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Significance of cord blood screening test for glucose-6-phosphate dehydrogenase enzyme deficiency

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Abstract
A tests including complete blood count, reticulocyte %, total bilirubin, and fluorescent spot test for glucose-6-phosphate dehydrogenase enzyme were performed on cord blood samples from (725) full term newborns, (396) males and (329) females, the CBC, reticulocytes and total bilirubin all are within normal limit, negative results for fluorescent spot test, i.e. glucose-6-phosphate dehydrogenase (enzyme) deficiency was identified in 55/725 (7.58%), 43/55 males and 12/55 females (10.8% of total males and 3.64% of total females). Advices were given to parents of the newborns with enzyme deficiency in order to avoid risk factors which may lead to haemolysis and to look for the signs of hyperbilirubinemia. Nine male newborns were readmitted to the hospital because of hyperbilirubinemia with indication for phototherapy, no one reach the bilirubin level of blood exchange, no one develop signs of neurological deficit.

Keywords: cord, blood, screening

Introduction

Glucose-6-phosphate dehydrogenase enzyme is an enzyme present in the cytoplasm of all body cells involving erythrocyte, the main role of this enzyme is to maintain a sufficient amount of NADPH, through the hexose phosphate pathway, (pathway responsible on ATP production). NADPH maintains the level of glutathione in the reduced form, which has a critical role in protecting cells from damage by oxidizing agents, the erythrocytes is usually are more susceptible than other cells. The G-6-PD gene is located on the long arm of X chromosome, (X-linked inheritance), two hundred seventeen gene mutations have been described worldwide, usually it is a missense mutation which may result in decrease enzyme stability or qualitative changes, the most common polymorphic variant is G-6-PD Mediterranean and G-6-PD A. It is the most common enzymopathy, it affect about 400 million individuals worldwide. Clinically may be asymptomatic, presented as neonatal jaundice, acute haemolytic anaemia in respond to oxidant agent, chronic non spherocytic haemolytic anaemia, the severity is highly depending on the level of the enzyme which already depend on the enzyme variant and also on the type of oxidant agents and duration of the exposure [1, 2, 3, 4, 5, 6]. WHO is classify G-6-pd deficiency according to the level of the enzyme and the severity of illness and adapted into five classes

Class I the residual enzyme activity less than 10% clinically may be presented by chronic non spherocytic haemolytic anaemia, neonatal jaundice, acute exacerbation.

Class II the residual enzyme activity is also less than 10%, clinically asymptomatic in the steady state.

Class III enzyme activity between 10-60% asymptomatic in the steady state.

Class IV, V were enzyme activity near 100, >100%, asymptomatic.

A total 280 study had been done on the prevalence of the G-6-PD deficiency in 88 countries, it ranges between 5%-25%, the highest prevalence rate in sub-Saharan African countries,The incidence of neonatal hyperbilirubinemia, is higher in cases of G-6-PD deficiency than in baby without deficiency. The clinical manifestation is started to appear from first to fourth day after birth, rarely at birth. Jaundice become more severe in premature baby, if associated with infection, environmental factor and if mother received oxidant drugs [7, 8, 9, 10]. Neonatal jaundice is one of the severe form of G-6-PD deficiency, dangerous neurological complication mostly belongs to Class I deficient variant. Kernicterus and permanent neurological deficit higher in enzyme deficiency, 20-30% of kernicterus is due to G-6-PD deficiency jaundice. Neonatal jaundice due to enzyme deficiency is twofold higher than in non-deficient [4, 11, 12].

Area with high prevalence rate of G6PD deficiency and morbidity- in Africa, Mediterranean and Middle Eastern countries, started to screen the neonates routinely by semi quantitative, quantitative enzymatic activities, and genetic screen, also assessment of cost effect and the role of early detection in prevent complication, had been studied [17,19].

Aim of the study

To assess the benefit of early detection of G-6-PD enzyme deficiency by simple available tests in order to avoid development of severe hyperbilirubinemia and haemolysis and thus prevent serious neurological complication which may be results from severe hyperbilirubinemia.

Methods

Cord blood samples from (725) newborns had been collected in in Al Salam Hospital in Mosul/Iraq. Both normal labors and cesarean section were included in this study, between June/2013-February/2014.

Tests which done for all was including

1. Complete blood count by auto-analyzer cell dyne 5 diff.
2. Reticulocytes percent using brilliant cresyl blue dye according to standard method [13].
3. Fluorescent screening test for G6PD deficiency. A semiquantitatve test, the principle of the test depends on the presence of NADPH in the lysate which fluoresces under UV light. Blood with G6PD deficiency lacks fluoresces because there is an inability to produce

sufficient amount of NADPH. Test give positive result if enzyme activity 20% or more [13].

4. Total bilirubin measured by Bilirubinmeter. Newborn babies diagnosed as a case of G-6-PD deficiency, their mothers had been advised to keep the newborns under observation and avoid factors which could be a trigger factor for haemolysis, and then followed for two weeks.

Results

From total 725 samples, 396 (54.6%) males, 329(45.4%) females. 55/725 (7.58%) give negative results with fluorescent spot test (G-6-PD deficiency).43/55 of affected babies are males, 12/55 are females, with ratio 3.6:1. 43/396 deficient males from total males included, constitute (10.8%), while percent of female with deficient enzyme 3.64% (12/329). After follow up and monitoring the newborns for hyperbilirubinemia development, nine male enzyme deficient babies develop jaundice and needed phototherapy. No one needed exchange transfusion. No baby had neurological complication. The results are summarized in table-1-.

Table 1: The results.

	Total	Males	Females
Samples	725	396(54.6%)	329(45.4%)
G6PD deficiency	55/725(7.58%)	43/396(10.8%)	12/329(3.64%)
hyperbilirubinemia	9(1.24%)	9/396(20.90%)	0.0

Other tests had been performed on the cord blood were complete blood picture concentrating on the haemoglobin results. Reticulocytes percent and bilirubin. We divided the results into two groups, first group for positive spot test(normal) and second group for those with negative spot test(enzyme deficient) and the results compared between the two groups as an attempts to discover a potential risk results. Results of haemoglobin, reticulocytes, and bilirubin for those with enzyme deficient are within accepted ranges [14, 15, 16], the mean of the three parameters are near the mean for those of normal enzyme activity. The results are summarized in table-2-.

Table 2: Results of haemoglobin, reticulocytes, and bilirubin

	+ve spot test(normal)	-ve spot test(enz. deficient)
Haemoglobin Range Mean	13.1-18.4 g/dl 16.73g/dl	16 - 18 g/dl 16.8 g/dl
Reticulocytes Range Mean	1.2 - 8% 3.2%	3 - 5.2% 4%
Bilirubin Range Mean	0.1-2.15 mg/dl 0.97 mg/dl	0.6 - 2 mg/dl 1.02 mg/dl

Discussion: Screening test for G6PD deficiency had been performed in many countries either as a routine screen test in area with high prevalence rate especially if associated with severe clinical state, as A and Mediterranean variants. Others apply special criteria for screen [8, 17]. The choice between two screening strategies either selective (high risk) or universal depends on the prevalence of the disease, severity of the enzyme variant and the cost effectiveness [23]. WHO recommend, if the prevalence of G6PD deficiency exceed 5% in males, the screen should be done routinely [24]. Many studies on the prevalence of G-6-PD deficiency done in Iraq in general -and in Mosul city, the capital of Nineveh province- where this study is performed. There are variation between the results performed most probably depends on the difference between the target groups, if healthy personals only are chosen or random study and probably due to ethnic groups. Study done in 1981 in Iraq, 12.4% males are enzyme deficient, similar to this study 10.8% for males while 8.8% for females which is more than double that of our study 3.64% for females, in general previous study done on all age groups and reveals that those bellow 5 years affected more [25]. Study done in Mosul (2012), over all prevalence is 5.8%, this study is 7.58% [26]. While in other epidemiological study, give similar result to this study Male: female 3.4:1 in Mosul, in this study the ratio is 3.6:1 [22]. In Misan (Iraq), study done on cord blood screen, total deficiency 8.82%, 13.97% for male, 2.59% for females [21]. According to molecular study done in Nineveh (Iraq) 2012-2013 and Bagdad (Iraq), the Mediterranean variant is the most common variant [20, 27]. So this study with studies done previously confirm that Mosul city belong to area considered as area of high prevalence G-6-PD deficiency. The importance and the benefit of cord blood screen for G-6-PD deficiency thoroughly studied around the world in order to avoid the high morbidity and mortality in area with high prevalence [5, 11, 18, 19, 29, 30,]. This study also confirm that cord blood screen (early diagnosed) and the advices which are given to the mothers will reduce the morbidity of the illness, as we illustrate only 9 newborns from 43 male deficient needs phototherapy, these result become significant if we know that the past family history of the affected babies, one of them give history of kernicterus and death during infancy and another give family history of exchange transfusion due to hyperbilirubinemia, while in this study with early detection no one indicated for exchange transfusion, no neurological deficit were reported in, these finding are also confirmed by other studies which concentrate on the comparison between development of kernicterus in screen and non-screened [19]. Study of haematological parameters (Haemoglobin, reticulocytes, and bilirubin) on cord blood have no role in detection cases with enzyme deficiency or those who have chance to develop hyperbilirubinemia.

Conclusion

Mosul is considered as area with high prevalence enzyme deficiency, Simple screening test for glucose-6-phosphate dehydrogenase deficiency is advised in Mosul in order to reduce the morbidity of the illness especially permanent neurological complication.

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