Introduction

Hypertension diseases in pregnancy are common and are associated with significant maternal and perinatal mortality and morbidity (Smith et al., 2005).

In hypertensive disorders of pregnancy, preeclampsia is a common and major complication causing significant morbidity and mortality in the fetus, new born infant and mother in both developed and developing countries (UK Department of Health and Social Security, 1994).

Redman et al.. (1976) have suggested that patients who subsequently develop preeclampsia have significantly higher levels of uric acid starting from 24 weeks gestation.

Elevated uric acid is another component of the preeclampsia syndrome that was recognized many years ago. It is one of the most consistent and earliest detectable changes in preeclampsia and has been cited as a better predictor of fetal risk than blood pressure (Roberts et al., 2005).



In the context of hypertension in pregnancy, plasma urate concentration clearly reflects the fetal prognosis. This is entirely consistent with reports that hyperuricemia correlates with the severity of preeclampsia (Pollak et al., 1960) and distinguishes reliably between pre-eclampsia and simple chronic hypertension (McFarlane, 1970). The data also indicate that in pregnant women with hypertension, measurement of plasma-urate is a better indication of the fetal consequences of pre-eclampsia than the measurement of blood-pressure itself. In established severe pre-eclampsia the diagnosis is usually clinically evident and the elevation of plasma-urate will simply confirm the diagnosis. But since urate retention is an ofthe early feature disorder. plasma-urate measurement is of the greatest value where the diagnosis of preeclampsia is in doubt or hypertension of unknown aetiology is present. If plasma-urate is found to be low the outlook for the fetus is excellent (Redman et al., 1976).

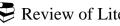
Roberts et al.. (2005) reported that in women gestational hypertension with or without proteinuria, elevated uric acid concentration identifies a group of pregnancies at increased risk for small for gestational age and preterm delivery compared with each condition in the absence of hyperuricemia.

The hyperuricemia of induced pregnancy hypertension is partly due to the failure of tubular secretion but placental ischemia may contribute to the elevation of uric acid in preeclampsia secondary to ischemia. The level of uric acid also correlate with levels of oxidative stress (Spickett, 1997). Therefore, preeclamptic hyperuricemia is probably caused by a combination of increased production, intrarenal "pretubular" vasoconstriction and hypovolemia. preeclampsia, a rise of uric acid can be seen to be a marker of the systemic disease process and increased risk rather than simply a sign of renal involvement.

The value of measuring plasma-urate concentrations in hypertensive pregnancy is greatest between 24 and 32 weeks gestation. Low value indicates a good prognosis for the fetus. Rising or high values at this time define a small number of very high risk cases which are better managed and treated in hospital (Redman et al., 1976).

Aim of the Work

This study aim to assess uric acid as a predictor of fetal outcome in gestational proteinuric hypertension.



Hypertensive Disorders In Pregnancy

Introduction

Hypertension is one of the most common medical complications of pregnancy and affects both maternal and fetal health. sometimes with life-threatening consequences. Hypertensive disorders are important causes of premature delivery, intrauterine growth restriction, and intrauterine fetal death. Maternal complications include those attributable to excessive increases in blood pressure, such as stroke, acute cardiac decompensation, and acute renal failure. Hypertensive disorders in pregnancy remain one of the leading causes of maternal death, worldwide, accounting for 10% to 20% of maternal deaths worldwide (Rajaram et al., 1995 and Chang et al., 2003).

large epidemiologic survey of hospital discharges reported that the of maternal rate mortality from hypertensive disorders in pregnancy is 1.4 per 100.000 deliveries (Zhang et al., 2003).

Because ensuring the well-being of the mother does not always ensure the most favourable fetal outcome, clinical management is challenging, and



decisions regarding the timing of delivery have profound lifelong effects on both the mother and the child. Although many, if not most, patients with hypertensive disorders in pregnancy are managed by obstetricians and specialists in perinatology, the often involved. internist is particularly when hypertension is severe and necessitates multi-drug therapy or when additional medical disorders, such as renal disease or pre-existing hypertensive conditions, are present (August, 2004).

Classification of hypertensive disorders in pregnancy

Accurate diagnosis of hypertension in pregnancy is of utmost importance, because pre-eclampsia is associated with adverse maternal and fetal outcome if not recognized early. Critical interventions such as decisions regarding the timing of delivery, are often clinical impressions ofthe based on disease responsible for the hypertension, thus, appropriate diagnosis may have significant, implications for the future health of the fetus (August, 2004).

According to the National High Blood Pressure Education (NHBPEP), Program 2000. (which recommended the original classification of *Hughes*, 1972), four categories of hypertension in pregnancy are recognized:

- 1. Pre-eclampsia-eclampsia, a syndrome occurring only in pregnancy and the puerperium and defined by the new onset of hypertension (systolic blood pressure of >140 mmHg or diastolic blood pressure of >90 mmHg) accompanied by new onset proteinuria, defined as 300 mg or more per 24 hours (eclampsia is the convulsive form).
- 2. Chronic hypertension, which is hypertension that preceded pregnancy and is due to essential or secondary hypertension.
- 3. Chronic hypertension with superimposed preeclampsia.
- 4. Gestational hypertension, which is high blood pressure appearing first after mid pregnancy, and is distinguished from pre-eclampsia by the absence of proteinuria.

(NHBPEPWG, 2000)

This category is broad, and include women who later develop diagnostic criteria for pre-eclampsia, as well as women with chronic hypertension in whom blood pressure decreased in early pregnancy, masking the true diagnosis. Gestational hypertension which resolves postpartum, and which was not in retrospect pre-eclampsia, is more likely to occur in women who



develop essential hypertension later in life (August. 2004).

In clinical practice, over diagnosis of preeclampsia may result in closer surveillance and possibly better outcomes. Thus, it may be prudent to consider a women with gestational hypertension to be at risk for pre-eclampsia (August, 2004).

Table (1): Classification of hypertension in pregnancy

Disorder	Description	
Pre-eclampsia- eclampsia	Multi-system disorder that usually manifests in the latter half of first pregnancy, characterized by hypertension, proteinuria, thrombocytopenia, mild renal dysfunction, and on occasion, abnormal results of liver function tests.	
Chronic hypertension	Hypertension that precedes pregnancy and that may represent essential hypertension or any form of secondry hypertension (e.g. renal disease, renovascular hypertension, pheochromocytoma, hyperaldosteronism).	
Chronic hypertension with superimposed preeclampsia	The development of worsening hypertension, newonset proteinuria, hyperuricemia, or thrombocytopenia in the latter half of pregnancy in a women with chronic hypertension.	
Gestational hypertension	Hypertension detected after mid pregnancy, no proteinuria. If blood pressure returns to normal by 12 weeks after delivery, then diagnosis is transient hypertension. If hypertension persists, then diagnosis is chronic hypertension.	

Modified from report of the National High Blood Pressure Education Working Group on Hypertension in Pregnancy. Am J Obstet Gynecol 2000: 183, S1-S22.

classification Thus hypertension separates induced by pregnancy, from hypertension that merely coexists with it. Unfortunately, chronic hypertension may be complicated by superimposition of preeclampsia or eclampsia (NHBPEP, 2004).

This classification is a more clinically focused classification, which diagnoses pre-eclampsia when de novo hypertension, in pregnancy, is accompanied by proteinuria or edema (NHBPEP, 2004).

Similar to the International Society for the Hypertension (ISSHP) Study of in Pregnancy classification, pre-eclampsia is diagnosed when denovo hypertension in pregnancy is accompanied proteinuria and isolated hypertension is referred to as transient hypertension of pregnancy (Brown et al., 1999).

The Australian Society for the Study of Hypertension in Pregnancy (ASSHP, 1993) describes all de novo hypertension as pre-eclampsia and subclassifying this as "mild pre-eclampsia", when hypertension is the only feature and "severe pre-eclampsia" when there is evidence of multi-system disorder in the mother.

Further classification has been proposed by *Redman and Jefferies (1988)*. They diagnosed preeclampsia in a pregnant women whose first diastolic blood pressure in the pregnancy was below 90 mmHg,



which rose by a minimum of 15 mmHg to a minimum reading of, at least, 90 mmHg.



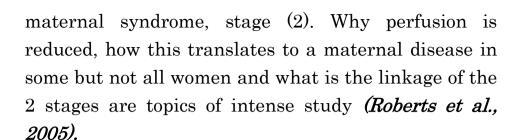
Pre-eclampsia

Pre-eclampsia is a major cause of maternal mortality (15-20% in developed countries) and morbidities (acute and long term), perinatal deaths, preterm births, and intrauterine growth restriction (Sibai et al., 2005).

Pre-eclampsia, which is a proteinuric gestational hypertension, accounts for the majority of the excess risks and is defined by the maternal syndrome. The maternal syndrome of pre-eclampsia is characterized by a systemic inflammatory response and its sequelae (Von Dadelszen et al., 2005).

Pre-eclampsia is a multi-system disorder that remains a major cause of maternal and foetal morbidity and death. To date, no treatment has been found that prevents the development of the disease (Rodrigo et al., 2005).

Pre-eclampsia is a pregnancy complication with serious consequences for mother and infant. The disorder is diagnosed by gestational hypertension and proteinuria but is far more than pregnancy induced hypertension. Pre-eclampsia is proposed to occur in 2 stages: Stage (1) reduced placental perfusion is postulated as the root cause and to lead to the



Pre-eclampsia is a placental-dependent disorder with both local and systemic anomalies with neonatal and maternal morbidity. It is manifested late in pregnancy, but the onset is during early stages of gestation (Mathiesen et al., 2005).

Hypertension is the most common medical disorder during pregnancy. Approximately 70 percent women diagnosed with hypertension pregnancy will have gestational hypertension preeclampsia. The term gestational hypertension preeclampsia is used to describe a wide spectrum of patients who may have only mild elevation of blood pressure to those with severe hypertension with various organ dysfunctions "acute gestational hypertension, pre-eclampsia, eclampsia, and the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP) (Coppage et al., 2005).

Hypertensive diseases in pregnancy are common and are associated with significant maternal and perinatal mortality and morbidity (Smith et al., 2005).

Risk factors for pre-eclampsia include: sociodemographical factors (extremes of reproductive age, socio-economic status, ethnic group), genetic factors, "multiple pregnancies. pregnancy factors gravidae, previous pre-eclampsia) or personal medical (obesity, chronic renal disese. history chronic hypertension, diabetes mellitus, thrombophilia). These risk factors and Doppler screening can help target interventions such as aspirin and calcium that have been proven to reduce the incidence of pre-eclampsia in high risk women (Smith et al., 2005).

Pre-eclampsia is a hypertensive disorder of pregnancy characterized by shallow placentation, inadequate placental perfusion, localized placental oxidative stress, a heightened maternal inflammatory response and subsequent maternal endothelial dysfunction. This Pathophysiology leads to an increase in maternal blood pressure, edema and proteinurea (Bainbridge et al., 2005).

Hypertensive disorders complicating pregnancy are common and form one of the deadly triad, along with hemorrhage and infection, that result in much of the maternal mortality related to pregnancy (Ventura and Collegues, 2000).

Better understanding of the diagnosis, categories, clinical manifestations, Pathophysiology and treatment of hypertension helps to maximize the chances of favorable outcome for both the mother and the fetus (Sibai et al., 1992).

Definitions or "Terminology"

Pre-eclampsia was defined according to the of the Internal Society for criteria Study Hypertension in Pregnancy as a diastolic blood of pressure >90mmHg in combination with proteinuria >0.3gm in a 24-hour urine sample (Alice et al., 1997). Proteinuria is an important sign of preeclampsia and the diagnosis is questionable in its absence (Chesley, 1985).

Mild pre-eclampsia: is defined s a diastolic blood pressure from 90 to 109mmHg combined with proteinuria of ≥300mg/24 hour or 1+ or 2+ on a urine dipstick.

Severe pre-eclampsia: is defined as pre-eclampsia with either a diastolic blood pressure of at least 110 mmHg or albuminuria of at least 5 gm/24 hour or both (Seven et al., 1997).



Severity of pre-eclampsia

The severity of pre-eclampsia is assessed by the frequency and intensity of the abnormalities listed in the next table. The more profound these aberrations, the more likely is the need for pregnancy termination. The differentiation between mild and severe preeclampsia can be misleading because apparently mild disease may progress rapidly to severe disease (Cunningham et al., 2005).

Table (2): Indication of severity of hypertensive disorders during pregnancy (Cunningham et al., 2005)

Abnormality	Mild	Severe
Diastolic blood pressure	<100 mmHg	110 mmHg or higher
Proteinuria	Trace to 1+	Persistent 2+ or more
Headache	Absent	Present
Visual disturbances	Absent	Present
Upper abdominal pain	Absent	Present
Oliguria	Absent	Present
Convulsions "eclampsia"	Absent	Present
Serum creatinine	Normal	Elevated
Thrombocytopenia	Absent	Present
Liver enzyme elevation	Minimal	Marked
Fetal growth retardation	Absent	Obvious
Pulmonary odema	Absent	Present