Hyperbilirubinemia in glucose-6-phosphate dehydrogenase-deficient male newborns in Al-Ahsa, Saudi Arabia

Sameer Y. Al-Abdi, SSCP, MRCPCH, *Taher A. Mousa,* DCH, MRCPCH, *Maryam A. Al-Aamri,* MBBS, *Najeeb G. Ul-Rahman,* MBBS, DCH, *Ayman I. Abou-Mehrem,* MD, CABP.

ABSTRACT

الأهداف: دراسة الخصائص السريرية والمخبرية لفرط بيليروبين الدم لدى المواليد الذكور المصابين بعوز إنزيم نازعة هيدروجين الغلوكوز – 6 – فوسفات (G6PD) في منطقة الإحساء – المملكة العربية السعودية.

الطريقة: تمت مراجعة السجلات الطبية للأطفال الذكور المولودين في مستشفى الملك عبد العزيز في الإحساء خلال الفترة من مايو 2008 حتى أبريل 2009م. ولقد اشتملت الدراسة مواليد الإحساء الذكور الأصحاء المصابين بعوز G6PD وغير المصابين بكثرة الكريات الحمراء، والذين قد ولدوا في الأسبوع 37 من الحمل أو بعده، وكانت أوزانهم عند الولادة ≤ 2.5 كغ، ولا يوجد لديهم سبب آخر لفرط بيليروبين الدم، والذين تم أخذ عينة منهم لفحص مصل بيليروبين الإجمالي (TSB) خلال الساعات الثمان والأربعين الأولى من الحياة. تمت مقارنة المواليد المصابين بفرط بيليروبين الدم مع المواليد غير المصابين بفرط بيليروبين الدم.

النتائج: ضمن 93 وليد مصاب بعوز G6PD استوفوا معايير الدراسة، كان هناك 67 مصابين بفرط بيليروبين الدم احتاجوا معالجة ضوئية، احتاج 13 منهم إلى معاودة المعالجة الضوئية. تم بدء المعالجة الضوئية بعمر 11±4 ساعة (متوسط ± انحراف معياري) ولمدة إجمالية 42±28 ساعة. مقارنة مع المواليد غير مصابين بفرط بيليروبين الدم، كان لدى المصابين بفرط بيليروبين الدم بشكل مهم إحصائياً نسبة عالية للهيماتوكريت (53±6 مقابل 49±8%، p=0.02)، و مستوى عالي للهيموغلوبين (176±18 غ/ل مقابل 166±21، p=0.04)، و نسبة قليلة للخلايا الشبكية (4.3±0.7 مقابل 5.2±1.0%، p=0.02).

خاتمة: يظهر فرط بيليروبين الدم بسبب عوزG6PD لدى مواليد الإحساء الذكور بمستويات عالية لكل من الهيماتوكريت والهيموغلوبين، و نسبة قليلة لخلايا شبكية مقارنة بنظائرهم غير مصابين بفرط بيليروبين الدم. ويتطلب فرط بيليروبين الدم معالجة ضوئية مبكرة ومتكررة. لذا ينبغي توفر متابعة مناسبة لهؤلاء المرضى و إجراء مزيد من البحوث للفهم بدقة فرط بيليروبين الدم لدى المواليد المصابين بعوزG6PD.

Objectives: To study the clinical and laboratory characteristics of hyperbilirubinemia in glucose-6-phosphate dehydrogenase (G6PD)-deficient male newborns from Al-Ahsa area (Ahsais).

Methods: The medical records of inborn male infants at King Abdulaziz Hospital (KAH) in Al-Ahsa area, Kingdom of Saudi Arabia from May 2008 through April 2009 were reviewed. Inclusion criteria were healthy non-polycythemic G6PD-deficient Ahsai males born at ≥37 weeks gestation, weighing ≥2.5 kg, with no other cause of hyperbilirubinemia, and were sampled for a total serum bilirubin (TSB) within the first 48 hours of life. Hyperbilirubinemics were compared with non-hyperbilirubinemic newborns.

Results: Among the 93 G6PD-deficient newborns that met the inclusion criteria, 67 were hyperbilirubinemic and required phototherapy, and 13 of them required re-phototherapy. Phototherapy was started at 11 ± 4 (mean ± SD) hours of life, and for a total duration of 42 ± 28 hours. Hyperbilirubinemics had statistically significant higher levels of both hematocrit (53 ± 6 versus 49 ± 8%, p=0.02) and hemoglobin (176 ± 18 versus 166 ± 21 g/L, p=0.04), and lower reticulocyte percentage (4.3 ± 0.7 versus 5.2 ± 1.0 %, p=0.02), when compared to non-hyperbilirubinemic newborns.

Conclusion: Hyperbilirubinemia in G6PD-deficient Ahsai male newborns was characterized by higher levels of both hematocrit and hemoglobin levels, and lower reticulocyte percentage compared to their non-hyperbilirubinemic counterpart. This hyperbilirubinemia required early phototherapy and re-phototherapy. Appropriate follow up should be made available to those high-risk newborns. Further research is needed to understand the exact mechanism of hyperbilirubinemia in G6PD-deficient newborns.

Saudi Med J 2010; Vol. 31 (2): 175-179

From the Department of Pediatrics, Neonatology Division, King Abdulaziz Hospital for National Guard, Al-Ahsa, Kingdom of Saudi Arabia.

Received 4th October 2009. Accepted 29th December 2009.

Address correspondence and reprint request to: Dr. Sameer Y. Al-Abdi, Consultant Neonatologist, Department of Pediatrics, Neonatology Division, MC 315, King Abdulaziz Hospital for National Guard PO Box 2477, Al-Ahsa 31982, Kingdom of Saudi Arabia. Tel: +966 (3) 5910000 Ext. 33386. Fax: +966 (3) 5910000 Ext. 33844. E-mail: abdis@ngha.med.sa

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an X-linked recessive enzymopathy that is a well-known cause of hyperbilirubinemia that may be severe enough to cause kernicterus, or death in newborns. The pathogenesis of G6PD deficiency associated neonatal hyperbilirubinemia is thought to be multifactorial.[1] However, there is compelling evidence that reduced bilirubin conjugation may play a larger role in the pathogenesis of G6PD-associated neonatal hyperbilirubinemia than hemolysis.[1,2] For example, the rate of neonatal hyperbilirubinemia increases if G6PD deficiency coexists with Gilbert's syndrome.[1] As the clinical presentation of G6PD deficiency may differ according to the geographic area and genetic mutation, G6PD-associated neonatal hyperbilirubinemia could be acute, unpredictable, and often requires exchange transfusion, or gradual that responds to phototherapy.[1,2] Cord blood screening for G6PD deficiency and predischarge bilirubin measurement was recommended as preventive measures of this hyperbilirubinemia and its devastating sequlae.[1]

An individual originally from Al-Ahsa in the Eastern province of the Kingdom of Saudi Arabia (KSA) is called Ahsai (plural, Ahsais). They are old Arabic Muslim population composed of civilian and Bedouin descents, with high prevalence of G6PD deficiency reported as 23% in males, and 13% in females.[3] The most common mutation in Ahsais is G6PD-Mediterranean (84%) that is considered the most severe variant, followed by G6PD-A- (5.8%).[4] There is only one study shedding light on G6PD deficiency in newborns in Al-Ahsa area.[5] However, it has some limitations as being a heterogeneous group of older than 48 hours, male and female newborns who were born at different gestational ages, with different birth weight categories, and admitted to pediatric ward for phototherapy. Since G6PD deficiency is underreported in Ahsai newborns, we aimed to study the clinical and laboratory characteristics of hyperbilirubinemia in G6PD-deficient male Ahsai newborns, who were sampled for total serum bilirubin (TSB) level within the first 48 hours of life.

Methods.

Clinical protocol and treatment. King Abdulaziz Hospital (KAH) for National Guard is the second largest hospital in Al-Ahsa area, commissioned to provide health care in 2002. In early 2008, a nurse driven cord blood screening for G6PD deficiency was added to the already established cord blood screening program for thyroid-stimulating hormone test (TSH), direct antiglobulin test (DAT), and blood grouping. Following delivery of the placenta, the midwife sends a venous umbilical cord blood to the lab to estimate G6PD level qualitatively via fluorescence spot test (Randox kit, Antrium, UK). The nurse traces the results of G6PD screening, which is usually available within a few hours, and if reported as abnormal, a venous blood sample is obtained for TSB measurement, and complete blood count (CBC). Then all the results will be shared with the physician. In addition, reticulocyte percentage and blood film is requested upon the physicians' discretion. Phototherapy will be started if TSB level is equal to, or more than phototherapy threshold, as follows: if TSB is ≥130 μmol/L within the first 24 hours (hrs) of life, ≥170 at 25-48 hrs, ≥230 at 49-72 hrs, ≥270 at 73-96 hrs, and ≥310 at >96 hrs. Phototherapy is discontinued if 2 consecutive TSB levels obtained, 8-12 hours apart, are below the phototherapy threshold. The practice at KAH is that a single phototherapy can be provided at the mothers' bedside, while intense phototherapy will be carried out only in the level II/III nursery with, or without extra parenteral fluids. Parents of G6PD-deficient newborns are educated on how to assess for jaundice, and advised to bring symptomatic newborns to KAH as soon as possible. Also, they are given bilingual (Arabic and English) pamphlet that included general information on G6PD deficiency, and a list of triggers of hemolysis that should be avoided.

Patients. We reviewed the medical records of male inborn infants at KAH from May 2008 through April 2009. Eligible for analyses were healthy G6PD-deficient Ahsai male newborns that were born at ≥37 weeks' gestation and weighed ≥2.5 kg, and had their first TSB level measurement within the first 48 hours of life. Baseline demographic and clinical data collected included: family's descent, gestational age, birth weight, mode of delivery, exclusive/mixed breast milk, cephalohematoma, diagnosis of infant of diabetic mother, other causes of hyperbilirubinemia, admission to level II/III nursery, and readmission to pediatric ward in the first 28 days of life, and as well as phototherapy requirement, intensity, timing, and duration. The family's descent was determined based on tribe name, medical history, and Saudi National ID card. The laboratory data collected included: levels and sampling time of first TSB, highest TSB, first hemoglobin, lowest hemoglobin, first hematocrit, highest hematocrit, and reticulocyte percentage, as well as DAT status. Newborns with any of the following were excluded: positive DAT, other known hemolytic disease (such as, pyropoikilocytosis, spherocytosis), cephalohematoma, sepsis, macrosomic infant of a diabetic mother or birth weight of >4 kg, timing of first TSB within >48 hours of life, first pre-phototherapy hematocrit of >65%, major congenital anomaly, admitted to level II/III nursery for non-hyperbilirubinemia, discharged against medical advice, and non-Ahsai descents.

Data analysis. Definition of hyperbilirubinemia and phototherapy was adopted for this study from the Australian Coding Standards (ICD-1-0-AM).[6] A newborn was considered hyperbilirubinemic if he required phototherapy >12 hours, and newborns who had no phototherapy or phototherapy ≤12 hours were considered non-hyperbilirubinemic.[6] Hyperbilirubinemic and non-hyperbilirubinemic G6PD-deficient newborns were compared with each other. Chi-square, T-test, and Mann-Whitney test were used to analyze categorical, parametric, and non-parametric data. The data were reported as mean ± SD or percentage. Statistical analysis was performed with Epi Info (CDC statistical software version 3.5.1), and Open Epi (version 2.2.1). A two-tailed *p*-value <0.05 was considered statistically significant for all the tests.

Results. A total of 2556 cord blood samples was screened for G6PD deficiency during the study period. Of these, 1548 were Ahsai newborns; 1312 civilians, and 236 Bedouins from a single tribe. G6PD deficiency was diagnosed in 185 civilian descent, and none in Bedouin descent. Only 93 out of 185 G6PD-deficient newborns met the inclusion criteria (67 hyperbilirubinemic, and 26 non-hyperbilirubinemic). Reticulocyte percentage was only carried out for 22 hyperbilirubinemic and 9 non-hyperbilirubinemic newborns. The baseline and laboratory characteristics of patients are shown in **Table 1**. There was no significant difference between hyperbilirubinemic and non-hyperbilirubinemic newborns in terms of gestational age, birth weight, rate of exclusive breast milk, and cesarean section. Hyperbilirubinemic had statistically significant higher pre-phototherapy first hematocrit level (p=0.02), and first hemoglobin level (p=0.04), and lower reticulocyte percentage (p=0.02) than non-hyperbilirubinemic newborns. Level of first TSB (p=0.002) and highest TSB (p=0.00001) was significantly higher, and highest TSB was significant at the later hours of life (p=0.002) in hyperbilirubinemic compared to non-hyperbilirubinemic newborns. Although statistically not significant, lowest hemoglobin level was higher (p=0.08) and hemoglobin drop rate was lower (p=0.3) in hyperbilirubinemic (n=29) than non-hyperbilirubinemic (n=10) newborns who had repeated CBC testing. The onset of phototherapy was at 11 ± 4 hrs of life, and phototherapy duration was 42 ± 28 hrs (median;35). There were 63 that required single phototherapy in the mothers' room, 4 newborns required intense phototherapy in level II nursery, and 13 (19%) newborns required re-phototherapy (2 phototherapy courses [n=11], and 3 phototherapy courses [n=2]). After discharge, there were 2 hyperbilirubinemic newborns readmitted to the pediatric ward, while none of the non-hyperbilirubinemic newborns developed hyperbilirubinemia, or required readmission. Only one newborn had the highest TSB ≥340 µmol/L (359 µmol/L), and none required exchange, or simple blood transfusion during the neonatal period, and none developed kernicterus.

Table 1 - Baseline and laboratory characteristics of G6PD-deficient Ahsai male newborns.

Characteristics	Hyperbilirubinemic newborns (n = 67)	Non-hyperbilirubinemic newborns (n = 26)	*P*-value
Birth weight (g)	3224 ± 373	3163 ± 374	0.5
Gestational age (weeks)	39 ± 1	39 ± 1	0.999
Exclusive breast milk (%)	30	35	0.7
Cesarean section (%)	15	19	0.6
First/Pre-phototherapy hematocrit			
Level (%)	53 ± 6	49 ± 8	0.02
Sampling time (hours of life)	7 ± 4	7 ± 2	0.9
First/Pre-phototherapy hemoglobin			
Level (g/L)	176 ± 18	166 ± 21	0.04
Sampling time (hours of life)	7 ± 4	7 ± 2	0.9
Lowest hemoglobin level (g/L)*	163 ± 20	148 ± 20	0.08
Hemoglobin drop rate (g/L)*	0.8 ± 1.1	1.4 ± 1.4	0.3
Reticulocyte†			
Level (%)	4.3 ± 0.7	5.2 ± 1.0	0.02
Sampling time (hours of life)	17±13	18 ± 13	0.9
First total serum bilirubin			
Level (µmol/L)	80 ± 29	65 ± 22	0.002
Sampling time (hours of life)	7 ± 3	7 ± 2	0.5
Highest total serum bilirubin			
Level (µmol/L)	191 ± 68	121 ± 57	0.00001
Sampling time (hours of life)	76 ± 42	49 ± 32	0.002

Data are presented as mean ± SD or percentage.
*in newborns who had repeated complete blood count (29 hyperbilirubinemic and 10 non-hyperbilirubinemic newborns),
†reticulocyte percentage was only carried out for 22 hyperbilirubinemic and 9 non-hyperbilirubinemic newborns

Discussion. High prevalence of G6PD deficiency in the Al-Ahsa area is rationalized by a past history of malaria endemicity.[5] Because malaria was confined to Ahsai civilians,[7] it is not surprising that our study showed G6PD deficiency occurs only in civilians. However, this observation was not reported, and it will be of clinical importance in term of risk factors of hyperbilirubinemia, and screening program for G6PD deficiency in Ahsais. Our study clearly showed that G6PD-deficient Ahsais developed hyperbilirubinemia within the first hours of life, and not the same as physiological hyperbilirubinemia as concluded by Al-Omran et al.[5] The inclusion of newborns older than 48 hours of life in that study may explain this discrepancy. Kaplan et al[8] reported an onset of hyperbilirubinemia within the first 3 hours of life in G6PD-deficient newborns. Our study showed that TSB of hyperbilirubinemic newborns peaked later than non-hyperbilirubinemic. A bimodal peak TSB is expected in the population with high prevalence of the Gilbert's syndrome in which the rate of bilirubin elimination is known to be bimodal.[9]

Our study showed that 72% of G6PD-deficient Ahsai newborns developed hyperbilirubinemia and required phototherapy, which is higher than other reports. For instance, the rate of G6PD deficiency associated hyperbilirubinemia was 13% in Saudi males from Yanbu, 22% in African-American males, and 49% in Indian males and females.[10-12] The high rate of hyperbilirubinemia and phototherapy requirement in our study may be explained by a high prevalence of the G6PD-Mediterranean in Ahsais (84%).[2] In newborns with G6PD-Mediterranean, the incidence of TSB (≥257 µmol/L) was reported as 31.6% in heterozygotes, and 50% in homozygotes Gilbert's syndrome.[13] Admittedly, the rate of phototherapy and subsequently hyperbilirubinemia in our study might be overestimated hence, our phototherapy threshold for the first 24 hours of life is on average 40 µmol/L lower than that recommended by the American Academy of Pediatrics (AAP) for newborns at medium risk.[14] For instance, the median of phototherapy duration in our study was 10 hours more than the median in a study that used the AAP phototherapy nomogram.[9] For the same reason, the rate of re-phototherapy in the present study was high (19%) in comparison to 0.5% of re-phototherapy in another large study.[13] However, the rate of TSB ≥340 µmol/L, and the need for exchange transfusion was decreased effectively in the study population, and whether the phototherapy duration could be reduced by using the AAP phototherapy nomogram without increasing frequency of hyperbilirubinemia sequelae in G6PD-deficient Ahsai newborns merits further study.

Noteworthy, our study showed that at a statistically significant level the hyperbilirubinemic newborns had paradoxically higher pre-phototherapy hematocrit and hemoglobin levels than their counterparts. This concurs with an old Greek study that showed the mean hemoglobin (183 g/L) of G6PD-deficient newborns with TSB of ≥274 µmol/L was significantly higher than the mean hemoglobin (168 g/L) of normal non-hyperbilirubinemic newborns.[15] Also an Indian study showed hemoglobin level of >18 g/L was more frequent among hyperbilirubinemic (42%) than non-hyperbilirubinemic (5%) G6PD-deficient newborns.[13] Our hematological observations may be a characteristic of G6PD-Mediterranean that accounts for 84% in Ahsais, 77% in Greeks, and 60.4% in Indians of G6PD deficiency.[4,16,17] Contrary, in Malay where the G6PD-Mediterranean only accounts for 26.4% of G6PD deficiency, the hemoglobin level was the same in hyperbilirubinemic and non-hyperbilirubinemic G6PD-deficient newborns.[2,18] Interestingly a recent Turkish study found that male adolescents and adults with unconjugated hyperbilirubinemia and Gilbert's syndrome had significantly higher hematocrit and hemoglobin levels than normal.[19] Further, that study demonstrated an association between unconjugated bilirubin level and hematocrit level in 7 hyperbilirubinemic males with Gilbert's syndrome. Statistically significant paradoxical lower reticulocyte percentage in hyperbilirubinemic than non-hyperbilirubinemic G6PD-deficient Ahsai newborns concurs with well-known limited role of the hemolysis in the pathogenesis of G6PD deficiency associated neonatal hyperbilirubinemia.[1,2] Therefore, the high paradoxical non-polycythemic hematocrit and hemoglobin levels in hyperbilirubinemic G6PD-deficient Ahsai newborns may indicate characteristic features of G6PD-Mediterranean and Gilbert's syndrome concordance that merit further study, since, prevalence of Gilbert's syndrome is unknown among Ahsais, and it is only 3.6% in Jeddah, KSA, and 3-12% worldwide.[20]

We believe that this homogenous study population with only G6PD deficiency as the identified risk for hyperbilirubinemia may improve the quality of parental counseling, and a further step in the predictability and pathophysiology of G6PD deficiency associated neonatal hyperbilirubinemia. However, there are some limitations in our study that should be noted in addition to its retrospective methodology. These are the low phototherapy threshold that may have resulted in over diagnosis of hyperbilirubinemic newborns, the small number of reticulocyte percentage that was carried out, and the small number of non-hyperbilirubinemic newborns. Therefore, further study is called for to confirm its results.

In conclusion, G6PD-deficiency associated hyperbilirubinemia in Ahsai male newborns is characterized by higher levels of hematocrit and

hemoglobin, and lower reticulocyte percentage compared to their non-hyperbilirubinemic counterpart. This hyperbilirubinemia required early phototherapy and re-phototherapy. Appropriate follow up should be made available to those high risk newborns, and further research is needed to understand the exact mechanism of hyperbilirubinemia in G6PD-deficient newborns.

Acknowledgment. *The authors gratefully acknowledge Mr. Saleh Al-Ghamdi and Mr. Mohammed Abukari from the Hematology Laboratory, Division of Laboratory Medicine of King Abdullaziz Hospital, Al-Ahsa, KSA for their valuable assistance.*

References

1. Kaplan M, Hammerman C. Glucose-6-phosphate dehydrogenase deficiency: a hidden risk for kernicterus. ***Semin Perinatol*** 2004; 28: 356-364.
2. Jalloh S, Van Rostenberghe H, Yusoff NM, Ghazali S, Nik Ismail NZ, Matsuo M, et al. Poor correlation between hemolysis and jaundice in glucose 6-phosphate dehydrogenase-deficient babies. ***Pediatr Int*** 2005; 47: 258-261.
3. Warsy AS, El-Hazmi MA. G6PD deficiency, distribution and variants in Saudi Arabia: an overview. ***Ann Saudi Med*** 2001; 21: 174-177.
4. Al-Ali AK, Al-Mustafa ZH, Al-Madan M, Qaw F, Al-Ateeq S. Molecular characterization of glucose-6-phosphate dehydrogenase deficiency in the Eastern Province of Saudi Arabia. ***Clin Chem Lab Med*** 2002; 40: 814-816.
5. Al-Omran A, Al-Ghazal F, Gupta S, John TB. Glucose-6-phosphate dehydrogenase deficiency and neonatal jaundice in Al-Hofuf area. ***Ann Saudi Med*** 1999; 19: 156-158.
6. National Centre for Classification in Health, Australian Coding standards for ICD-10-AM/ ACHI/ACS. 5th edition. National Centre for Classification in Health: University of Sydney (Australia); 2006. p. 221
7. McNiel JR. Pediatric practice in Eastern Saudi Arabia. ***J Trop Pediatr Afr Child Health*** 1966; 11: 82-87.
8. Kaplan M, Algur N, Hammerman C. Onset of jaundice in glucose-6-phosphate dehydrogenase-deficient neonates. ***Pediatrics*** 2001; 108: 956-959.
9. Valaes T. Severe neonatal jaundice associated with glucose-6-phosphate dehydrogenase deficiency: pathogenesis and global epidemiology. ***Acta Paediatr Suppl*** 1994; 394: 58-76.
10. Muzaffer MA. Neonatal screening of glucose-6-phosphate dehydrogenase deficiency in Yanbu, Saudi Arabia. ***J Med Screen*** 2005; 12: 170-171.
11. Kaplan M, Herschel M, Hammerman C, Hoyer JD, Stevenson DK. Hyperbilirubinemia among African American glucose-6-phosphate dehydrogenase-deficient neonates. ***Proc Natl Acad Sci U S A*** 1997; 94: 12128-12132.
12. Verma M, Singla D, Crowell SB. G6PD deficiency in neonates: a prospective study. ***Indian J Pediatr*** 1990; 57: 385-358.
13. Kaplan M, Renbaum P, Levy-Lahad E, Hammerman C, Lahad A, Beutler E. Gilbert syndrome and glucose-6-phosphate dehydrogenase deficiency: a dose-dependent genetic interaction crucial to neonatal hyperbilirubinemia. ***Pediatrics*** 1992; 90: 401-405.
14. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. ***Pediatrics*** 2004; 114: 297-316.
15. Valaes T, Karaklis A, Stravrakakis D, Bavela-Stravrakakis K, Perakis A, Doxiadis SA. Incidence and mechanism of neonatal jaundice related to glucose-6-phosphate dehydrogenase deficiency. ***Pediatr Res*** 1969; 3: 448-458.
16. Menounos P, Zervas C, Garinis G, Doukas C, Kolokithopoulos D, Tegos C, et al. Molecular heterogeneity of the glucose-6-phosphate dehydrogenase deficiency in the Hellenic population. ***Hum Hered*** 2000; 50: 237-241.
17. Sukumar S, Mukherjee MB, Colah RB, Mohanty D. Molecular basis of G6PD deficiency in India. ***Blood Cells Mol Dis*** 2004; 33: 141-145.
18. Ainoon O, Yu YH, Amir Muhriz AL, Boo NY, Cheong SK, Hamidah NH. Glucose-6-phosphate dehydrogenase (G6PD) variants in Malaysian Malays. ***Hum Mutat*** 2003; 21: 101.
19. Buyukasik Y, Akman U, Buyukasik NS, Goker H, Kilicarslan A, Shorbagi AI, et al. Evidence for higher red blood cell mass in persons with unconjugated hyperbilirubinemia and Gilbert's syndrome. ***Am J Med Sci*** 2008; 335: 115-119.
20. Bakhotmah MA, Gasem AA, Bairotee B. Asymptomatic unconjugated hyperbilirubinemia (Gilbert syndrome) among Saudis in Jeddah. ***Ann Saudi Med*** 1995; 15: 422-423.

Related topics

Saeidi R, Heydarian F, Fakehi V. Role of intravenous extra fluid therapy in icteric neonates receiving phototherapy. ***Saudi Med J*** 2009; 30: 1176-1179.

Bicakci Z. A hemolysis trigger in glucose-6-phosphate dehydrogenase enzyme deficiency. Vicia sativa (Vetch). ***Saudi Med J*** 2009; 30: 292-294.

Al-Ani SS, Baker AA, Al-Athmani AK, Al-Jesmi BJ. Neonatal screening of glucose-6-phosphate dehydrogenase deficiency in Khorfakkan, United Arab Emirates. ***Saudi Med J*** 2008; 29: 1826-1828.

Davutoglu M, Guler E, Olgar S, Kurutas EB, Karabiber H, Garipardic M, et al. Oxidative stress and antioxidant status in neonatal hyperbilirubinemia. ***Saudi Med J*** 2008; 29: 1743-1748.