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Original Article

The First Case of a Class I Glucose-6-phosphate Dehydrogenase Deficiency, G6PD Santiago de Cuba (1339 G > A), in a Chinese Population as Found in a Survey for G6PD Deficiency in Northeastern and Central China

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In Liaoning Province in northeastern China, we found a G6PD-deficient patient at the age of 3. By the classification of the World Health Organization, this patient was categorized as class I (very severe G6PD deficiency). When we investigated the *G6PD* gene of the patient, we found that he had a replacement of G to A at nucleotide 1339. As a result, the amino acid at position 447 should change from Gly to Arg. This replacement is known as G6PD Santiago de Cuba, because it was first discovered in a Cuban boy who showed heavy chronic anemia. Today, 28 G6PD variants have been reported in the Chinese population, and all are categorized as class II (severe deficiency) or class III (mild deficiency); in class II or III deficiency, anemia is not present in daily life, but hemolytic attack can occur when the carrier ingests certain oxidative medicines or foods. This is the first report of a G6PD-deficient Chinese patient in the category of class I. We intended to find other G6PD-deficient cases in northeastern China and tested several hundred blood samples, but no cases of G6PD deficiency were found (0/414). In central China, where falciparum malaria was endemic from the 1950s to 1970s, we found two G6PD-deficient cases (2/27) and the other members from their families whose variant type was G6PD Kaiping (1388G > T), which is a common variant in the Chinese population.

Key words: hemolytic anemia, Chinese, glucose-6-phosphate dehydrogenase, G6PD Santiago de Cuba, malaria

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is one of the most frequent hereditary abnormalities. The gene *G6PD* is distributed in 13 exons on the X-chromosome, and the length of the open reading frame is 1545 bases [1]. Almost all cases of G6PD deficiency are caused by one amino-acid change due to a point mutation of the genomic DNA, and about 140 molecular abnormalities of the G6PD genotype have been identified [2]. As an enzyme, the monomer of G6PD consists of 515 amino acids; 2 monomers form a homo-dimer attaching at the site of the dimer interface. Once the amino acid sub-

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stitution occurs near the dimer interface, G6PD activity becomes very low. The dimer formation may be important for the function of the active enzyme [3]. The World Health Organization (WHO) categorizes G6PD-deficiency variants into 3 classes according to their severity. The class I variant shows very low G6PD activity (less than 1% of that in a normal individual), and carriers of these genes suffer from heavy anemia because hemolysis occurs chronically. The class II variant shows low G6PD activity (less than 10% of residual enzyme activity) and does not pose as serious a problem in daily life. Hemolytic attack occurs only when the carrier ingests certain foods or medicines. The class III variant shows 10–60% of residual enzyme activity and hemolysis occurs only in rare cases [4]. Females, but not males, can be heterozygous for the class I or class II G6PD variants, and such carriers are sometimes categorized into class III, because half of their red blood cells lack the G6PD enzyme activity, while the other half have full activity.

We have proviously investigated variants of G6PD deficiency in Asian countries [5–12], where this abnormality is highly prevalent in malaria-endemic areas. We have introduced a rapid diagnosis method for malaria [13] and rapid G6PD-deficiency tests [14–16] in malaria-endemic areas. Using these methods, patients are notified of the results of blood examination within 30 min and are able to receive anti-malarial medicine including primaquine [17, 18]. Primaquine can kill gametocytes, the sexual stage of malaria parasites, which are the cause of malaria transmission to mosquitoes. However, when G6PD-deficient persons take primaquine, a hemolytic attack can occur. Without G6PD, erythrocytes cannot prepare a sufficient amount of reduced pyridine nucleotide and reduced glutathione, and cannot prevent oxidant attack by primaquine. Thus, primaquine should not be administered to malaria patients before confirming their G6PD activity. In our previous studies, we have diagnosed more than 200 G6PD-deficiency cases and found 15 variants of G6PD deficiency in Southeast Asian countries. These G6PD variants were all categorized as class II. Among them, we discovered three new G6PD variants, which we designated G6PD Surabaya [5], G6PD Bajo Maumere [10], and G6PD Bao Loc [11].

Numerous studies have investigated G6PD deficiency in the Chinese population. Twenty-two molecular variants were reported from the southern part of China, which includes many malaria-endemic areas [19–22]. Some other variants were reported from Chinese populations in Taiwan [23–26], Singapore [27], Malaysia [12, 28], Indonesia [5] and Hawaii [29]. These G6PD variants were all categorized as class II or class III. In this report we present the first Chinese case of G6PD deficiency categorized as class I. We also conducted a G6PD test in northeastern and central China to investigate the G6PD variants present in these areas.

Materials and Methods

This study was approved by the Ethical Committees of China Medical University, Jichi Medical University, Shenyang Infectious Disease Hospital, and Hubei Center for Disease Control and Prevention.

A case report. A 3-year-old boy who showed heavy anemia was admitted to Shengjing Hospital of China Medical University, Shenyang. His erythrocyte number was 1.25×10^{12}/L, his hemoglobin concentration was 45 g/L, and his total bilirubin level was 24.3 μmol/L. He had had infant jaundice since birth, and this condition was still present upon admission. He was first diagnosed with hemolytic anemia, and then with G6PD deficiency, because his G6PD activity was found to be less than 1% of the normal level. By the classification of the World Health Organization [4], he was categorized as class I. Artificial nutrition and recuperation led to a recovery of his scores (RBC: 2.98×10^{12}/L; Hb: 93 g/L), and he was discharged. We asked his family members for permission to analyze their G6PD activity and sequence their *G6PD* gene, and received informed consent (Fig. 1A).

Participants in the G6PD test. We asked outpatients of Shenyang Infectious Disease Hospital, Shenyang, if they would agree to be tested for G6PD activity upon providing a venous blood sample for other purposes, *e.g.*, for an RBC count, a WBC count, or blood sugar levels. From patients who provided informed consent, we collected about 10 μl of blood onto a filter sheet, which was then dried and stored at −20℃. There were 414 males and 105 females who agreed to be tested for G6PD activity. In

addition, we visited a junior high school in Suizhou, which is in Hubei Province in central China, and received informed consent from the principle and students to test G6PD activity. Fifty students (27 males and 23 females) participated in this test. Five microliters of blood was taken from the ear lobe and put in a tube containing reagents for the G6PD test, which Hirono *et al.* described [15]. Finally, we were introduced to 2 students' families by the Suizhou Center for Disease Control and Prevention. Members of the 2 families had been diagnosed with G6PD deficiency and had previously had episodes of hemolysis (Fig. 1B and 1C).

G6PD test. Fujii's method was used at Shenyang Infectious Disease Hospital and Shengjing Hospital [14], and Hirono's method was used at the junior high school in Suizhou [15]. A 10 μl blood sample was taken from each D6PD-deficient individual and kept on a filter sheet for analysis of the *G6PD* gene.

Analysis of the G6PD gene. The filter papers containing blood samples were dried, sent to Jichi Medical University, and kept at −20℃. DNA was eluted from the filter paper by heating at 80℃ for 10 min in DNA extraction buffer. DNA extraction and purification were conducted using a DNA purification kit according to the manufacturer's instruction (Amersham Pharmacia Biotech, Buckinghamshire, UK). Since genomic G6PD consists of 13 exons, we prepared primers for these exons [11], amplified each exon by PCR, and read the DNA sequence (ABI PRISM 310; Applied Biosystems, Foster City, CA, USA). Both strands of each exon were sequenced. To indicate the mutation point, the nucleotide number of the cDNA sequence was used.

Results

We read all the exons encoding the *G6PD* gene of the first patient and found a replacement of G to A at nucleotide 1339 in exon 11 (Fig. 2A). As a result, the amino acid was expected to change from Gly to Arg at position 447 in the molecule. The sequencing results also confirmed that his mother was a heterozygote of G6PD Santiago de Cuba (Fig. 2B) and his grandfather was a hemizygote of the same variant.

All blood samples collected from the 414 males and 105 females at the Shenyang Infectious Disease Hospital in Liaoning Province showed normal G6PD activity. The rate of G6PD deficiency was thus 0% (0/414).

In Hubei Province in Central China, we found 2 males with G6PD deficiency among 50 students (7.4%; 2 in 27 males). As described above, we also collected blood samples from 2 families with G6PD deficiency and analyzed their *G6PD* genes. After providing the informed consent, 5 individuals from the 2 families participated. We found that all of these individuals had the G6PD Kaiping (1388G > T) variant, which is one of the most frequent types of G6PD

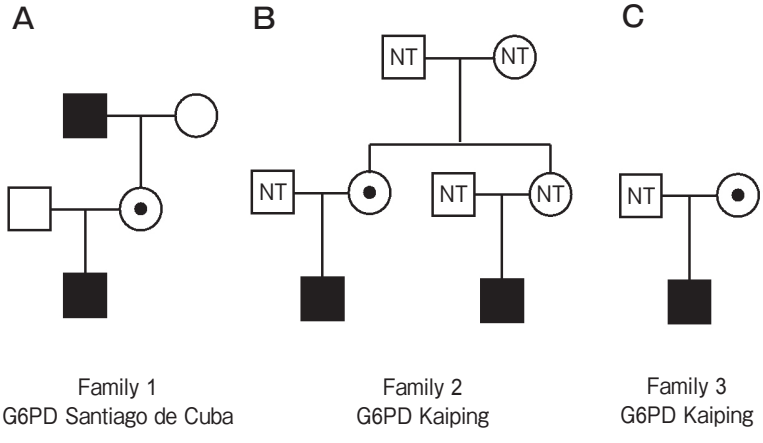

Fig. 1 Family trees of G6PD deficiency. ■, hemizygote of G6PD deficiency; ⊙, heterozygote of G6PD deficiency; □ and ○, full activity of G6PD; NT, not tested. **A**, Family 1 was found in Liaoning Province in northeastern China. **B** and **C**, Families 2 & 3 were from Hubei Province in central China.

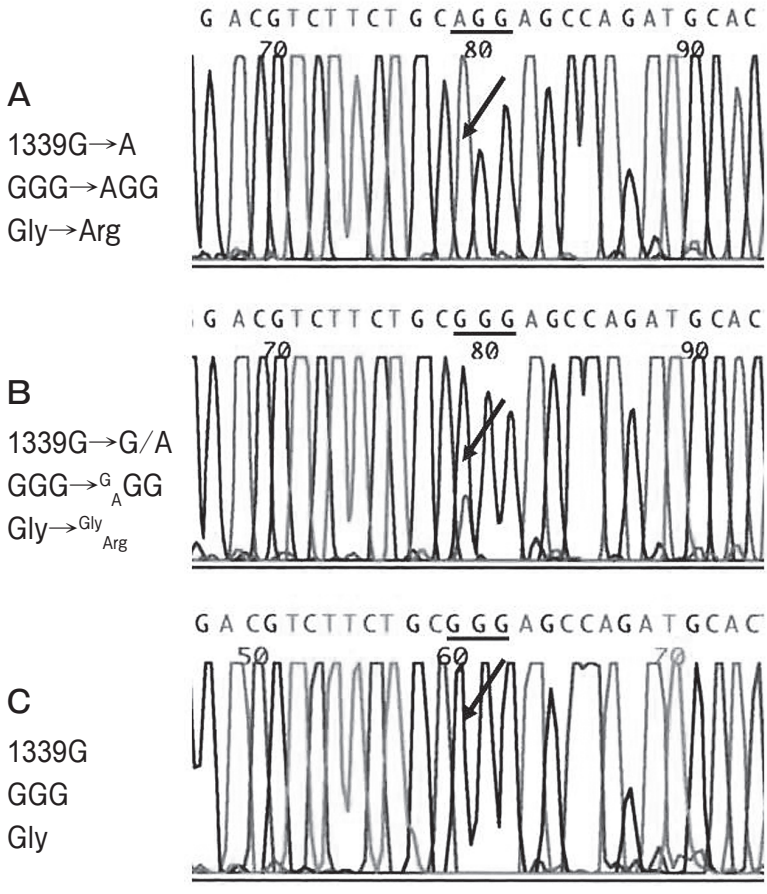

Fig. 2 **A**, Part of the DNA sequence in exon 11 from a hemizygous boy with G6PD Santiago de Cuba; **B**, Part of the DNA sequence in exon 11 from a heterozygous mother with G6PD Santiago de Cuba; **C**, Part of the DNA sequence in exon 11 from the boy's father with normal G6PD. *Arrows* show 1339A, 1339G/A, and 1339G.

variant in the Chinese population.

Discussion

Mutation 1339 G > A was first discovered in a Cuban boy, who showed heavy chronic anemia, and was therefore designated G6PD Santiago de Cuba [30]. Because the G6PD activity of this variant is very low, patients with this mutation show chronic hemolysis and anemia. Thus this variant is categorized as class I. Since the amino-acid substitution occurs at site 447, which is close to the dimer interface site [3], the variant molecule might not be formed properly, causing the enzyme activity to decline.

In the literature, 28 types of G6PD variant have been reported in the Chinese population [19–29], and all are categorized as class II or class III, because they do not show chronic hemolytic anemia. In such patients, accidental hemolysis occurs only when they ingest certain oxidative medicines or foods. The present case and his family members with the G6PD Santiago de Cuba variant are thus the first reported cases of class I G6PD deficiency in a Chinese population.

In addition to Cuba and China, the G6PD Santiago de Cuba variant has also been reported in Japan [31]. The patient lived in Iwate Prefecture in northern Japan, and also suffered form chronic hemolysis and anemia. This is the only known case of G6PD Santiago de Cuba in the Japanese population. Fiorelli *et al.* reported that G6PD variants causing chronic hemolytic anemia are all sporadic, and almost all arise from independent mutations [32]. Moreover, because this variant, G6PD Santiago de Cuba, has been reported in Cuba, Japan and China, and the number of cases is very few, it is not likely to spread by genetic drift. This suggests that its origin is unlikely to be a common ancestor and that it is probably a new mutation that has arisen independently.

Among the blood samples from 414 males and 105 females collected in Liaoning Province in northeastern China, there were no cases of G6PD deficiency. This result suggests that the frequency of G6PD deficiency is very low in this area. Similar results have been reported by Jiang *et al.*, who found that the prevalence of G6PD deficiency was 0% (0/1,000) in Shandong Province in northern China [21]. Luzzatto *et al.* reported that the frequency of G6PD deficiency was high in malaria-endemic areas [33]. Individuals with G6PD deficiency are relatively resistant to falciparum malaria, and thus there is natural selection for G6PD-deficient people in areas with malignant malaria [34]. As a result, the frequency of G6PD deficiency is higher in malaria-endemic areas than in areas where

falciparum malaria has not existed. In northern areas of China, no falciparum malaria has existed historically. This is likely the reason that we found no G6PD-deficient cases but sporadic individual in this area.

Falciparum malaria was endemic to Hubei Province in the 1950s to 1970s [35], which is probably why the frequency of G6PD deficiency was high (7.4%) in our very small sampling of this area. Although we could not collect more samples from this area, this rate was similar to that from the southern part of China. Studies of G6PD deficiency in China have been done mainly in the southern part of the country. A high frequency of G6PD deficiency (5.2%) has been reported in Yunnan Province, the Guangxi Zhuang Autonomous Region, Guandong Province and Fujian Province [21]. Our results suggested that the distribution of G6PD deficiency in the northern regions of China was different from that in the central and southern areas. Based only on our findings, we might speculate that the frequency of G6PD deficiency and falciparum malaria are positively correlated in China.

In the Chinese population, the most common variants of G6PD are G6PD Kaiping (1388G > A), G6PD Canton (1376G > T), G6PD Gaohe (95G > A), G6PD Quing Yuan (392C > T) and G6PD Chinese-5 (1024C > T) [36]. These variants are frequently detected in Malaysia [37], Indonesia [10] and Vietnam [11], suggesting that they spread from China to these countries. Historically, Chinese people have migrated and settled in many countries and geographical regions. When G6PD variants in mainland China are compared with those in other areas, we can detect gene flows between Chinese and other ethnicities. For instance, G6PD Mediterranean (563C > T), which is common in Mediterranean countries, is detected in the Chinese population living in Singapore [27], but this variant is never seen on the mainland of China. We previously found G6PD Chatham in a Chinese individual living in Surabaya, Indonesia [5]. This variant has not been reported in mainland China, but is common in Indonesia [10] and Iran [38].

In conclusion, a patient with G6PD deficiency was found in northeastern China. This patient and his family members had a mutation of G6PD Santiago de Cuba, which was classified as class I according to its very low enzyme activity. This is the first reported case of a class I G6PD deficiency in the Chinese population. In addition, our screening results suggest that the difference in the distribution of G6PD deficiency in China may be related to the endemicity of falciparum malaria.

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References

1. Chen EY, Cheng A, Lee A, Kuang WJ, Hillier L, Green P, Schlessinger D, Ciccodicola A and D'Urso M: Sequence of human glucose-6-phosphate dehydrogenase cloned in plasmids and a yeast artificial chromosome. Genomics (1991) 10: 792–800.
2. Cappellini MD and Fiorelli G: Glucose-6-phosphate dehydrogenase deficiency. Lancet (2008) 371: 64–74.
3. Fujii H and Miwa S: Red blood cell enzymes and their clinical application. Adv Clin Chem (1998) 33: 1–54.
4. WHO working group: Glucose-6-phosphate dehydrogenase deficiency. Bull WHO (1989) 67: 601–611.
5. Iwai K, Hirono A, Matsuoka H, Kawamoto F, Horie T, Lin K, Tantular IS, Dachlan YP, Notopuro H, Hidayah NI, Salim AM, Fujii H, Miwa S and Ishii A: Distribution of glucose-6-phosphate dehydrogenase mutations in Southeast Asia. Hum Genet (2001) 108: 445–449.
6. Matsuoka H, Arai M, Yoshida S, Tantular IS, Pusarawati S, Kerong H and Kawamoto F: Five different glucose-6-phophate dehydrogenase (G6PD) variants found among 11 G6PD-deficient persons in Flores Island, Indonesia. J Hum Genet (2003) 48: 541–544.
7. Matsuoka H, Wang J, Hirai M, Yoshida S, Arai M, Ishii A and Baral MP: Two cases of glucose-6-phophate dehydrogenase deficient Nepalese belonging to the G6PD Mediterranean-type, not India-Pakistan sub-type but Mediterranean-Middle East sub-type. J Hum Genet (2003) 48: 275–277.
8. Matsuoka H, Wang JC, Hirai M, Arai M, Yoshida S, Kobayashi T, Jalloh A, Lin K and Kawamoto F: Glucose-6-phosphate dehydrogenase (G6PD) mutations in Myanmar: G6PD Mahidol (487G > A) is the most common variant in the Myanmar population. J Hum Genet (2004) 49: 544–547.
9. Matsuoka H, Nguon C, Kanbe T, Jalloh A, Sato H, Yoshida S, Hirai M, Arai M, Socheat D and Kawamoto F: Glucose-6-phosphate dehydrogenase (G6PD) mutations in Cambodia: G6PD Viangchan (871G > A) is the most common variant in the Cambodian population. J Hum Genet (2005) 50: 468–472.
10. Kawamoto F, Matsuoka H, Kanbe T, Tantular IS, Pusarawati S, Kerong HI, Damianus W, Mere D and Dachlan YP: Further investigations of glucose-6-phosphate dehydrogenase variants in Flores Island, eastern Indonesia. J Hum Genet (2006) 51: 952–957.
11. Matsuoka H, Thuan DT, van Thien H, Kanbe T, Jalloh A, Hirai M, Arai M, Dung NT and Kawamoto F: Seven different glucose-6-phosphate dehydrogenase variants including a new variant distributed in Lam Dong Province in southern Vietnam. Acta Med Okayama (2007) 61: 213–219.

12. Wang JC, Luo EJ, Hirai M, Arai M, Abdul-Manan E, Mohamed-Isa Z, Hidayah N and Matsuoka H: Nine different glucose-6-phosphate dehydrogenase (G6PD) variants in a Malaysian population with Malay, Chinese, Indian and Orang Asli (aboriginal Malaysian) backgrounds. Acta Med Okayama (2008) 62: 327–332.
13. Kawamoto F and Billingsley PF: Rapid diagnosis of malaria by fluorescence microscopy. Parasitol Today (1992) 8: 69–71.
14. Fujii H, Takahashi K and Miwa S: A new simple screening method for glucose 6-phosphate dehydrogenase deficiency. Nippon Ketsueki Gakkai Zasshi (Acta Haematol Jpn) (1984) 47: 185–188.
15. Hirono H, Fujii H and Miwa S: An improved single-step screening method for glucose-6-phosphate dehydrogenase deficiency. Jpn J Trop Med Hyg (1998) 26: 1–4.
16. Tantular IS and Kawamoto F: An improved, simple screening method for detection of glucose-6-phosphate dehydrogenase deficiency. Trop Med Int Health (2003) 8: 569–574.
17. Tantular IS, Iwai K, Lin K, Basuki S, Horie T, Htay HH, Matsuoka H, Marwoto H, Wongsrichanalai C, Dachlan YP, Kojima S, Ishii A and Kawamoto F: Field trials of a rapid test for G6PD deficiency in combination with a rapid diagnosis of malaria. Trop Med Int Health (1999) 4: 245–250.
18. Jalloh A, Tantular IS, Pusarawati S, Kawilarang AP, Kerong H, Lin K, Ferreira MU, Matsuoka H, Arai M, Kita K and Kawamoto F: Rapid epidemiologic assessment of glucose-6-phosphate dehydrogenase (G6PD) deficiency in malaria-endemic areas in Southeast Asia using a novel diagnostic kit. Trop Med Int Health (2004) 9: 615–623.
19. Cai W, Filosa S, Martini G, Zhou Y, Zhou D, Cai L and Kuang Y: Molecular characterization of glucose-6-phosphate dehydrogenase deficiency in the Han and Li nationalities in Hainan, China and identification of a new mutation in human G6PD gene. Zhonghua Yi Xue Yi Chuan Xue Za Zhi (Chinese J Med Genet) (2001) 18: 105–109 (in Chinese).
20. Ren X, He Y, Du C, Jiang W, Chen L and Lin Q: A novel missense mutation (G1381A) in the G6PD gene identified in a Chinese man. Chinese Med J (Engl) (2001) 114: 399–401.
21. Jiang W, Yu G, Liu P, Geng Q, Chen L, Lin Q, Ren X, Ye W, He Y, Guo Y, Duan S, Wen J, Li H, Qi Y, Jiang C, Zheng Y, Liu C, Si E, Zhang Q, Tian Q and Du C: Structure and function of glucose-6-phosphate dehydrogenase-deficient variants in Chinese population. Hum Genet (2006) 119: 463–478.
22. Yan T, Cai R, Mo O, Zhu D, Ouyang H, Huang L, Zhao M, Huang F, Li L, Liang X and Xu X: Incidence and complete molecular characterization of glucose-6-phosphate dehydrogenase deficiency in the Guangxi Zhuang autonomous region of southern China: description of four novel mutations. Haematologica (2006) 91: 1321–1328.
23. Chang JG, Chiou SS, Perng LI, Chen TC, Liu TC, Lee LS, Chen PH and Tang TK: Molecular characterization of glucose-6-phosphate dehydrogenase (G6PD) deficiency by natural and amplification created restriction sites: five mutations account for most G6PD deficiency cases in Taiwan. Blood (1992) 80: 1079–1082.
24. Perng LI, Chiou SS, Liu TC and Chang JG: A novel C to T substitution at nucleotide 1360 of cDNA which abolishes a natural Hha I site accounts for a new G6PD deficiency gene in Chinese. Hum Mol Genet (1992) 1: 205.
25. Tang TK, Huang WY, Tang CJ, Hsu M, Cheng TA and Chen KH: Molecular basis of glucose-6-phosphate dehydrogenase (G6PD) deficiency in three Taiwan aboriginal tribes. Hum Genet (1995) 95: 630–632.
26. Chen BH, Lin SR, Chiang CH and Chao MC: Molecular characterization of Chinese G6PD deficiency by using polymerase chain reaction/single strand conformation polymorphism. Kaohsiung J Med Sci (1998) 14: 197–202.
27. Saha S, Saha N, Tay JS, Jeyaseelan K, Basair JB and Chew SE: Molecular characterisation of red cell glucose-6-phosphate dehydrogenase deficiency in Singapore Chinese. Am J Hematol (1994) 47: 273–277.
28. Ainoon O, Joyce J, Boo NY, Cheong SK, Zainal ZA and Hamidah NH: Glucose-6-phosphate dehydrogenase (G6PD) variants in Malaysian Chinese. Hum Mutat (1999) 14: 352.
29. Hsia YE, Miyakawa F, Baltazar J, Ching NS, Yuen J, Westwood B and Beutler E: Frequency of glucose-6-phosphate dehydrogenase (G6PD) mutations in Chinese, Filipinos, and Laotians from Hawaii. Hum Genet (1993) 92: 470–476.
30. Vulliamy TJ, D'Urso M, Battistuzzi G, Estrada M, Foulkes NS, Martini G, Calabro V, Poggi V, Giordano R, Town M, Luzzatto L and Persico MG: Diverse point mutations in the human glucose-6-phosphate dehydrogenase gene cause enzyme deficiency and mild or severe hemolytic anemia. Proc Natl Acad Sci USA (1988) 85: 5171–5175.
31. Hirono A, Fujii H, Takano T, Chiba Y, Azuno Y and Miwa S: Molecular analysis of eight biochemically unique glucose-6-phosphate dehydrogenase variants found in Japan. Blood (1997) 89: 4624–4627.
32. Luzzatto L and Notaro R: Malaria. Protecting against bad air. Science (2001) 293: 442–443.
33. Fiorelli G, Martinez di Montemuros F and Cappellini MD: Chronic non-spherocytic haemolytic disorders associated with glucose-6-phosphate dehydrogenase variants. Baillieres Best Pract Res Clin Haematol (2000) 13: 39–55.
34. Guindo A, Fairhurst RM, Doumbo OK, Wellems TE and Diallo DA: X-Linked G6PD deficiency protects hemizygous males but not heterozygous females against severe malaria. PLoS Med (2007) 4: 516–522.
35. Chen SQ, Zhang SQ and Xu BZ: Burden of malaria and strategies for preventing and treating malaria in Hubei Province. Chin J Parasit Dis Con (2001) 14: 316 (in Chinese).
36. Zhao F, Ou XL, Xu CC, Cai GQ, Wu XY, Huang YM, Zhu WF and Jiang QC: Rapid detection of six common Chinese G6PD mutations by MALDI-TOF MS. Blood Cells Mol Dis (2004) 32: 315–318.
37. Ainoon O, Yu YH, Amir Muhriz AL, Boo NY, Cheong SK and Hamidah NH: Glucose-6-phosphate dehydrogenase (G6PD) variants in Malaysian Malays. Hum Mutat (2003) 21: 101.
38. Noori-Daloii MR, Hajebrahimi Z, Najafi L, Mesbah-Namin SA, Mowjoodi A, Mohammad Ganji S, Yekaninejad MS and Sanati MH: A comprehensive study on the major mutations in glucose-6-phosphate dehydrogenase-deficient polymorphic variants identified in the coastal provinces of Caspian Sea in the north of Iran. Clin Biochem (2007) 40: 699–704.