Association of -582 A> G HAMP-P Polymorphism and Iron Status of Javanese β Thalassaemia Carriers

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Thalassaemia is a genetic disorder most commonly found in Indonesia. β thalassaemia is a diverse group of blood disease which may include congenital haemolytic disorder due to mutations in the β globin chain gene. Iron overload in thalassaemia β is influenced by polymorphisms of genes involved in various metabolic pathways that play a role in iron metabolism including HAMP gene. HAMP is hepcidin encoding gene. Hepcidin maintains plasma iron level by regulating the mobilization of iron deposit from hepatocytes and controlling intestinal iron absorption and iron release from macrophages. -582 A> G HAMP-P gene polymorphism changes transcriptional activation responses to stimulatory factors 1 and 2 (USF1 / USF2) and cMyx / Max heterodimers, prompting promoter to be less responsive to USF1 / USF2 or cMyx / Max, hence transcriptional activity-582G (mutant) allele was 20% lower than the-582A (wild type) allele. The role of -582 A> G HAMP-P gene polymorphism as genetic modifiers on iron status in β thalassaemia is still controversial. The purpose of this study was to examine the effect of -582 A> G HAMP-P gene polymorphism on iron status of Javanese β thalassaemia carriers as reflected in serum levels of iron, transferrin saturation and ferritin.

This study was explanational analytic research with cross sectional design. Thirty-six adult javanese β thalassaemia trait carriers who are parents and siblings of β thalassaemia major patients who came to red cross office in Semarang city during the period 2010 - 2011 that met the inclusion criteria are included as the sample of the study. All recipients have signed a letter of agreement to participate as research probands. -582 A> G HAMP-P gene polymorphism was examined by using PCR-RFLP method [1].

There were 36 β thalassaemia carriers (23 female and 13 male); The mean of serum iron, transferrin saturation and serum ferritin level in female β thalassaemia carriers was 69.6 ± 24.8 mg / dl, 25.6 ± 8, 6% and 95.6 ± 69.7 ng / ml, respectively. The mean of serum iron, transferrin saturation and serum ferritin level in male β thalassaemia carriers was 89.2 ± 23.7 mg / dl, 31.6 ± 11.5% and 150.5 ± 90.9 ng / ml, respectively. These iron status are in the range of normal reference values. Genotype frequency of -582 A> G HAMP-P gene polymorphism is 50 % AA (wildtype), 47.2 % AG (heterozygous mutant) and 2,8% GG (homozygotes mutant). -582 A> G HAMP-P gene polymorphisms did not modify iron status. There was no significant difference in serum iron levels between the AA (wild type) genotype and AG or GG on female (p = 0.240) and male (p = 0.206) probands. There was no significant difference in transferrin saturation between genotypes AA (wild type) and AG or GG on female (p = 0.228) and female (p = 0.260) probands. No significant differences in serum ferritin levels between the AA (wild type) genotype and AG or GG on female (p = 0.806) and male (p = 0.754) probands. The finding of this research contradicts with the previous study which concludes that there is an increased iron overload in poly transfused thalassaemia major patients with HAMP-P 582 G (mutant) genotype. Probably because of low iron intake and predominantly non-heme iron in diet of the probands, the mild decrease in the expression of the gene has no effect on the iron status, however in the case of poly transfused thalassaemia major probands with highly iron deposits, the decreased expression of hepcidin -582 G (mutant) variant will accelerate iron overload.

-582 A> G HAMP-P gene polymorhism is commonly found in Javanese ethnic β thalassaemia carriers. However -582 A>G HAMP-P gene polymorphism does not modify iron status of β thalassaemia carriers.

Keywords: β thalassaemia carrier, HAMP, iron status

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