration of primaquine, an 8-aminoquinoline, for the treatment of malaria. Its incidence and clinical presentation vary considerably among different ethnic groups[2].

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The distribution is similar to that of the Thalassemia and is thought to be due to the selective advantage of these phenotypes against endemic malaria infection in the past[3-7].

Populations with common G6PD deficiency are distributed in the Mediterranean regions, across the Middle East, India, Indochina, and South China as well as middle Africa. Its incidence in the Arab world ranges from 8% to 50%[8-19].

G6PD is a cytoplasmic enzyme in the hexose monophosphate pathway responsible for the production of glutathione. It helps to protect the red blood cells from oxidative damage. G6PD B+ is the predominant enzyme, while G6PD A+ (a non-deficient normal variant) exists in polymorphic low frequency. The Mediterranean variants, is the most common deficient variant in Saudi Arabia, United Arab Emirates and Bahrain[20].

G6PD deficiency is an X-linked recessive genetic disorder. The gene located on chromosome Xq28 region, with a higher frequency in males than in females. While most of the G6PD deficient variants resulted in compensated hemolysis and no anemia in the steady state, some causes chronic nonspherocytic hemolytic anemia (CNSHA). The clinical spectra includes Acute massive intravascular hemolysis due to agent such as anti-malarial, Sulfonamides, Sulfones, Nitrofurans, naphthalene (mothballs), aspirin, fava beans. Diabetes ketosis_and infection may cause hemolysis, such as, viral respiratory infection, viral hepatitis and bacterial pneumonia. G6PD deficiency may also cause neonatal jaundice (NNJ) with kernicterus[21-28].

The Situation in Bahrain

The estimated population in 2007 was 1,039,297; it was based on the 2001census data (646,551). The majority of Bahraini Arabs are originally from Arabian Peninsula. The crude birth rate was estimated to be 15.4 per 1000 population in 2007[29].

Falciparum malaria was endemic in Bahrain until 1970, later it was eradicated. The malaria associated genetic defects of red cells such as SCD, Thalassemia and glucose 6 phosphate dehydrogenase deficiencies were expected to be common. A new-born screening study conducted in Bahrain during the year 1984-1985, showed that 20% had G6PD deficiency[30,31].

The student screening project aims to determine the prevalence of the genetic blood disorders such as sickle cell anemia, Thalassemia and glucose 6 phosphate dehydrogenase deficiency, and identify the geographic distribution and variation among regions. It also aims to create awareness of hereditary anemias through prior comprehensive educational campaign.

METHOD

A student screening project was conducted among the 60424 school children studying at the 11th grade in 38 schools from 1999 to 2008. It is a collaborative project between Ministry of Health, Ministry of Education and Bahrain Hereditary Anemia Society.

The project includes planning, educational sessions, blood collection, laboratory testing, data processing, distribution of cards, data analysis and reporting. Informed consent was obtained from the parents, and students were fully informed about these diseases through educational lectures, and informational booklets. The blood samples were collected from the students by laboratory technicians. Samples were tested for G6PD deficiency by

fluorescence spot test using one ml of whole blood collected in ethylenediamine tetraacetic acid tube. A coded form was issued to each student with the result. At the initial stages of the project, the ethical and legal issues such as informed consent, equity, confidentiality, no discrimination, no stigmatization and freedom of choice were all taken into consideration.

This is a cross sectional interval study, performed annually for a period of ten years. The obtained data was coded, processed and analyzed by using SPSS.

RESULT

Seventy five percent of the student samples were found to be normal and free of G6PD deficiency. The number of students found to be affected with G6PD homozygous between 1999 to 2008 were: (year 1999) 1320 (23.22%), (year 2000) 1337 (23.48%), (year 2001) 1519 (24.33%), (year 2002) 1401 (23.77%), (year 2003) 1126 (20.78%), (year 2004) 1432 (22.96%), (year 2005) 1334 (20.98%), (year 2006) 1333 (20.99%), (year 2007) 1311 (20.56%), (year 2008)1365 (22.14%). Total = 13478/60,424 = 22.3%, see Table 1 and Figure 1.

Table 1: G6PD Prevalence among Students in Bahrain (99-2008)

Year	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**
Diseases										
Heterozygous	105	14	11	4	16	9	16	52	37	26
No and %	1.85%	0.25%	0.18%	0.06%	0.30%	0.14%	0.25%	0.82%	0.58%	0.42%
Homozygous	1320	1337	1519	1401	1126	1432	1334	1333	1311	1365
No and %	23.22%	23.48%	24.33%	23.77%	20.78%	22.96%	20.98%	20.99%	20.56%	22.14%
Total No.	5685	5694	6244	5894	5418	6237	6358	6352	6376	6166

In 1999, higher G6PD deficiency prevalence rates were found in the region of Sitra (45%), Western area (36%), Jidhafs (34%), Northern area (31%) and Central area (31%). The prevalence were lower in Isa town (17%), Muharaq (11%), Riffa (8.3%) and Hidd (5.4%), The prevalence rates among males and females homozygous were 11.37% and 11.86% respectively; 55% of the affected were females and 45% were males. Carrier rate was low (1.85%), because female carriers could not be detected accurately by this method. Twenty-one percent of G6PD deficient students had sickle cell trait and 1.68% had sickle cell disease.

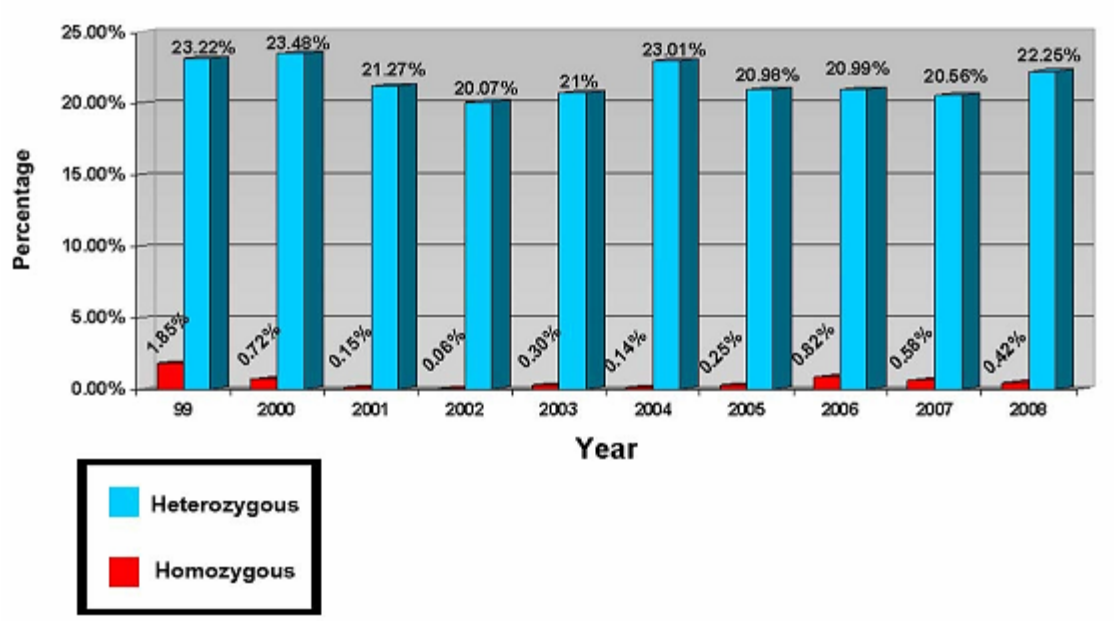

Figure 1: G6PD Prevalence among Students in Bahrain (99-2008)

DISCUSSION

The frequency of G6PD deficiency is high in Bahrain, but it is comparable with the other Gulf countries. G6PD deficiency has been found at a frequency of 25% in Omanis male population, while the highest frequency was 65% in males living in Qatif Oasis of Eastern Saudi Arabia[8,9]. The majority of the affected individuals were asymptomatic, and they are not aware of their condition.

The male to female ratio in our study was nearly 1:1, as the number of female students in this study was more than male students 60%: 40%. The other causes may be the method used in this study and the higher frequency of the disease in the country. Homozygous affected females were not uncommon, as females may be affected through lionization. Patients have little clinical implication. Few cases were admitted with hemolytic crisis although fava bean is one of traditional food recipes in the country. On the other hand, there is higher rate of neonatal jaundice.

The molecular basis of G6PD-deficiency among Bahraini population showed that 90% of patients had mutation 563, in addition to the silent mutation 1311, which was identical to the characteristic of the Mediterranean mutation[32]. These data revealed the high molecular homogeneity of G6PD-deficiency in Bahrain. It is identical to the Mediterranean mutation in European and Mediterranean countries, and was different from that reported from the Indian subcontinent, where the silent 1311 mutation is not detected. The possibility that the Mediterranean variant arose somewhere in the Mediterranean and then spread through the interaction between Europeans with the Arabs and other ethnic groups in the Middle East. However, the possibility that the latter variant arose independently in Arabia, and its frequency increased because of various selective forces such as Malaria cannot be ruled out[33-36].

Testing for G6PD is carried out during the pre marital counseling investigations, but the result does not influence the marriage decision as the majority of the affected people lead normal life[37].

Early detection of genetic trait, like G6PD deficiency, by neonatal screening is feasible and cost-effective. It allows the early preventive measures against severe jaundice and kernicterus. Other preventive strategies later in life include education of patient and doctors, and the provision of a list of agents to be avoided. It is obvious that such genetic trait does not warrant prenatal diagnosis or the advice for termination of pregnancy.

CONCLUSION

The mean prevalence rate of G6PD deficiency in Bahrain was 22.3%, for homozygous. No significant change in the prevalence rate during the past 10 years was observed. More studies are needed to explore the clinical effect of this condition, more research should be undertaken to study its effect on newborns jaundice.

The technique is not accurate or sensitive in diagnosing the carriers. Further studies are needed to explore the clinical effect of this condition and to estimate the magnitude of the carriers.

Due to lionization many of carriers cannot be identified, because females has two X chromosome, if one is affected and it is inactive, the enzyme level will be normal.

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