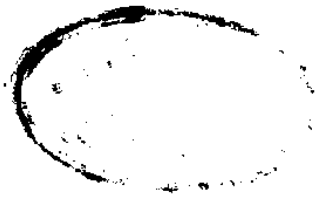
AUTOIMMUNE ANTIBODIES IN PREGNANCY INDUCED HYPERTENSION

Thesis

Submitted for partial fulfilment of M.S.

in Gynaecology and Obstetrics



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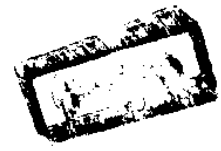

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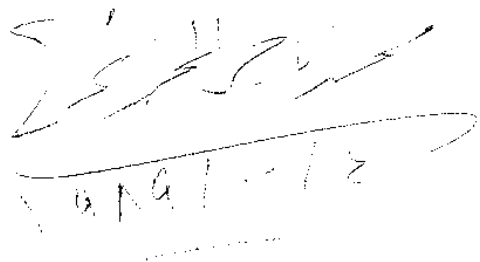

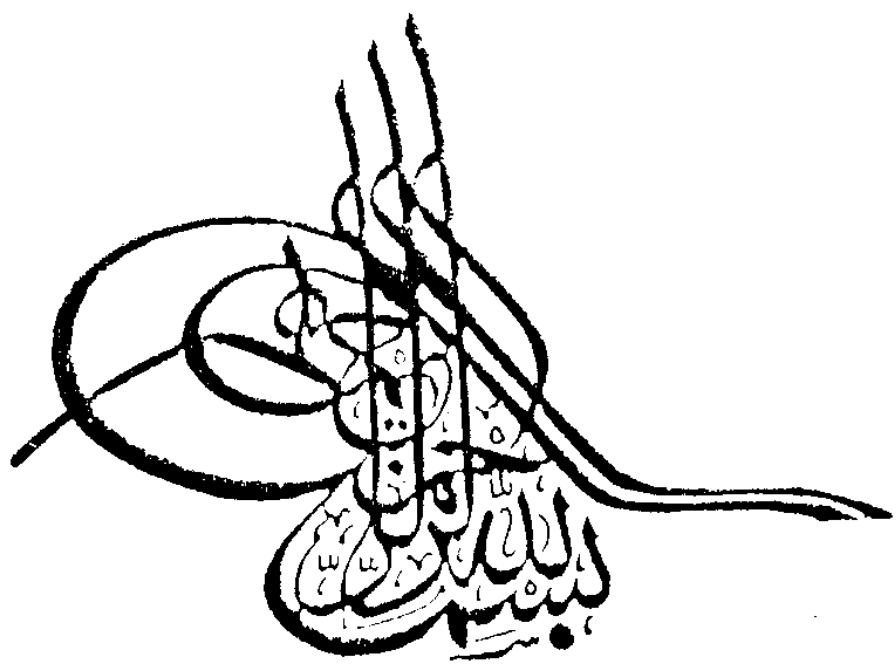

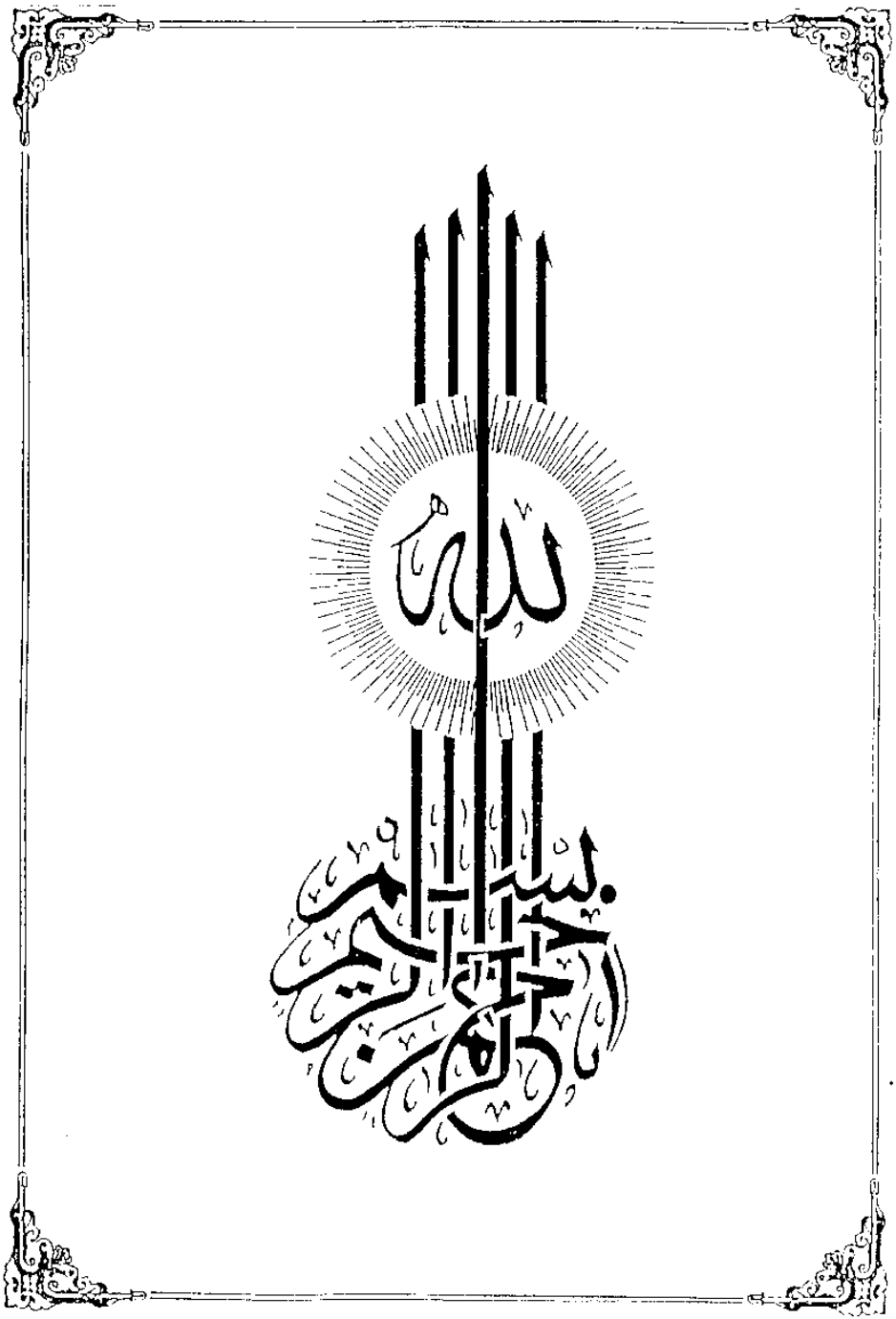

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CONTENTS

INTRODUCTION

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Pregnancy induced hypertension (PIH) is one of the serious complications of pregnancy and is held responsible for a number of maternal, and fetal morbidity and mortality (Chamberlain et al, 1975). So it is considered as a sort of crossroad where the interest of the obstetrician,the physician, the nephrologist, the cardiologist and neonatologist join together (Romanini, 1988).

Eclampsia was referred to by Hippocrates, ancient Egyptian, Chinese, Indian and Greek writings (Jenkins et al, 1988). Mauriceau, (1668) drew attention to the particular association of the disease with primigravidity and, realizing that the convulsions ceased after delivery, logically advocated prompt delivery as treatment.

Eclampsia and epilepsy were only distinguished by the cessation of convulsions after delivery in eclampsia. This distinction was not absolute and some confusion still occurs for patients with single post-natal fit (Jenkins et al, 1988).

Lever, (1843) noted that the proteinuria he had found in eclamptics disappeared after delivery, whilst that in women with the clinically similar condition of glomerulonephritis did not . It was not until the beginning of the twentieth

century, when measurement of the blood pressure was introduced, that the "strong swollen pulse" of the ancient writers were recognized as hypertension (Jenkins et al, 1988).

In this century much was known about the clinical features of the disease although a definitive agreement on the blood pressure parameters that have to be considered does not yet exist (Adriano , 1988). On the other hand what has still to be discovered about the etiology and pathophysiology is rather more (Romanin, 1988).

As our understanding of immunological mechanisms has grown, many diseases of unknown etiology have been shown to have an immunological basis, such as diabetes mellitus and collagen diseases, So, recent awareness of the possible range of immunologic manifestation has stimulated reappraisal of certain ill- understood clinical problems in the field of reproduction for possible immune etiological factors.

Materno-fetal immunological interactions have been studied largely in the last few years. The commonly held concept of the fetus as an intrauterine allograft is not valid now (Billington, 1988), since there is no vascular continuity with the maternal host nor any evidence of cell traffic into the fetal circulation. Also it has become

Increasingly evident that the mother and fetus are immunologically aware of each other and that their immune systems may interact. This evidence had led to a persistent belief that maternal recognition of the implanting embryo and the generation of a protective immune response is an absolute requirement for normal pregnancy. The break of such protective immune response may provide the conceptual basis for the pathogenesis of certain pregnancy disorders among which PIH lies. The immune factors may act as trigger mechanisms if other variables are "permissive" in a "domino effect" (Jenkins et al, 1988).

Recent studies have shown that among patient with PIH some of the auto-antibodies such as antinuclear antibodies (ANA), antimitochondrial antibodies (M antibodies), anti-smooth muscle antibodies, antiphospholipid antibodies (includes lupus anticoagulant (LAC) and anticardiolipin (ACA) antibodies) occur more frequently than were previously reported in the literature for the normal population (Airoldi et al, 1988; Garcia et al, 1984; Branch et al, 1989; Alanen et al, 1984).

However other studies have shown that the incidence of ANA in normal pregnant women is significantly higher than in nonpregnant women (Farnam et al, 1984).

So at present the role or even the presence of the auto-antibodies in normal pregnancy or in PIH is still debatable.So, PIH remains the main killer of pregnant women and their unborn children in the Third World, but is fastly disappearing as a cause of such in the developed world.

This "disease of theories" may eventually disappear without its complex etiology having been unrevealed. Those thousands of researchers who have tackled its mysteries in vain would then have to acknowledge defeat as the disease disappeared from the stage. Alternatively, the disease may return with a vengeance as new reproductive technologies alter feto-maternal relationships. (Jenkins, 1988).

AIM OF THE WORK

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In view of the considerable controversy regarding the presence or absence of autoantibodies namely antinuclear, antimitochondrial, antismooth muscle and antiparietal cell antibodies in maternal sera during normal pregnancy, the first objective of the present work is an attempt to throw light upon this issue.

The second objective in this study is to find out the occurrence of these antibodies in patients with PIH.

The third objective is to compare the previous immunologic parameters in the normotensive pregnancies and those complicated by hypertension and proteinuria "pre-eclampsia and eclampsia" which may contribute to the possible immunopathogenesis of PIH.

In the present study the term PIH is used to denote hypertension developing during the third trimester in the absence of positive data suggestive of hypertension or proteinaria antedating pregnanay (Davey, 1985). This category includes pre-eclampsia and eclampsia.

REVIEW OF LITERATURE

AUTOIMMUNITY

The immune system has the potential for recognizing and responding to an enormous range of antigen determinants. This depends upon the activities of T and B lymphocytes, which are equipped with receptors for a correspondingly diverse repertoire of antigenic specificities.

These will inevitably include some that are directed towards antigens present on the body's own cells and tissues.

The potential for such self-recognition may be an important component of the immune functions in general.

However small amount of autoantibodies in normal subjects may facilitate the removal of some metabolic and catabolic products. Also these naturally occuring auto-antibodies may also serve to prevent the initiation of a damaging autoimmune response by binding to self- mimicking epitopes on microbes. (Taylor, 1988).

The self recognition served by the immune system depends mainly on the recognition of cell- surface antigens encoded by the major histocompatibility complex (MHC).

In general, the tissue antigens present during fetal and neonatal life are recognized as "self" and so are tolerated

by the host. No antibodies or hypersensitivity reactions are developed to them, a type of immune response called immune tolerance which means that the body is tolerant to its own antigens which have " self markers" the ability to recognize them is learned during development and maintained by continuous contact during life.

The possible mechanisms involved in such immune tolerance was summarized by Lachmann et al, (1982) as following:

(1) Absent T helper cells, so that no assistance is given to autoreactive B cells in producing the relevant antibody. This may be due to early exposure of the antigen to the incompletely developed immunologic cells or clones,rendering them a "forbidden clones" or destructed clones.

(2) T suppressor cell system may also provide a back-up function,particularly in relation to antigens encountered after the neonatal period.

The outcome of these controlling factors is maintenance throughout life of the lack of response to self tissues which, coupled with responsiveness to foreign antigens, is fundamental to the normal working of the immune system.