



**SPECTRUM OF β -GENE MUTATIONS IN PATIENTS DIAGNOSED IN
UKMMC**

By

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DECLARATION

I hereby declare that this thesis is based on my original work and has not been submitted previously or currently for any other degree student at Universiti Teknologi MARA or any other institution.



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ABSTRACT

β -thalassemia and HbE are autosomal recessive disorders that affect the synthesis of β -globin gene. These defects mainly caused by point mutations on chromosome 11. Due to the multi-ethnicity of Malaysia, each ethnic population has its own common mutation. The aim of this study was to characterize β -globin gene mutation present in Malay and Chinese patients of UKMMC using multiplex ARMS polymerase chain reaction (MARMS-PCR). Initially, 120 samples were selected based on presence of hypochromic microcytic red blood cells and raised HbA₂, HbF, HbE and Hb Variant. Presences of the different types of mutation were then tested by using ten primers of common β -globin gene mutations using MARMS-PCR. Once the mutation was detected, heterozygosity and homozygosity of the mutation was identified. Out of the 120 samples, 80 samples were detected with increase HbA₂, HbF, HbE and Hb Variant. MARMS-PCR managed to detect 75 samples with mutation while another 5 were uncharacterized. It was also found that 52% from the sample were HbE patients with positive for CD26(G-A). As for the group of β -thalassemia it was noted that the most common β -thalassemia mutation were CD41/42(36.1%), followed by IVS1-5(G-C)(33.3%). Among the Malay patients, HbE and IVS 1-5 were the most common mutation seen whereas CD41/42 was most common among the Chinese. Genotyping result showed all HbE and 33 of the β -thalassemia samples were heterozygotes. Only 3 samples were homozygotes which all from IVS1-5. Hence the study managed to provide the pattern of β -gene mutations for the two main ethnics in Malaysia.

Keywords: β -thalassemia, HbE, MARMS-PCR, common mutations

CHAPTER 1

INTRODUCTION

1.1 Background of Study

β -gene mutation diseases are conditions that relate to reduction in the synthesis of β -globin chain. Diseases associated with β -gene mutations are one of the several types of disorders under hemoglobinopathies. The term hemoglobinopathies embraces all genetic haemoglobin diseases and they can be classified into two categories; thalassemia and abnormal hemoglobin diseases. As for haemoglobin, it is a globular protein found in red blood cells that is responsible for taking up oxygen and transporting it throughout the body. It consisted of four heme groups and two pairs of globin chains. Two different forms of globin chains are used to build normal haemoglobin which is called alpha (α) and beta (β) globins. Alpha globin is coded by four genes on chromosome 16 while beta globin is made up of two genes on chromosome 11.

Thalassemia is the commonest single gene disorder in Malaysia and is a paradigm of monogenetic diseases. It is a heterogeneous group of genetic disorders that resulted from reduced rate of synthesis of the globin chains of hemoglobin. Thalassemia is an autosomal recessive disorder inherited from the parents. There are two types of thalassemia based on the two major globin chains; α and β thalassemia. However, the most common case of thalassemia is β -thalassemia. β -thalassemia is a condition when there is a quantitative reduction in synthesis of β -globin chain which is mainly caused by point mutation. It is further categorized into minor and major β -thalassemia. Minor β -thalassemia is a circumstance when one of the β -globin chains is mutated. In Malaysia, study has shown that 4.5% of the total 28.9 million people are β -thalassemia trait (George et al., 2012). On the other hand, β -thalassemia major or Cooley's anemia is when both β -globin chains are missing due to mutation. It is a crucial condition where