Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a widespread abnormality of red cell enzyme, which gives rise to hemolysis under oxidative stress. In Saudi Arabia, however, G6PD deficiency has a variable frequency in different regions. The prevalence and genotypes of G6PD deficiency are not known until now in Jeddah province. Accordingly, we design this study to investigate the frequency of the Mediterranean mutation and other mutations that may involve exon 6 and exon 7 of the G6PD gene in this region of Saudi Arabia. All samples were collected in a short period from July 2005 to October 2005. Twenty five Saudi males and 22 Saudi females, (their ages ranged between 18 and 45) were screened for G6PD deficiency by quantitative spectrophotometric assay at the Maternity and Children Hospital in Jeddah for premarital screening were found to be deficient in G6PD. The CBC was performed to all blood samples obtained from those patients. During this period 47 normal subjects (15 males and 32 females) blood samples were randomly collected from the same hospital as a control group in order to compare the CBC of the control group with the CBC results from the G6PD deficient patients. Also, those 47 subject were visiting the hospital for the same reason. The G6PD deficient subjects were further analyzed for the genetic mutations which affect exon 6 and exon 7 of the G6PD gene. The DNA of the G6PD deficient subjects was extracted from the blood samples and amplified by the polymerase chain reaction (PCR). Mutation analysis was performed by using the conformation sensitive gel electrophoresis (CSGE) followed by direct automated sequencing to the samples which gives positive results in the CSGE. All detected mutations were in exon 6 of the G6PD gene, while no mutations were detected in exon 7. The results obtained for the deficient subjects showed that 6 subjects had the Mediterranean mutation and one subject had the Sibari mutation as a novel mutation not reported before in Saudi Arabia. However, the frequency of Mediterranean mutation appeared to be low 6/47 (12.8%) compared to the eastern region of Saudi Arabia. The absence of the Mediterranean and Sibari mutation from the remaining forty patients should signify the existence of other mutations in their G6PD gene. So, it is recommended to use molecular methods for the detection of other G6PD mutations. The need for utilizing screening measures for early detection of G6PD deficiency before marriage is recommended.