I. INTRODUCTION

Graves' disease (GD) is a typical organ-specific autoimmune disease that affected world-wide population. The pathogenesis involves the autoimmune of thyroid gland are characterized by lymphocytic infiltration and the presence of autoantibodies (Feliciano, 1992). The disease is due to autoantibodies to the thyroid stimulating hormone receptor that mimicked the thyroid-stimulating hormone (TSH) activity by binding to the TSH receptor (TSHR) and overstimulating the thyroid function. Graves' disease is mostly found simultaneously with other autoimmune endocrine diseases such as Type I diabetes mellitus (IDDM), Addison's disease or non-endocrine autoimmune disorders include myasthenia gravis, rheumatoid arthritis (RA) within the same individual or family and predominate in female (Weetman, 1994). Several autoimmune diseases have shown associations with the genes of the major histocompatibility complex (MHC) class II (Statsny, 1983). For two reasons, the extreme degree of polymorphism that exists in this system and the existence of the polymorphic immune response genes that was concerned the immunopathogenesis and suscepitibility to certain diseases, were assumed the subject of HLA and disease association. Exactly how particular histocompatibility genes predispose to autoimmunity still not clear.

HLA-DQ and HLA-DR are highly polymorphism and are in strongly linkage disequilibrium (Bidwell, 1988). The complexity has been further compounded by developments in technology. The old techniques such as cytotoxic, serological, two-dimensional gel electrophoresis and restriction fragment length polymorphism (RFLP) analysis have contributed to this field but they are not capable of resolving all HLA specificities because of a lack of sensitivity and suitable reagents (Bidwell, 1988, Brown, et al., 1993). The ability of the DNA typing with sequence-specific oligonucleotide probes (SSOP) has been enhanced by the use of polymerase chain reaction (PCR) as a method for amplifying specific segments of genome DNA (Saiki et al., 1989). Based on the cloning and sequencing results of many investigator, up to 13 alleles of HLA-DQA1, 25 of HLA-DQB1 and 135 of HLA-DRB1 having been defined (Bodmer, 1995).

Studies in different ethnic population led to the observation that HLA-A1, HLA-B8 and HLA-DR3 were associated with the disease in Caucasians (Farid et al., 1979), The relative risks associated with HLA-DR3 within Caucasians has varied widely from figures as high as 7.4 in subtype 3a (Mangklabruk et al., 1991). The extension studies gave an increasing data of the frequency of the HLA-DQA1*0501 in Graves' patients with relative

risk of 3.7 (Yanagawa et al., 1993). It has been reported that a different HLA association exists in Graves' disease of Orientals. Many studies of Oriental populations were shown that HLA-B46 and HLA-DR9 (Yeo et al., 1989), HLA-DR4 (Luo et al., 1994) in Chinese and HLA-A2, HLA-B46, HLA-Cw11 and HLA-DPB1*0501 (Dong et al., 1992) in Japanese were significantly associated with Graves' disease. With regard to HLA antigens in Japanese, Tamai reported a negative association between HLA-DQB1*0501 and Graves'disease (1.5% vs 11.4%) (Tamai et al., 1994).

The purpose of the present study is to determine the frequency of different alleles at HLA-DQ and HLA-DR loci of Graves' patients who resided in the northern Thailand. It was undertaken to investigate the role of HLA factor in contributing to disease development in Graves' disease. This analysis should be useful in understanding the role of these genes and disease susceptibility or finding the genetic marker for susceptibility or resistance to Graves' disease.