ATRIAL NATRIURETIC PEPTIDE CONCENTRATIONS IN PREGNANCY INDUCED HYPERTENTION (P. I. H.)

THESIS

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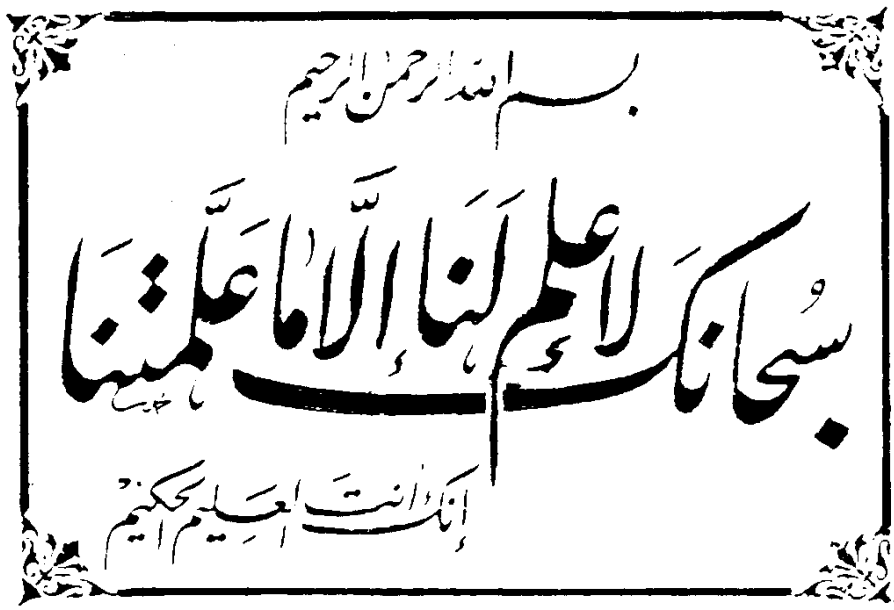

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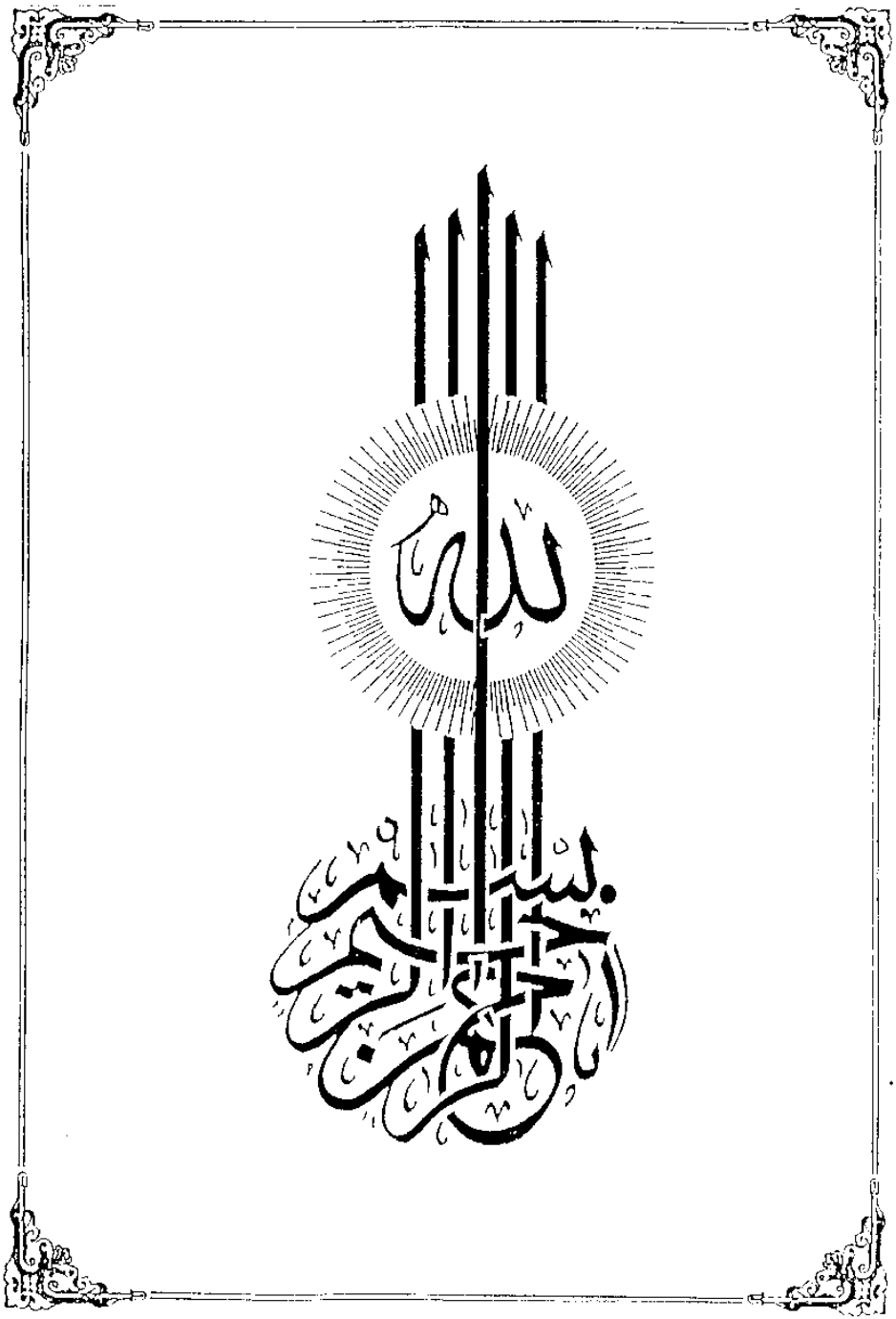

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ABBREVIATION

ANP	:	Atrial Natriuretic peptide
cAMP	:	Cyclic adenosine monophosphate
cGMP	:	Cyclic guanosine 3'5' monophosphate
DOC	:	Deoxycorticosterone
HLA	:	Human leucoytic antigen
PIH	:	Pregnancy induced hypertension

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INTRODUCTION

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AIM OF WORK

INTRODUCTION
AND
AIM OF THE WORK

Hypertensive disorders complicating pregnancy are common and form one of the great triade along with haemorrhage, infection and continues to be responsible for a large number of maternal deaths. *[Cunningham et al., 1989].*

Pregnancy induced hypertension is a syndrome of unknown aetiology; different theories were postulated but none of them could stand the test of time *[Pauerstein, 1987].*

Cardiac atria have long been suspected of participating in the regulation of blood volume *[Thomsen et al., 1987],* this has usually been ascribed to reflex stimulation of neural stretch receptors located in the subendocardium which results in enhanced urine flow and salt excretion *[Ballermann and Brenner, 1985].*

In *1981, De Bold et al.* provided direct evidence for humoral mediator "atrial natriuretic peptide", by showing that saline extracts of cardiac atria, but not the ventricles, elicit a marked increase in urinary salt and water excretion when injected into normal rats.

Atrial natyiuretic peptides are a group of biologically active peptides synthesized and secreted by the atrial myocytes. Three separate forms (α, β,τ) of the peptide have been isolated from human atrial cells *[Kangawa et al., 1985]*. The biologically active sirculating form of the atrial natriuretic peptide (ANP) is a 28 amino acid structure derived from a large molecular weight prohormone *[Gutkowska et al., and Kangawa et al., 1985]*.

Besides the significant matriuretic and diuretic effects, atrial natriuretic peptide induces an increase in renal blood flow and glomerular filteration rate. However the actual mechanism (s) responsible for natriuresis remains unclear with evidence consistent for both haemodynamically induced natriuresis and inhibitory effect upon tubular sodium reabsorption *[Borenstein et al., 1983]*. ANP has also been shown to inhibit vascular smooth muscle contraction induced by angiotensin II and noradrenaline and it reduces the secretion of both renin and aldosterone. *[Thomsen, et al., 1987]*. Thus it complements the activity of other known regulators of blood pressure and blood volume *[Bond et al., 1989]*.

In fact plasma levels of ANP change in various pathologic states associated with generalized oedema or volume expansion such as congestive heart failure, renal failure and some hypertensive disorders *[Sato et al., 1986]*.

Atrial stretch consequent to haemodynamic changes or volume expansion appears to be one of the most important stimuli for atrial natriuretic peptide release *[Burnett et al., 1986 and Sato et al., 1986]*. ANP secretion is also increased in response to high sodium diet and conversely, a low sodium diet decreases its plasma concentrations *[Sagnella et al., 1985]*.

A striking change in hoemodynamics occurs in women during pregnancy that may alter plasma ANP levels *[Hirai et al., 1988]*. Normal pregnancy is characterized by expanded plasma volume, *[Gallery et al., 1979 and Thomsen et al., 1987]* therefore elevated levels of plasma ANP in normal pregnancy might be expected. There is no consensus in the leterature that atrial natriuretic peptide is increased in pregnancy.

A role for ANP in pregnancy induced hypertension has also been proposed. Since patients with pregnancy induced hypertension, typically have decreased plasma volume, normal or even low plasma ANP concentrations would have been expected. Conversely *Thomsen et al. [1987] and Miyamoto et al. [1988]* reported substantively increased ANP levels in those patients with PIH. However the role of endogenous atrial natriuretic peptide in hypertensive disorders is debatable.

The present study aims to asses the effect of pregnancy as well as pregnancy induced hypertension on plasma atrial natriuretic peptide concentrations in a trial to find its significant role in PIH state .Also to correlate the plasma ANP level with the clinical and other biochemical findings in this study.

REVIEW OF LITERATURE

ATRIAL NATRIURETIC PEPTIDE

Since its isolation, 1981, atrial natriuretic peptide has received attension as a potentially important mediator of volume homeostasis *[Bond et al., 1989]*.

Atrial natriuretic peptide acts on the kidney to promote excretion of salt and water, thus decreasing the extracellular fluid volume and maintaining homeostasis *[Ballerman and Brunner, 1986]*.

Beside the natriuretic and diuretic effects, atrial natriuretic peptide (ANP) inhibits vasoconstriction induced by angiotensin II and nor adrenaline and reduces secretion of both renin and aldosterone. *[Atlas et al., 1986 and Thomsen et al., 1987]*.

Nomenclature

Atrial natriuretic peptide was described by different authors and gave it different names as: atrial natriuretic factor I, II, III *[Atlas et al., 1984]*, α, β and human natriuretic polypeptides *[Kangawa and Matsu, 1984]*.

Atrin [Ballermann and Brenner, 1985] cardionatrin *[Mills, 1984]*, atriopeptin I, II, III *[Geller et al., 1984]* and auriculin *[Maack et al., 1984]*.

Origin

Atrial natriuretic peptide is a hormone synthesized in atrial myocytes, stored there in granules and released as a result of increased intraatrial pressure or atrial stretching *[Yamaji et al., 1985]*.

Also it has been shown that foetal umbilical arterial level of ANP is higher than the umbilical venous level or maternal plasma level. This implies that there may be a primary foetal synthesis of atrial natriuretic peptide and the localization of placental ANP receptors supports a functional role of circulating foetal ANP *[Hatijis et al., 1988]*.

Robbillard et al. (1988) carried out an important work on human foetuses to determine whether an increase in intravascular volume load would stimulate ANP secretion in the foetases as it does in the adult. He found that ANP is present as a circulating hormone, in the human foetus by mid gestation at which time foetal release of ANP is increased in response to intravascular volume expansion.