Lipid Profiles and Platelets Counts of Pre-eclamptic women in Selected Rural Areas of Northern Nigeria

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Thesis
Lipid Profiles and Platelets Counts of Pre-eclamptic women in Selected Rural Areas of Northern Nigeria

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Abstract

Pre-eclampsia is one of the most common and potentially life-threatening complications of pregnancy. It affects five to eight percent of all pregnancies and is one of the leading causes of maternal mortality and preterm delivery in North East and North western Nigeria, ignorance and misconception about the disease plays an imperative role in the effect of the diseases on women, like wise accurate, affordable and sufficient routine test to be use clinically to identify the disease in whom it may develop and effective intervention or approaches that help in reducing pre-eclampsia is unclear on unavailable in health centres, in Nigeria approximately 37,000 women die annually because of Pre-eclampsia/eclampsia related complication WHO (2004). Objective of the study is to study lipid profiles in women with pre-eclampsia in rural areas of northern Nigeria. The mean age among the three groups is 25.18±0.86 in Non Pregnant non hypertensive, 24.52±0.53 in pregnant non hypertensive and 24.03±0.65, there is also a significant difference in the mean Triglycerides SEM of 4.21±0.89 of the pre-eclamptic group as compare to the other two groups which have lower means, No significant difference seen in the LDL, among the three groups, there were significant difference in the pre-eclamptic group urine specific gravity SEM of 1.127±0.007, platelets SEM of 0.46±0.34x105, and hemoglobin 1.34±0.001. Conclusion Pre-eclampsia is common in rural areas of Northern Nigeria due to presence of high risk factors in the study areas; this can be explained by the presence of high maternal mortality in the three states respectively. In summary, the findings reported in this research suggest that the women who develop pre-eclampsia had disturbed lipid profile due to abnormal lipid metabolism. Increased triglycerides levels and delayed triglycerides clearance, decrease High density lipoprotein, severe proteinuria of greater than 500mg in 24hrs urine or 3+ using dipstick and high blood pressure are the reasons for the development of preeclampsia. The findings in this study may be relevant for understanding the pathophysiology of Pre-eclampsia and the future treatment by lipid modifying regimens of this life-threatening condition. Recommendation In efforts to identify women at risk of developing pre-eclampsia during pregnancy, a question about family history of pre-eclampsia should be included during antenatal clinics.

Introduction

Pre-eclampsia is a complex pregnancy complication associated with increased blood pressure accompanied by proteinuria, edema, or both Davey et al., (1988). This condition seems to be linked to oxidative stress within the placenta. Increased production of lipid peroxides, thromboxane and/or cytokines triggered vascular and organic dysfunction have been observed in pre-eclampsia Lefèvre et al., (1997). Pre-eclampsia (PE) is one of the causes of high morbidity for both mother and fetus, especially in developing countries Vanderjagt et al., (2004). Pre-eclampsia is characterized by hypertension, proteinuria, and edema. Without intervention, pre-eclampsia progresses to eclampsia, this is characterized by malignant hypertension and epileptiform convulsions requiring emergency caesarian section Packer et al., (2005). Several risk factors have been identified in women who developed pre-eclampsia. They include nulliparity, history of pre-eclampsia in previous pregnancy, extremes of maternal age, multi fetal gestation, several preexisting maternal diseases (chronic hypertension, diabetes mellitus, chronic kidney disease, vascular or connective tissue disease, thrombophilia, high body mass index (BMI)), and possibly, long interval between pregnancies. Of these, obesity (where the risk of pre-eclampsia increases three-fold), is the most common. As over 30% of women of reproductive age are obese, increased BMI may be responsible for 30-40% of all cases of pre-eclampsia. Despite known risk factors, it is not possible to predict which woman will develop pre-eclampsia during pregnancy. Reproductive implications of pregnancy complicated by hypertensive disorder are well known, and women are advised regarding risk of pre-eclampsia in subsequent pregnancies Pre-eclampsia foundation (2006), Ness et al., (2003) and Chambers et al., (2001).

Numerous screening tests for pre-eclampsia have been proposed over the past few decades. A
screening test should be safe, valid, reliable, and acceptable to the population, reproducible, appropriate for the population, and economical. Pre-eclampsia is an appropriate disease to screen, as it is common, important, and increases both maternal mortality and perinatal mortality. However, to date, no test has been shown to appropriately screen for pre-eclampsia (Friedman et al., 2001). Although measurement of urinary kallikrein has been shown to have high predictive value, it was not reproducible (Kyle et al., 1997 and Miller et al., 1996). While recent works on sFlt-1, PI GF, and VEGF are promising, their positive predictive values in predicting pre-eclampsia are yet to be evaluated in a prospective fashion. (Kyle et al., 1997 and Miller et al., 1996).

Currently, the clinical value of an accurate predictive test for pre-eclampsia is not clear since we lack effective prevention. Intensive monitoring in women, who are at increased risk of developing pre-eclampsia, when identified by a predictive test, may lower the incidence of adverse outcome for both mother and the neonate. However, the effectiveness of such a strategy must be rigorously investigated (Villar et al., 2009).

In northern Nigeria Pre-eclampsia accounts for up to 40 percent of maternal deaths Population Council (2009), pre-eclampsia and eclampsia are problems usually associated with a woman's first pregnancy (primigravida) Population Council (2009). Given the tendency toward and culture of early marriage in the North, the majority of those affected by this condition are teenagers.

1.4: Laboratory values for pre-eclampsia

Renal
Proteinuria of >300 mg/24 h, Urine dipstick >3+, Protein/creatinine ratio >0.3*, Serum uric acid >5.6 mg/dL**, Serum creatinine >1.2 mg/dL**.

Low platelets/coagulopathy
Platelet count Hemolysis
Abnormal peripheral smear*, Indirect bilirubin >1.2 mg/dL**, Lactate dehydrogenase >600 U/L*.

Elevated liver enzymes
Serum AST >70 U/L**
* ACOG 2001 and
** Zhou et al., (1997)
1.1: Incidence of Pre-eclampsia
The incidence of pre-eclampsia varies greatly worldwide. WHO estimates the incidence (or number of new cases) of pre-eclampsia to be seven times higher in developing countries (2.8% of live births) than in developed countries (0.4%) which is due to poor health seeking behaviours, availability of health care facilities and personnel Dolea et al., (2003). In Nigeria the incidence is higher in the Northern part of the country with prevalence rate of 17%. FMOH 2009
1.2: Progression of Pre-eclampsia to Eclampsia
Only a relatively small proportion of all women with pre-eclampsia progress to the more potentially deadly eclampsia, however, once again, a pre-eclamptic woman in a developing country is three times more likely to progress to eclampsia than a woman in a developed country. The WHO estimates that eclampsia develops in 2.3% of pre-eclamptic women in the developing world, compared with 0.8% of pre-eclampsia cases in developed countries Royal Collage Obstetricians and Gynecologists London (2006).

1.3: Challenges to Defining the Problem: Variations in Death Rates from Eclampsia
Reliable statistics about women dying due to eclampsia are difficult to obtain because of the poor quality of vital statistics registration systems and hospital records in many developing countries. In addition, a sizable number of deliveries take place at home, and thus there are no records at all for these births. Therefore, data on women who die from eclampsia are only available from a limited number of countries Nevertheless, it is clear that the case fatality rates for eclampsia vary greatly across countries, with the risk of death from eclampsia being much higher in developing countries than in developed ones Aaserud et al., (2005).

1.5: CURRENT SERVICE PROVISION:
Screening for women at risk of pre-eclampsia is an important part of antenatal care. Routine screening for pre-eclampsia is based on measurement of blood pressure and urinalysis for proteinuria. Once women have been identified as being at high risk, they can be targeted for more intensive antenatal surveillance and prophylactic interventions such as early delivery. Most current strategies for risk assessment are based on the obstetric and medical history and clinical examination. Pregnant women are assessed at their first antenatal clinic (prior to 12 weeks if possible) for risk factors for pre-eclampsia including age, nulliparity, long pregnancy interval, prior history of pre-eclampsia, high body mass index (BMI), history of diabetes mellitus and hypertension. If a woman has any of the risk factors, an increased schedule of blood pressure screening is provided. Otherwise, they have blood pressure measurement and urinalysis for proteinuria at 16, 25, 28, 31, 34, 36, 38 and 40 weeks. No other blood tests to detect pre-eclampsia are recommended and routine Doppler ultrasound scans of the uterine or umbilical artery are not recommended National Collaborating Centre for Women’s and Children’s Health (2003).

1.6: DYSLIPIDEMIA
The dyslipidemia of pre-eclampsia is best understood in the context of lipid changes during normal pregnancy, in normal pregnancy circulating lipids are carried primarily in lipoproteins, which are composed primarily of free and esterified lipids, proteins (apolipoprotein), and phospholipids. The two main cholesterol-carrying lipoproteins are LDL and high-density lipoproteins (HDL). The triglyceride-enrichment of LDL and HDL contributing to hypertriglyceridemia may be due to increased cholesteryl ester transfer protein (CETP) activity during normal pregnancy. Supra-normal increases in serum triglyceride and free fatty acids develop as early as 10 weeks gestation in women destined to develop pre-eclampsia. Nearly 50% of women with preeclampsia have triglyceride concentrations > 400 mg/dL. Total cholesterol and LDL cholesterol concentrations are usually not different whereas HDL cholesterol is decreased in clinically evident preeclampsia. Metabolic changes producing hypertriglyceridemia generally shift the spectrum of LDL subfractions toward a proportional increase of smaller, denser LDL. Small, dense LDL particles are relatively depleted of cholesteryl esters, and enriched in protein. Proportional increases in small, dense LDL with heightened susceptibility to oxidative modification may account for part of the increased cardiovascular risk in individuals with the small, dense LDL phenotype. The normal pregnancy rise in plasma triglyceride is associated with a shift from predominantly large and buoyant low density lipoprotein (LDL) to intermediate and small, dense LDL (36 week’s gestation), with partial reversal by 6 weeks postpartum. LDL size correlated negatively with triglycerides (R= -0.61, P<.001). Pre-eclampsia, however, evidence for the interaction of plasma lipids, reactive oxygen species, and endothelial cell dysfunction is largely indirect. In contrast to atherosclerosis; for example, there are currently no positive or negative reports on isolation of oxidized lipids from vascular tissues in preeclampsia (Sibai 1991).

Early pregnancy dyslipidemia is associated with an increased risk of Pre-eclampsia Enquobahrie (2004). In pregnancy, lipolysis of TG-rich lipoproteins is reduced because of decreased lipolytic activities of the mother Alvarez et al. (1996) and Kinnunen et al. (1988), whereas placental VLDL receptors are up-regulated (Wittmaack et al., 1995). This results in a rerouting of TG-rich lipoproteins to the fetoplacental unit Winkler et al., (2000). However, in Pre-eclampsia, the vascularization of the fetoplacental unit may be impaired, resulting in yet-undefined compensatory mechanisms that may further increase synthesis of maternal Triglyceride (TG) levels. In addition, the decreased catabolism of TG-rich lipoproteins by reduced placental uptake and the putative concomitant decrease of lipoprotein lipolysis results in the accumulation of TG-rich remnant lipoproteins in the maternal circulation. Remnant lipoproteins may induce platelet activation and endothelial dysfunction, thus leading to the major clinical symptoms of PE.

1.8: JUSTIFICATION

Pre-eclampsia and maternal and neonatal mortality is common in rural areas of Northern Nigeria due to presence of high risk factors. This research is aim at identifying the level of cholesterol, triglyceride, High/Low density Lipoproteins and Platelets counts in predicting the onset of pre-eclampsia among those at risk of developing the disease in rural areas and provide data on current status of the disease in the research area which will help plan interventions that will reduce the prevalence of the disease and its debilitating effect on women.

1.9: Limitation of the study

As is the case with any large-scale study in which routinely collected data are used, this study involved a number of weaknesses. Lack of pre-pregnancy weights to assess pre-pregnant status and weight gains during pregnancy would have helped to further elucidate the pathologic mechanism underlying the relationship between lipid alteration, BMI and development of pre-eclampsia, lack of comprehensive medical history of some of the participants. There is also the possibility of unknown errors in ascertainment of cases; cost of reagents has also limited the sample size.

1.1.1: Hypothesis:

Lipid alteration in Pregnancy is not associated with pre-eclampsia in people living in rural areas.

1.1.2: General objectives

To study lipid profiles in women with pre-eclampsia in rural areas.

1.1.3: Specific Objectives

1. To determine the relationship between plasma triglyceride levels, platelets counts, diastolic blood pressure and severity of pre-eclampsia
2. To quantify the relation between maternal body mass index, lipid profile and the risk of developing pre-eclampsia
3. To examine whether maternal socio-cultural and economic status, is associated with pre-eclampsia, and if so, to what extent known risk factors for pre-eclampsia.

Literature Review

The etiology of pre-eclampsia remains unknown and...
several theories have been proposed to explain the pathophysiology. A current hypothesis implicates the placenta as the source for maternal pathology. Most prevalent are theories where trophoblastic invasion of the uterine spiral arteries is incomplete, resulting in relative placental ischemia, followed by release of antiangiogenic proteins from the placenta that lead to endothelial dysfunction. This final common pathway, systemic maternal endothelial dysfunction, results in hypertension, increased vascular permeability, and the activation of the coagulation cascade, while the effects of antiangiogenic proteins also affect the filtering mechanism of the kidney and are responsible for the new onset proteinuria. Changes in the levels of circulating angiogenic proteins, implicated in pathogenesis of pre-eclampsia, have been detected in the mother's blood, prior to onset of clinical disease. This latter observation is important in terms of developing preventive or therapeutic interventions. However, as appealing as this hypothesis is, it remains unproven Pre-eclampsia foundation (2006) and Ness et al., (2003).

Recently decreased expression of reducing systems thioredoxin and glutaredoxin in placenta from pregnancies with pre-eclampsia and intrauterine growth restriction have been documented Pankaj (2008). Placental tissue from normal pregnancies, severe pre-eclampsia with fetuses small for gestational age, mild pre-eclampsia with fetuses small for gestational age and pregnancies with small fetuses for gestational age without any sign of pre-eclampsia was collected immediately after delivery Pankaj (2008). The levels of these proteins were increased approximately 2- to 3-fold in the pre-eclamptic placenta compared to the normal placenta. These results indicated that the pre-eclamptic placenta were exposed to oxidative stress and that the protein thiol/disulphide oxidoreductases were adaptively induced in pre-eclamptic placenta, suggesting possible roles for thioredoxin, glutaredoxin, and protein disulphide isomerase in protecting placental functions against oxidative stress caused by pre-eclampsia Birtcher (2000). 

During early human pregnancy, cytotrophoblast cells invade the uterine spiral arteries, replacing the endothelial layers of these vessels with the subsequent destruction of the medial elastic, muscular, and neural tissue Fisher et.al, (1999), August et.al, (1995), Hanretty et al., (1988). By the end of the second trimester of pregnancy the uterine spiral arteries are lined exclusively by cytotrophoblast, and endothelial cells are no longer present in the endometrial or superficial myometrial regions. This remodeling of the uterine spiral arteries results in the formation of a low resistance arteriolar system with a dramatic increase in blood supply to the growing fetus. In preeclampsia, invasion of the uterine spiral arteries is limited to the proximal decidua, with 30% to 50% of the spiral arteries of the placental bed escaping endovascular trophoblast remodeling Fisher et.al, (1999), August et.al, (1995), Hanretty et al., (1988). Myometrial segments of these arteries remain anatomically intact and un dilated, and adrenergic nerve supply to the spiral arteries is not affected. The mean external diameters of the uterine spiral arteries in women with preeclampsia are less than one half of the diameters of similar vessels from uncomplicated pregnancies Hanretty et al., (1988). This failure of vascular remodeling prevents an adequate response to increased fetal demands for blood flow that occur as gestation progresses. Inappropriate integrin expression by the extravillous cytotrophoblast may explain the shallow pattern of invasion and lack of arterial remodeling that occurs in pre-eclampsia Fisher et al., (1999).

This failure of trophoblast invasion in pre-eclampsia results in a reduction in uteroplacental perfusion, with the placenta becoming increasingly ischemic as gestation progresses Fisher et.al, (1999) and August et.al, (1995). This concept of placental hypoxia in preeclampsia is supported by reports of decreased clearance rates of various radioactive compounds and steroids by the pre-eclamptic placenta Hanretty et al., (1988). In addition, placentas from women with preeclampsia display an increased frequency of placental infarcts Fisher et al., (1999, August et al., (1995), Hanretty et al., (1988) and Brosens et al., (1972) and altered morphology evidenced by abnormal cytotrophoblast proliferation and increased formation of syncytial knots. Further empirical evidence for a key role of the placenta in the etiology of preeclampsia is the generally rapid recovery that patients experience following delivery Fisher et al., (1999), August et al., (1995) Hanretty et al., (1988), Roberts et al., (1991) and Brosens et al., (1972).

**CD3 Zeta Protein expression in pre-eclampsia**

Pre-eclampsia is characterized by decreased suppression of CD3-zeta expression, inferring increased T-cell function compared to normotensive pregnancies. Maternal immunologic function appears to be altered in normal pregnancy. For example, infection from intracellular pathogens (viz., tuberculosis and malaria) and viruses (i.e. hepatitis, herpes simplex) are more severe (Luft, et al.,1984) =This implies that that cell-mediated (also known as T helper cell type 1 or Th1) immunity is depressed in pregnancy. Bedenicki et al., 1999 has illustrated that suppression
of Th1 type immunity in pregnancy is linked to down-regulation of the CD3-zeta chain complex. CD3-zeta is the intra membranous part of the T-cell receptor that is critical for T-cell proliferation. Secretion of IL-2, a Th1 cytokine that stimulates T cell (along with B cell and natural killer cell) growth, is mediated through this complex (Taylor et al., 2002). Thus, one would expect that successful pregnancy would involve decreased CD3-zeta expression to inhibit cell-mediated/Th1 immunity to protect the fetal allograft from rejection.

Pre-eclampsia, meanwhile, may be considered as an excessive maternal inflammatory response to pregnancy Redman, 1999. Recent publications Saito et al., and Sunder-Plassman et al have shown that cytokine expression is up regulated in pre-eclamptic pregnancies compared to normotensive pregnancy controls. For example, Saito et al., 1999 illustrated that pre-eclamptic patients exhibited significantly higher Th1 type cytokine production than normotensive patients. Sunder-Plassman et al., (1989) further showed that serum levels of IL-2 are increased in pre-eclamptics.

Pre-eclampsia is likely the end result of altered relationship between mother and fetus. Perhaps preecclampsia represents a shift in the maternal immune system that changes maternal tolerance to a semi-allogeneic fetus. Study by Garrett K. Lam et al., 2003 has confirmed a possible role for modification of the Th1/Th2 ratio by demonstrating a lack of suppression of TcR/CD3-zeta expression in a strictly defined population of pre-eclamptic women. There may be some serum factor, as yet to be identified, that exists in normal pregnancies and leads to the down-regulation of CD3-zeta. Presumably, this factor is lacking in pregnancies complicated by pre-eclampsia.

Sleeping Disorders Breathing in Pre-eclampsia

Sleep-disordered breathing (SDB) includes snoring, upper airway resistance syndrome, and obstructive sleep apnea (OSA)-hypopnea syndrome. OSA-hypopnea syndrome is characterized by recurrent episodes of upper airway collapse and obstruction during sleep and is associated with recurrent oxygen desaturations and arousals from sleep Young et al., (1993).

These disorders represent a continuum of SDB, with snoring at one end of the spectrum and OSA hypopnea syndrome at the other end. The exact prevalence of OSA among pregnant women is unknown. The prevalence of OSA is estimated to be 5% to 6% among women of reproductive age Young et al., (1993). Apnea is defined as the complete cessation of air flow for a minimum of 10 seconds. Apneas are usually associated with oxygen desaturations or sleep fragmentation (arousals).

Physiologic changes of pregnant women, including progressive weight gain and upward displacement of the diaphragm, may predispose women to OSA. Estrogen and progesterone levels rise significantly during the course of pregnancy. Estrogen induces hyperemia, nasopharyngeal mucosal edema, Elkus and Popovich 1992 and vasomotor rhinitis, which can lead to a narrowing of the upper airway with increased resistance to Air flow. Nasal obstruction, especially chronic nocturnal nasal congestion, has been shown to be an independent risk factor for SDB in the general adult population. Young et al (2001), Young et al., (1997). Hence it is plausible that upper airway congestion secondary to estrogen-mediated mechanisms and/or physiologic hypervolemia of pregnancy may increase the risk of SDB among pregnant women. Reduced upper airway dimensions, which is a risk factor for SDB, has been demonstrated among women in the third trimester of pregnancy. Izci et al., (2006), Pilkington et al., (1995) these physiological changes may be particularly pronounced in females with PE Izci et al., (2003).

Sleep disorder breathing (SDB) it more likely to occur in females with pre-eclampsia than in females with uncomplicated pregnancies and respiratory disturbances contribute to the functional abnormality of the blood vessels seen in females with pre-eclampsia Yion et al., 2008.

Role of the renin-angiotensin system in the pathogenesis of pre-eclampsia

Pre-eclampsia is a hypertensive disorder unique to pregnancy with consistent involvement of the kidney. The renin-angiotensin system (RAS) has been implicated in the pathogenesis of preeclampsia. In the gravid state, in addition to the RAS in the kidney, there is a tissue-based RAS in the uteroplacental unit. Increase renin expression observed both in human pre-eclampsia and in a transgenic mouse model with a human pre-eclampsia-like syndrome supports the concept that activation of the uteroplacental RAS, with angiotensin II entering the systemic circulation, may mediate the pathogenesis of pre-eclampsia AbdAlla et al., (2001).

Pre-eclampsia may present with variable manifestations of the multiple systems involved but is most consistently associated with renal involvement. The RAS has been implicated in the pathogenesis of pre-eclampsia Nielsen et al., (2000). Many of the previous investigations of the RAS in pregnancy and pre-eclampsia involved, out of contemporaneous necessity, measurements of the components of the RAS in the peripheral blood or ANG II infusion and
support the following observations. First, while renin, angiotensinogen, ANG II, and aldosterone are increased in the peripheral blood in normal pregnancy Skinner (1972), in patients with preeclampsia, plasma renin activity and aldosterone are paradoxically suppressed with relatively higher levels of aldosterone for the given level of renin Brown et al., (1992) and Symonds et al., (1972), suggesting increased adrenal sensitivity to ANG II. Second, normal pregnancy is associated with decreased vascular responsiveness to ANG II Abdul-Karim and Assali (1961), and preeclampsia is associated with increased sensitivity to ANG II that may develop before the clinical manifestations of the disease Gant et al., (1973). A decrease in ANG- Alexander et al., 2000, the vasodilatory arm of the RAS in the maternal peripheral plasma, has been reported in pre-eclampsia Merrill et al., (2000). All other components of the renin-angiotensin aldosterone system, except serum ACE, were reduced in pre-eclamptic subjects compared with normal pregnant subjects.

The effect of ANG- Alexander et al., 2000 on uterine blood ?ow is unknown. Hayashi et al., (1977) prospectively investigated the response of endogenous ANG II levels in 55 primi gravid patients during the last half of pregnancy. Blood samples were obtained from patients in the lateral and supine recumbent positions. They identi?ed that the mean supine ANG II level was signi?cantly higher between 29 and 34 wk of gestation in patients destined to develop pre-eclampsia than in those who remained normotensive Hayashi et al., (1977).

This difference in the ANG II levels is partially explainable by lower plasma renin activity levels in the controls compared with pre-eclamptic subjects in this study. In women with chronic hypertension who develop superimposed preeclampsia initially, at 20- and 28-wk gestation, the RAS remains elevated, similar to women who are not destined to develop preeclampsia. In women who develop pre-eclampsia, plasmarenin activity at 32 and 38wk and aldosterone at 32wk are lower compared with controls August et al., (1990). These observations suggest that after the establishment of increased sensitivity to ANG II, renal renin and adrenal aldosterone secretions are apparently suppressed. The renal renin juxtaglomerular cell granularity in manifest preeclampsia is decreased Hill et al., (1988), which is consistent with the decrease in renal renin secretion. Maternal circulating rennin in human pregnancy represents renal renin because it responds appropriately to renal-type physiological stimuli Brown et al., (1997). The decrease in renal renin secretion may thus explain why the maternal circulating level of renin is decreased in women with manifest pre-eclampsia.

**Adenosine Receptor Expression in Pre-eclampsia**


Several changes in placental morphology and function have been described in pregnancies complicated by pre-eclampsia Fox (2007) and Benirschke (2006), the mechanisms associated with these alterations are not well understood, however placental hypoxia as a result of impaired trophoblast invasion in PE. Studies by Yoneyama et al., (2002) shows Adenosine receptor concentration and expression was significantly higher in placentas of PE women when compared to uncomplicated pregnancies. Higher maternal and fetal plasma adenosine concentrations have been reported in PE, and maternal adenosine concentration correlates with the severity of the PE Yoneyama et al., (2002).

**2.1:FUNCTION OF VASCULAR ENDOTHELIUM**

The vascular endothelium has many important functions, including control of smooth muscle tone through release of vasoconstrictor and vasodilatory substances, and regulation of anticoagulation, antiplatelet, and fibrinolysis functions via release of different soluble factors Taylor et al., (1999) and Roberts’s et al., (1989). It has been suggested that release of these factors from the placenta in response to ischemia results in endothelial dysfunction of the maternal circulation Taylor et al., (1999) and Roberts’s et al., (1989). Evidence of endothelial dysfunction as an early event in preeclampsia suggests that it is a possible cause, and not a result, of the pregnancy specific disorder. Additionally, in women who develop pre-eclampsia, preexisting maternal factors such as chronic hypertension, diabetes, and hyperlipidemia may predispose the maternal endothelium to further damage Taylor et al., (1999) and Roberts’s et al, (1989).

**2.2: ENDOTHELIAL DYSFUNCTION**
Many markers of endothelial dysfunction have been reported in women who develop preeclampsia, suggesting that preeclampsia is an endothelial cell disorder (Taylor et al., 1999 and Roberts et al., 1989). An imbalance of anticoagulation and procoagulation forces is found in pre-eclampsia as increases in proteins of the coagulation cascade have been reported in women with pre-eclampsia. Circulating levels of fibronectin are significantly increased in women who develop pre-eclampsia, with measurable increases observed as early as 20 weeks of pregnancy Taylor et al., (1999) and Roberts’s et al., (1989). Plasma thrombomodulin, an antiocoagulation factor, is also significantly elevated in women with preeclampsia, with elevations detected as early as 24 weeks into the pregnancy Taylor et al., (1999) and Roberts’s et al., (1989). Biomarkers may also reflect severity of the disorder as circulating levels of fibronectin and thrombomodulin increase relative to severity of disease Taylor et al., (1999) and Roberts’s et al., (1989). Von Willebrand factor, another coagulation cascade factor, is also elevated in women with preeclampsia Taylor et al., (1999) and Roberts’s et al., (1989). The majority of studies reported so far found increased TNF alpha and IL-1 levels, and increased levels of soluble TNF alpha receptors and IL-1 receptor antagonist. Serum levels of IL-2 are also increased in pre-eclampsia Sunder et al., (1989). Increases in plasma ceruloplasmin, complement activity, α1-antitrypsin and haptoglobin, and reduced albumin and transferrin in pre-eclampsia, are characteristic of an acute-phase reaction that may be related to the increased IL-6 levels Vince et al., (1995). Dysfunctional endothelial cells undergo activation and produce leukocyte-endothelial adhesion molecules that mediate adherence of inflammatory cells. This inductive process is mediated by cytokines produced by inflammatory cells and activated endothelial cells.

2.3: Other Factors Contributing To Etiology of Preeclampsia

Platelets also appear to play an important role in the etiology of preeclampsia. Enhanced platelet activation, as determined by whole blood flow cytometry, and increased levels of platelet endothelial cell adhesion molecule-1 (PCAM-1) also occur in women who develop pre-eclampsia Taylor et al., (1999) and Roberts’s et al., (1989).

Plasma levels of other adhesion cell molecules are also significantly elevated in women who develop preeclampsia Taylor et al., (1999). These include vascular adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1), and E-selectin. Plasma levels of ICAM-1 and VCAM-1 have been reported to be significantly elevated at 3 to 15 weeks before onset of clinical manifestations. Elevations in ICAM-1 were evidenced at 18 weeks gestation, thus suggesting that markers of endothelial dysfunction may serve as predictors of preeclampsia during pregnancy. In summary, endothelial dysfunction may serve as a causative factor in pre-eclampsia and is not just a result of the disorder. Many markers of endothelial dysfunction may function as predictors of the syndrome in women who develop pre-eclampsia as many are significantly elevated at weeks before observance of clinical manifestations.

2.4: Risk Factors of Developing Preeclampsia

Women having history of pre-eclampsia or eclampsia during their first pregnancies are at higher risk of a repeating the disease Adelusi et al., (1986), although the disease generally occurs at a greater gestational age Steegers et al., (1998). The recurrence risk of pre-eclampsia is best predicted by the degree of proteinuria. The recurrence risk of pre-eclampsia in women who had had proteinuria of 300-500mg g/24 hours was 12.2% compared with 22.3% in women who had had proteinuria of >300mg/24 hours in their index pregnancy Visser et al. (1999). In general, estimation of the risk ratio is difficult, because most of the studies lack controls, and the incidence of eclampsia and pre-eclampsia may be different in different populations Adelusi et al., (1986).

Beyond family history, other maternal cardiovascular risk factors have been found to be associated with increased risk of HDP. Prepregnancy blood pressure has been shown to have a linear, positive correlation with preeclampsia Magnussen et al., (2007)

2.5: Diagnostic and screening of pre-eclampsia

Apart from the measurement of blood pressure, dipstick analysis of urine for protein is the most commonly performed antenatal screening test. The presence of proteinuria is seen as a possible indication of many complications in pregnancy, from urinary tract infection to chronic renal disease and it remains central to the diagnosis of pre-eclampsia in a hypertensive pregnancy. It has both diagnostic and prognostic implications when it is found though the optimal methods for detection and quantification in primary and secondary care remain controversial National Collaborating Centre for Women’s and Children's Health (2003).

In non-pregnant women daily urine protein excretion averages 20-80 mg/day (with an upper limit of 150 mg/day). This is made up of 40% albumin, 15-20% immunoglobulin (IgG 5-10%, IgA 3% and light chains 5-10%) and the remainder is Tamm-Horsfall glycoprotein derived from the tubules and the lower urinary tract Abbate et al., (1999). The movement of protein across capillary walls in most vascular beds is
limited by mechanical, electrochemical and hemodynamic restrictions Abbate et al., (1999). However, movement in the glomerular capillary is influenced by protein size, configuration and charge. The protein filtered by the glomerulus is reabsorbed, through proximal tubular epithelial cells by endocytosis and lysosomal degradation. This reduces protein excretion but is a process that is easily saturated and therefore can be overwhelmed by a high glomerular protein load which may result in swelling and rupture of the lysosomal particles within the epithelial cells. The resultant interstitial swelling and fibrosis these causes are common in chronic proteinuric renal disease Abbate et al., (1999)

Extensive changes occur in the renal system in pre-eclampsia. As part of the end organ pathology preeclamptic glomeruli undergo structural changes with pronounced endothelial vacuolisation and hypertrophy of the cytoplasmic organelles first defined as glomerular endotheliosis by Spargo et al., (2005) Such alterations were thought to be pathognomonic of pre-eclampsia but it is now accepted that no one feature of glomerular endotheliosis is specific to pre-eclamptic nephropathy. Under light microscopy the glomeruli appear swollen and bloodless and in contrast to the nephropathy seen in glomerulonephritis and diabetic nephropathy, cellular hyperplasia is absent Sheehan (1980). There is however, mesangial and endothelial cell hypertrophy with encroachment on the capillary lumen. In the largest postmortem study to date, 50% of affected glomeruli demonstrated extreme swelling with herniation of capillary loops into the proximal tubule Sheehan at el., (1983).

2.6: Prognostic role of proteinuria

Despite the prognostic role of proteinuria, it remains a poorly assessed clinical sign in pregnancy Suzuki et al., (1987). Although accepted by common consensus amongst obstetricians that proteinuria is most reliably measured by biochemical assay of a 24 hour urine sample, this is an impractical screening test and the most commonly performed front line investigation for proteinuria is semi-quantitative dipstick urinalysis. It is widely believed that the results of dipstick urinalysis correlate with the results of total protein measurements performed on 24-hour urine collections and this has led to an inevitable dependence on the dipstick for both clinical decision making and research definitions of pre-eclampsia. Thus women may be classified as having significant proteinuria on the basis of a variety of tests Suzuki et al., (1987).

The substantial risk of pre-eclampsia to fetus include intrauterine growth restriction, death and prematurity where as the mother is at risk of seizures (eclampsia), renal failure, pulmonary edema, stroke, and death

Pre-eclampsia is a syndrome, which affects virtually all maternal organ systems Enquobahrie et al., (2004). Despite considerable research, the cause or causes of pre-eclampsia remain unclear and there are no clinically useful screening tests to identify women in whom it will develop (Caren et. al., (2004).

Most classification systems for the hypertensive disorders of pregnancy have repeatedly placed emphasis on the appearance and progression of proteinuria above a threshold of ≥300mg/24 hours to separate gestational hypertension from preeclampsia. This threshold therefore defines significant proteinuria. Although it is now accepted that proteinuria is not inevitable in preeclampsia it still remains a cardinal sign of the syndrome and one of the two features, along with hypertension that clinicians use to screen the pregnant population for early detection of the disease (Davison 1986). In pre-eclampsia the glomerular barrier is certainly altered and there is an increased excretion of protein including albumin. When total protein excreted (TPE) exceeds 1 g/24 hours, tubular protein reabsorption will be saturated and individual proteins excretion rates will be related to their molecular weights. The term selective proteinuria is used when large protein molecules are retained and non-selective proteinuria is used when the glomerular barrier looses this ability. The proteinuria of preeclampsia is considered to be non-selective (Davison 1986).

Proteinuria and clinical outcome

The incidence of proteinuria (and/or hypertension) arising in pregnancy varies according to the definition (Redman and Jefferies 1988) and to parity, age and underlying medical disease, (Dekker et al., 1995 and Garnr et al., 1990) but in most populations it will occur in more than 10% of pregnant women. Proteinuria can be caused by the pregnancy itself, or may exist from before conception (being unrelated to the pregnancy) (Redman and Jefferies 1988). However as pregnancy may be the first point of medical contact for many women, pre-existing proteinuria may be first diagnosed at this time (Dekker et al., 1995 and Garnr et al., 1990).

Some studies suggest a proportional link between the level of proteinuria and adverse clinical outcome. Page et al., (1976) in a prospective study of almost 13,000 pregnant women found that significant proteinuria, (defined as 2+ or more on dipstick analysis) was associated with an increase in stillbirth rates, fetal growth restriction and neonatal morbidity, when associated with hypertension. Other studies suggest that it is the presence of proteinuria rather than the severity, which is associated with poorer outcomes. There is evidence
that even the finding of trace proteinuria in pregnant women with hypertension is associated with an increase in adverse outcome (North et al., 1999). When screening for proteinuria, it has been suggested that a test should be associated with a low false negative rate (high sensitivity) to avoid missing significant proteinuria and hence pre-eclampsia (Halligan et al., 1999). There has always been controversy over the difficulty of interpreting trace proteinuria. Lowering the threshold for dipstick proteinuria to trace or 15 mg/dl may improve detection and reduce false negative rates.

2.7: Female sex hormones

The endogenous female sex hormones have significant effect on serum lipids Patrizia et al. (1999). In the late phase of pregnancy, estrogen decreases the production of VLDDs and decreases maternal lipolytic activity Karl et.al. (2003). Together with the increased expression of the VLDL/apoE receptors in the placenta Wittmaack et.al, (1995), this may result in a coordinated rerouting of TG-rich lipoproteins from the mother toward the fetoplacental unit to meet the nutritional demands of the growing fetus Winkler et.al, (2000). However, in PE constrained fetal utilization of nutrients may result in chronic fetal distress and growth retardation. Therefore, during gestation, the effect of estrogen in enhancing very low density lipoprotein (VLDL) production and decreasing hepatic lipase activity plays a key role in the accumulation of triglycerides in lipoproteins of density higher Alvarez et.al, (1996).

Estrogen increases vasodilatation and inhibits the response of blood vessels to injury and the development of atherosclerosis. Estrogen-induced vasodilatation occurs 5 to 20 minutes after estrogen has been administered and is not dependent on changes in gene expression; this action of estrogen is sometimes referred to as nongenomic. The estrogen-induced inhibition of the response to vascular injury and the preventive effect of estrogen against atherosclerosis occur over a period of hours or days after estrogen treatment and are dependent on changes in gene expression in the vascular tissues Register et al., (1998).

Estrogen alters serum lipid concentrations, coagulation and fibrinolytic systems, antioxidant systems, and the production of other vasoactive molecules, such as nitric oxide and prostaglandins, all of which can influence the development of vascular disease. Estrogen has both rapid and longer-term effects on the blood-vessel wall. The mechanisms that mediate the rapid effects of estrogen are not fully understood. Current data suggest that estrogen influences the bioavailability of endothelial-derived nitric oxide and, through nitric oxidemediated increases in cyclic guanosine monophosphate, causes the relaxation of vascular smooth-muscle cells. The longer-term effects of estrogen, about which more is known, are due at least in part to changes in vascular-cell gene and protein expression that are mediated by estrogen receptor a, b, or both. Estrogen-regulated proteins influence vascular function in an autocrine or paracrine fashion Register et al., (1998). However, additional vascular target genes regulated by estrogen receptors need to be identified Barret-Connor (1997).

2.8: Nitric Oxide and pre-eclampsia

Substantial evidence indicates that Nitric oxide (NO) production is elevated in normal pregnancy Sladek et al., (1997). Plasma and urinary levels of cGMP, the second messenger of NO, increase during pregnancy Sladek et al., (1997). Marked increases in 24-hour urinary nitrate/nitrite excretion have also been reported during pregnancy Sladek et al., (1997). Increases in NO production appear to play an important role in the renal vasodilatation of pregnancy Sladek et al., (1997). Recent studies by Conrad and others Sladek et al., (1997) clearly demonstrated that the renal vasodilatation in the pregnant rat is due to an increased NO production. Because NO appears be an important physiological vasodilator in normal pregnancy, NO deficiency during preeclampsia might be involved in the disease process. Studies from several laboratories have found that chronic NO synthase inhibition in pregnant rats produces a hypertension associated with peripheral and renal vasoconstriction, proteinuria, intrauterine growth retardation, and increased fetal morbidity, a pattern that closely resembles the symptoms of human pregnancy-induced hypertension Conrad (1990). However, whether there is a reduction in NO production during pregnancy-induced hypertension is unclear. Much of the uncertainty originates from the difficulty in directly assessing the activity of the NO system in a clinical setting Chronic reductions in uterine perfusion pressure in pregnant rats resulted in increases in arterial pressure and decreases in renal plasma flow and glomerular filtration rate, but no difference in urinary nitrate/nitrate excretion relative to control pregnant rats Alexander et al., (1999).

Homocysteine Concentrations in Pre-eclampsia

Homocysteine is an essential amino acid required for the growth of cells and tissues in the human body. Maternal hyperhomocysteinemia is associated with a number of placenta-mediated diseases such as preeclampsia (Mignini et al., 2005). Homocysteine concentrations are slightly increased in normotensive pregnancies that later develop preeclampsia and are
considerably increased once preeclampsia is established. However, because of a lack of consistency in data, dose-response relationship, and biologic plausibility, the observed association cannot be considered causal from the current literature (Ingec et al., 2005).

2.9: Body Mass Index and Preeclampsia
Women categorized as obese by BMI measurement during the first trimester of pregnancy have decreased endothelium-dependent and endothelium-independent vasodilation at each trimester as compared to lean women, although both groups showed improvement throughout the pregnancy. At four months postpartum, the improved endothelium-dependent vasodilation persisted in the lean women, but not in the obese women. Stewart et al., (2007) In addition to confirming the reduction in endothelium-dependent and independent vasodilation, a study by Ramsay et al reported that elevated BMI in early pregnancy is associated with increased systolic blood pressure, triglyceride concentration, insulin levels and lower HDL, although LDL and glycosylated hemoglobin were found to be similar Ramsay et al., (2002).

Elevated BMI early in pregnancy has been repeatedly shown to be associated with increased risk of preeclampsia Sahu et al., (2007), Bhattacharya et al (2007), Leeners et al., (2006), Ramos et al., (2005), Kabiru et al.,(2004).

Excessive weight gain during pregnancy is associated with increased risk of preeclampsia in women who are overweight at their first prenatal visit, but not in those who are of normal weight. Kabiru et al.,(2004) similarly a weight gain of at least 2 pounds per week has been found to significantly associated with developing preeclampsia Sibai et al., (1997). Although one study has shown that early gestational BMI had a similar predictive capacity to prepregnancy BMI Wendland et al., (2007).

A number of studies have investigated BMI before pregnancy. Although there have been some studies that did not find an association between prepregnancy BMI and Preeclampsia, (Thadhani et al., 1999) these have been in the minority this is most likely because prepregnancy BMI and elevated blood pressure are on the same causal pathway and BMI measured, for example, in the second trimester represents a combination of whatever BMI the woman entered pregnancy with and her weight gain and fluid retention during the pregnancy. This does not give enough information to sort out whether it is prepregnancy BMI or intra-pregnancy weight gain that is important. Additionally, since preeclampsia can be associated with edema, one might get a false association between elevated intra-partum BMI and preeclampsia simply due to the fluid retention. Sahu et al., (2007), The association between elevated prepregnancy BMI and preeclampsia has been widely and consistently reported, Magnussen et al.,(2007), Doherty et al., (2007), Abenhaim et al.,(2007), Forest et al., (2005) , Baeten et al.,(2001), Thadhani et al.,(1999), Barden et al., 1999, and Eskenazi et al.,(1991) and remains significant even after adjustment for weight gain during pregnancy Murakami et al., (2005) Unfortunately, some of these results may be confounded by a higher prevalence of Prepregnancy chronic hypertension in the obese group Doherty et al., (2007). Prepregnancy BMI has been associated with elevated blood pressure during pregnancy Miller et al., (2007).

A systematic review concluded that the risk of preeclampsia doubled with each 5-7 kg/m2 increase in prepregnancy BMI Miller et al., (2007), and data from Bodnar et al., (2005) demonstrate that the risk of preeclampsia increases even within the standard BMI categories Bodnar et al., (2005). Elevated prepregnancy BMI Forest et al., (2007, Magnussen et al., (2007, Doherty et al., (2007), Abenhaim et al., (2007) and Thadhani et al., (1999) and increased weight gain during Pregnancy Saftlas et al., (2000) have also been associated with increased risk of gestational hypertension.

Girouard et al., (2007) report an increased weight gain in adulthood, before the first pregnancy, in women who go on to develop HDP as compared to the control group, Girouard et al., (2007) again suggesting an underlying metabolic predisposition that predates the pregnancy.

Family history of cardiovascular disease has been shown to be associated with increased risk of developing pre-eclampsia Magnussen et al., (2007) and Ness et al., (2003) and gestational hypertension, Ness et al., (2003) although confidence intervals are close to the null Ness et al., (2003). Another study by Rose et al., (2005) examining risk factors for severe pre-eclampsia found no association with family history of cardiovascular disease, but did find an association with familial hypertension and hypercholesterolemia Rose et al., (2005).

Paternal history of early myocardial infarction also strongly predicted severe pre-eclampsia, family history of type 2diabetes has also been shown to increase the risk of preeclampsia Magnussen et al., (2007) and Qiu et al., (2003). Beyond family history, other maternal cardiovascular risk factors have been found to be associated with increased risk of pre-eclampsia. Prepregnancy blood pressure has been shown to have a linear, positive correlation with preeclampsia Magnussen et al., (2007). Elevated prepregnancy total cholesterol and low density lipoprotein (LDL) have also
been associated with increased risk of preeclampsia, although unfortunately the study measured levels in the non-fasting state Magnussen et al., (2007).

A study by Duckitt et al., (2005) examining self-reported elevated cholesterol and found that a history of elevated cholesterol was associated with increased risk of preeclampsia, but not gestational hypertension Thadhani et al., (1999). Prepregnancy diabetes also increases the risk of preeclampsia Duckitt et al., (2005).

2.2.1: Diet and Nutrition in Preeclampsia

Various hypotheses have been put forward to link pre-eclampsia with specific dietary deficiencies, either before or during pregnancy. For example, calcium and fish oil supplementation were suggested based on observations of an association between dietary intake and the incidence of pre-eclampsia in various communities. Zinc Mahomed (2008) Atallah et al., (2004) and magnesium supplements were suggested as interventions that might optimise normal physiological function during pregnancy Makrides (2008). Antioxidants such as vitamin C and E, selenium and garlic have been suggested to counteract oxidative stress. Folic acid may correct raised blood levels of homocysteine Makrides (2008). Certain dietary factors have been linked to pre-eclampsia. For example, Mayan Indians in Guatemala, who traditionally soak their corn in lime before cooking, have a high calcium intake and a low incidence of pre-eclampsia and eclampsia. This led to the hypothesis that an increase in calcium intake during pregnancy might reduce the incidence of pre-eclampsia among women with low calcium intake. Similarly, the observation that Greenland Inuits who eat a lot of oily fish have a low incidence of pre-eclampsia provided the basis for the hypothesis that fish oil might prevent this condition Dyerber at al., (1985). Other dietary factors that have been suggested to have a role in preventing pre-eclampsia include magnesium, zinc, selenium, antioxidants such as vitamin C and E, folic acid, garlic and rhubarb Dyerber at al., (1985).

Diet is an important issue in maternal health, since optimal fetal development requires adequate nutrients. Maternal malnutrition during the prenatal period has been associated with spontaneous abortion, poor growth and development, learning impairment and behaviour problems of the offspring Kramer (2000), Laurence et al.,(1980). Some nutrient deficiencies can be dealt with by strengthening the training and practice of antenatal care providers, enabling them to dispense supplementation, such as iron, calcium and vitamin tablets. Understanding the dietary patterns of pregnant women and the associated factors leads to proper planning of nutrition education programs.

The demand for both energy and nutrients is increased during pregnancy Picciano (1996). For well-nourished women, only a small amount of additional energy is required because the body adapts to the increased energy requirements and becomes more energy efficient through reduced physical activity and a lowered metabolic rate. Although the average-sized, well-nourished woman requires 10460 kJ/d (2000 kcal/d) during the last trimester of pregnancy (Hyttten 1983), many women in developing countries restrict their food intake during pregnancy to have smaller infants, on the premise that smaller infants will carry a lower risk of delivery complications (Brems et al., 1988). Recent evidence suggests, however, that infants who are small or disproportionate at birth have increased health risks later in life Godfrey (1998), Barker a & b.

The single most important thing that a pregnant woman need for her baby is to eat a healthy, well-balanced diet. A well-balanced diet is one that includes foods from all food groups in appropriate amounts, so as to ensure proper nutrition. Proper nutrition ensures that all essential nutrients (carbohydrates, fats, protein, vitamins, minerals and water) are supplied to the body to maintain optimal health and well-being. Good nutrition is essential for normal organ development and functioning; normal reproduction, growth and maintenance; for optimum activity level and working efficiency; for resistance to infection and disease; and for the ability to repair bodily damage or injury. While pregnancy is a normal alternative condition for the female body, it is stressful, and all nutritional needs are increased in order to meet the needs of the pregnancy Amy (1995).

A study conducted at Harvard University found that by eating at least 75 grams of protein per day, pregnant women could prevent diseases of pregnancy such as pre-eclampsia. During pregnancy a woman's blood volume increases as much as 40 to 60 percent, and in order to reach this necessary level and maintain it, a woman's body needs adequate protein, salt, calcium, potassium and water from her diet.

Management of Pre-eclampsia

Efforts to prevent pre-eclampsia have been disappointing (Sibai 1998). To date, a systematic review of 14 trials using low-dose aspirin (60-150 mg/d) in women with risk factors for pre-eclampsia concluded that aspirin reduced the risk of pre-eclampsia (OR 0.86, 95% CI, 0.76-0.96) along with perinatal death, but did not significantly affect birth weight or the risk of abruption (Coomarasamy et al., 2003). Low-dose aspirin in unselected nulliparous women seems to reduce the incidence only slightly.
Rest and exercise are known to affect hypertension.

**Life style choices**

Rest and exercise are known to affect hypertension. Whether changes in a woman’s level of activity during pregnancy influences her risk of pre-eclampsia is less clear. For normotensive high risk women, two small trials of uncertain quality suggest that rest, for up to four hours a day at home, may reduce the risk of pre-eclampsia. For those with hypertension, it is unclear whether rest in hospital offers any advantage over normal activity. Taking more exercise may reduce the risk of pre-eclampsia, although again data are sparse. As none of this evidence is strong, the balance between rest and exercise should depend on each woman’s personal preference (Lelia et al., 2006).

**Recurrence**

In general, the recurrence risk of pre-eclampsia in a woman whose previous pregnancy was complicated by pre-eclampsia near term is approximately 10% (Chesley 1978). If a woman had severe pre-eclampsia (including HELLP syndrome and/or eclampsia), she has 20% risk of developing pre-eclampsia sometime in her subsequent pregnancy (Chames et al., 2003; Sibai et al., 1995, Sullivan et al., 1994, Sibai et al., 1992, Adelusi and Ojengbede 1986 and Lopez-Llera et al., 1974).

**Seizure Prophylaxis**

Magnesium sulfate is the drug of choice for seizure prophylaxis in women with pre-eclampsia. Although the precise mechanism of its anti seizure activity is unknown, several randomized studies showed that magnesium sulfate is better than benzodiazepam or phenytoin in preventing the onset of initial eclamptic seizures and recurring seizures (Sibai 2004).

Therapy is started at the beginning of labor or prior to cesarean section and continued 24 hours postpartum in most cases. The duration of postpartum therapy may be modified depending on the severity of the disease. Treatment is started by administering an intravenous (IV) loading dose of 4-6 g magnesium sulfate, followed by a maintenance dose of 1-3 g/h. Proposed mechanisms of action of magnesium sulfate therapy are prevention of calcium ion transport, cerebral blood vessel dilatation, and prevention of platelet aggregations (Sibai 2004, 1998).

Patients receiving magnesium sulfate should be monitored carefully for signs and symptoms of magnesium toxicity. Magnesium toxicity manifests initially as loss of patellar reflexes and shortness of breath. Therefore, the patellar reflexes must be checked every 4 hours and oxygen saturation and respiratory rate must be monitored. As magnesium sulfate is excreted by the kidney, urine output should be monitored closely and should be at least 30 mL/h. If magnesium toxicity is suspected, a blood test for magnesium level should be performed. Most practitioners feel comfortable with a level below 9.0 mg/dL. However, patients have been reported to show
signs of toxicity below 6.0 mg/dL. Therefore, clinical evaluation of the patient should continue even if the serum magnesium level is below 9.0 mg/dL (Sibai 2004, Witlin and Sibai 1998).

Magnesium sulfate therapy for seizure prophylaxis should be administered to all women with severe pre eclampsia during induction or labor. However, prophylaxis for mild pre eclampsia is controversial. ACOG recommends magnesium sulfate in severe pre-eclampsia. However, ACOG has not recommended magnesium sulfate therapy in all cases of mild pre-eclampsia. Some practitioners withhold magnesium sulfate if blood pressure is stable and/or mildly elevated and if the laboratory values for liver function tests and platelets are mildly abnormal and/or stable. Others feel that even patients with gestational hypertension should receive magnesium, since a small percentage of these patients may either have or develop pre-eclampsia. The ultimate decision should depend on the comfort level of the labor and delivery staff in administering IV magnesium sulfate. An estimated 100 patients need to be treated with magnesium sulfate therapy to prevent one case of eclampsia (Sibai 2004, Witlin and Sibai 1998).

Plasma volume expansion:
Some women with severe pre-eclampsia have a restricted circulating plasma volume and are hemoconcentrated. This has led to the recommendation that plasma volume should be expanded with either colloid or crystalloid solutions, in an effort to improve maternal systemic and uteroplacental circulation. However, intravascular volume expansion carries a serious risk of volume overload, which may lead to pulmonary or cerebral edema. Also, large volume expansion often requires invasive monitoring of intravascular pressure, procedures carrying risks of their own (Bolte et al., 2001 and Dekker and Sibai 1998).

Materials and Method

This study was carried out in Primary Health Care Centers (PHC) in Funtua Katsina State, Mubi Adamawa State and Monguno Borno State. Some of the pre-eclamptic women were on admission in the PHC while other were selected during the antenatal clinics of the same PHC. The non pregnant non hypertensive were recruited from the relatives of some patient in the PHC and people within the vicinity of the center, and some of the staffs at the PHC volunteer to participate. The pregnant non hypertensive were recruited during antenatal clinics. The states were selected due high rates of maternal mortality FMOH (2008).

Settings
Munguno Local Government Area of Borno State has an area of about 7,000 square kilometers with a population of 375,023 Report of census 2006. Out of this 206,263 (55%) are women. Women aged 15-49 years (reproductive age) are 131,258 (35% of the total population). The ethnic groups in the local government are: Kanuri, Shuwa Arab, Gamargu, Fulani and Hausa, Report of census 2006. The local government has one general hospital at the local government headquarters, which is being manned by the Borno State Hospitals Management Board, 28 Primary Health Care centers and 18 dispensaries. Source: Monguno Local Government Health Statistics Office).

Mubi North LGA of Adamawa State has a population of 225, 705, Report of census 2006. 46% (103,824) are women. Women aged 15-49 years (Reproductive age) are 58,683 (26% of the total population). The ethnic groups in the local government are Fali, Gude, Fulani and Hausa Report of Census 2006.

The local Government has one general hospital at the local government Headquarters, which is being manned by Adamawa state Hospitals Management Board, 31 Primary health Care centers and 42 dispensaries. Statistic Unit of the Adamawa state Ministry of Health Yola 2008.

Funtua Local Government Area of Katsina State become a Local Government in 1967, with a total population of 225,571, out of this 47% (106,868) of the total population are women. Women aged 15-49 years (reproductive age) are 72,182 (32% of the total Population) Report of census 2006. The inhabitants of the Local Government are predominantly Hausa and Fulani by tribe. Their main occupation is farming and Animal rearing Funtua LGA official website and Report of Census 2006.

The Local Government has one General Hospital located at the LGA headquarters, which being managed by the Katsina State Health Service management Board in collaboration with the Ministry of Health, 28 Primary health care Centers, 72 dispensaries, Sources Funtua Local Government Health Department.

Ethical approval was obtained from Ahmadu Bello University Teaching Hospital Shika, Zaria Ethical Committee, and the PHC management. Informed verbal and written consent have been obtained from the subjects and their relatives.

A total 199 subjects were recruited for the study between April to September 2010, each group contain equal number of respondents from the state. Adamawa has 22 subjects in each group, Katsina 29
and Borno 34. Group A for each state has non-pregnant non hypertensive women; Group B for each state has women having normal pregnancy without hypertension; Group C for each state has Pregnant Hypertensive women with pre-eclampsia.

3.1: Exclusion Criteria
All maternal abnormally in pregnancies except pre-eclampsia were excluded.

Blood sample collection.
Blood sample was obtained in the morning by puncture of the antecubital vein as describe by Francois and Sandra 2009, Fuchs and Schiller 2009. The following parameters were tested: Lipid profile, Packed Cell volume (PCV), Hemoglobin and Platelets counts.

3.2: Blood pressure Measurement
Blood pressure was measured in a sitting position with sphygmonanometer after at least 10 minutes of rest. Systolic blood pressure was recorded at the appearance of sounds, and diastolic blood pressure was recorded at disappearance of fifth-phase korotkoff. Wichman el al., (1984). Cuff size was usually 12x22cm and measurement was repeated after 30 minutes for 12 hours the average of the measurement was used in the analysis Duley (1992).

3.3: Body Mass Index Measurement
Height was measured by Seca Anthropometer and weight by Omron weighing scale. Body Mass Index (BMI) was calculated from the formula BMI= weight in Kg divided by square of height in meter, percentage fat and fat mass was measured using Omron Body Fat Analyzer Model HBF-301 which is a hand-held device that reports body fat percentage in just seven seconds. Tasks 3 through 5 were read verbatim from the instruction manual. Task #1: the device is turn on, Task #2: the device is program. (This involved four steps): a). Input height, b). Input weight, c). Set age, d). Confirm gender.

Task #3: participants were asked to put their middle finger around the electrode grooves. With their thumb and index finger, securely grasp the upper portion of the electrode, then their ring and little fingers wrap around the lower portion of the electrode then press their palms firmly against the electrodes. Task #4: Stand with your feet shoulder width apart and arms straight out in front of you at a 90 degree angle. Task #5: Start the device, after seven seconds fat mass, percentage fat and BMI appears on the screen of the device (Rosenthal et al., 1994).

3.4: Lipid analysis
For Determination of serum total cholesterol venous blood sample was obtained using 5mls syringes after over night fasting and stored in non EDTA containers before analyzing for total cholesterol, triglycerides, HDL-C, and LDL-C using Cholesterol Quantization Kit. For Determination of serum total cholesterol, Chemistry assays were performed by automated analyzer utilizing Cholesterol analyzing kits according to manufacturer's instructions GLAXO ITC 234122 Model 2009. Instrument set-up, run procedures, and maintenance policies were strictly adhered to according to the manufacturer's instructions. Triglyceride level was measured after hydrolysis by lipoprotein lipase by assay of released glycerol, and the inter-assay CV was 5.3% Sullivan et al., (1985). HDL-cholesterol was measured using dextran sulfate (50,000 MW) and magnesium chloride, and the inter-assay CV was 2.5 % Warnick et al., (1988). LDL-C was calculated according to the method of Friedewald (2001). After extrapolation of VLDL-C from the fasting triglyceride divided by five, then: LDL  C = Total cholesterol (VLDL  C + HDL  C).

Packed Cell Volume
The packed cell volume (PCV) was determined using the micro-hematocrit method by centrifuging heparinized blood in a capillary tube at 10,000 RPM for five minutes. This separates the blood into layers and the result is read using the Hematocrit reader.

Hemoglobin
The hemoglobin was measure using photometer; the blood sample was diluted to a ratio of 1:250. The dilution is made by accurately taking a tiny sample of the blood into a pipette and delivering it into a container containing an agent which dissolves the red blood cells, and cyanide, which converts the hemoglobin to a more easily measurable form. This mixture, after standing for three to ten minutes, is then placed in a photometer where the light attenuation at 560 nm (green) is compared to that of standard solutions. From these comparisons, the concentration of hemoglobin was calculated.

Platelets Count
Blood samples were taken by antecubital venipuncture into Becton Dickinson(tm) Vacutainer tubes (Becton Dickinson, Rutherford, NJ, USA) containing tripotassium EDTA. All samples were analyzed on a Coulter Counter model JT2T (Coulter Electronics Ltd, Luton, UK) two to six hours after collection, to minimize changes in platelet size.5-7 Strict quality control procedures were adopted; tri-level controls and external quality assurance programmed were used on a regular basis to ensure the accuracy and precision of the instrument.

3.5: Urinalysis
Mid Stream Early morning urine was collected from all subjects for analysis, all women were carefully instructed regarding the procedure of urine collection in the specimen bottles. The urinalysis was carried out
using dipstick, to determine Protein and Glucose (McPherson et al., 2006), the results were recorded based on the color change as describe by reference list from Uppsala University Hospital 2008.

3.6: Statistical analysis

Data were expressed as SEM, descriptive statistics was use to analyze the questionnaire. Student t-test and Scheffe Post Hoc Test was conducted to analyse the significant difference between mean values, using SPSS version 16.0 at p

Results

Table 1: Shows the demographic and clinical characteristics of Non pregnant non Hypertensive, Pregnant non Hypertensive and Pre-eclamptic women respectively, the mean age among the three groups is 25.18±0.86 in Non Pregnant non hypertensive, 24.52±0.53 in pregnant non hypertensive and 24.03±0.65 ANOVA and Scheffe Post Hoc test showed that there were no significant difference among the three age groups, the only significant difference were the age at marriage with the preeclamptic group having a mean age of 18.23±0.21 at p

Systolic and diastolic blood pressure BP mmHg were significantly different at P

The SEM of the HDL-Cholesterol is 1.00±0.33 in the pre-eclamptic group is significantly different from that of the Non pregnant non hypertensive which has 3.22±0.16 and pregnant Non hypertensive 3.38±0.21 (P

Table 3 shows Pearson correlation coefficients of BP, BMI, Weight, age, triglyceride, high density lipoprotein, parity and history of BP in pregnancy among pre-eclamptic group. There is positive correlation of 0.471 between systolic and diastolic BP which is significant at r=0.01, while positive correlation also exist between BMI, height, weight and systolic BP. There is also negative correlation between age and triglyceride but it is not significant triglyceride correlates positively and significantly with systolic and diastolic BP respectively while age correlate positively and significantly with parity and history of BP during pregnancy, but there is negative correlations between parity diastolic BP and weight but it is not significant, proteinuria was between 2+ and 3+ on dipstick testing, and platelet counts were significantly decreased in pre-eclamptic women.

Table 4 shows correlation of socio-cultural background of pre-eclamptic women, where positive and significant correlation at 0.01 exists between ages, age at first marriage likewise there is correlation at 0.05 between age and number of wife. Age at first marriage, age, parity, history of hypertension and number of wives are negatively correlated with significant level of 0.01 and 0.05.

Discussion

There are few studies conducted in subjects with lower socio-economic background and lower age range in regards to pre-eclampsia. This study compared socio-cultural factors and lipid alteration in respect to severity or occurrence of pre-eclampsia, demographic characteristics of the cases were similar which shows high value of triglyceride serum cholesterol and low value of high density lipoprotein. There were no difference between the three groups in respect to age, gravid, parity and gestational age the mean systolic and diastolic blood pressures was in agreement with other studies Malik et al., (1995) and Prineas et al., (1980), The BMI is consistently related to fat mass and % fat in all the three groups with no significant difference. BMI has been proposed as useful indicators of metabolic aberration, however, studies by Grundy et al., (2004) have found evidence of the metabolic syndrome, consisting of abdominal obesity, elevated triglycerides, decreased HDL cholesterol, elevated blood pressure in pre-eclamptic women which was also similar to the finding of this study. In a large study from Finland by Pouta et al., (2004) found that women with pre-eclampsia were found to have increased waist circumference, waist/hip ratio, and BMI and serum insulin levels compared to those with normotensive pregnancies, even when examined at the relatively young age of 31. This study also finds differences in lipid parameters among the study groups.

In this study, total cholesterol and low-density lipoprotein (LDL) were similar between pregnant groups, but high-density lipoprotein (HDL) values were higher for the pre-eclamptic, and triglycerides were higher. Importantly, these women were also relatively young (SEM of 24.03±0.65) Pre-eclampsia is characteristically associated with hypertriglycerideremia Increased levels of triglycerides with reduced high density lipoprotein -cholesterol have been observed in this study, consistent with findings elsewhere studies on pre-eclamptic women Ray et al., (2006) Enquobahrie et al., (2005) and Gractacose et al., (2003), Hypertriglycerideremia is probably a consequence of competition between chylomicrons and very low-density lipoprotein cholesterol for the lipoprotein lipase Enquobahrie et al., (2005). Dietary fats, including cholesterol, are absorbed from the small
intestines and transported into the liver by lipoproteins called chylomicrons. Chylomicrons are large droplets of lipids with a thin shell of phospholipids, cholesterol, and protein. Once chylomicrons enter the bloodstream, an enzyme called lipoprotein lipase breaks down the triglycerides into fatty acid and glycerol. After a 12- to 14-hour fast, chylomicrons are absent from the bloodstream. Thus, individuals who are having a lipid profile done should fast overnight to ensure that chylomicrons have been cleared National Cholesterol Education Program (2001) and Birtcher et al., (2000).

The liver removes the chylomicron fragments, and the cholesterol is repackaged for transport in the blood in very low-density lipoproteins (VLDLs), which eventually turn into low-density lipoproteins (LDL). LDL cholesterol (LDL-C) the "bad cholesterol" consists mainly of cholesterol. Most LDL particles are absorbed from the bloodstream by receptor cells in the liver. Cholesterol is then transported throughout the cells. Diets high in saturated fats and cholesterol decrease the uptake of LDL particles by the liver. LDL particles are also removed from the bloodstream by scavenger cells, or macrophages, which are white blood cells that bury themselves in blood vessels such as arteries. Scavenger cells prevent cholesterol from reentering the bloodstream, but they deposit the cholesterol in the inner walls of blood vessels, eventually leading to the development of plaque National Cholesterol Education Program (2001) and Birtcher et al., (2000).

High-density lipoproteins (HDLs) are a separate group of lipoproteins that contain more protein and less cholesterol than LDL. HDL cholesterol (HDL-C) is also called "good cholesterol." HDL is produced primarily in the liver and intestine, and it travels in the bloodstream, picks up cholesterol, and gives the cholesterol to other lipoproteins for transport back to the liver National Cholesterol Education Program (2001) and Birtcher et al., (2000).

Classically, chylomicron clearance occurs in two sequential steps: (1) triglycerides hydrolysis by lipoprotein lipase, (2) uptake of the remnant by the liver. Delay in the second step leads to accumulation of remnants in plasma and is generally thought to represent the atherogenic risk of hypertriglyceridermia. There is considerable variation in the measurement of total protein in urine, most probably a consequence of differences in the analytical specificities of the methods as well as variation in the calibration of the methods. This may have contributed to the variation in the diagnostic performance among the studies, significant proteinuria of 150mg-180mg/24hrs urine has been established in the preeclamptic group of this study which is similar to finding of Nisell et al., (1995), Lindheir et al., (1986) and Davison (1986) who reported 300mg/24hrs of protein in urine of preeclamptic women, while Waugh et al., (2003) between 150mg/24hrs-200mg/24hrs and Higby et al., (1995) who recorded between 120mg/24hrs-200mg/24hrs. The mean platelets count is significantly low when compared to pregnant non hypertensive and non pregnant non hypertensive groups this study observe severity of preeclampsia and decrease of platelets counts like wise women with low platelets counts in the group have higher value of triglyceride, higher diastolic and the pathological edema is seen and pre-eclampsia is associated with deficient intravascular production of prostacyclin, a vasodilator, and excessive production of thromboxane, a platelet-derived vasoconstrictor and stimulant of platelets these lead to decrease in platelets count among the preeclamptic group and is consistent with findings of Yaprap et al., (2007), Duley et al., (2004) and Jaremo et al., (2000) who all found that platelet count were significantly low in severe pre-eclampsia groups. This result proposes a possible relationship between the platelet count and the severity of preeclampsia.

It is known that, iron preparations are widely used during pregnancy and this can influence the hemoglobin values, the hemoglobin values in this study were significantly different between the groups with the non pregnant and pregnant non hypertensive having higher values than the pre-eclamptic groups though not all the pregnant and the pre-eclamptic groups in this study attends regular ANC visits the idea about the iron usage during the pregnancy is not known, but the finding differs with Yaprap et al., (2007) who found no significant difference in the hemoglobin values between the pre-eclamptic and non pre-eclamptic women.

Studies evaluating the correlation between the severity of preeclampsia and socio-cultural background in rural areas of Northern Nigeria are scanty as most of the studies were carried out in urban centers and studied the influence of early marriage, educational background, antenatal care (ANC) and history of hypertension in pregnancy on pre-eclampsia this study however tries to correlate parity, age at first marriage, history of hypertension. This study find a significant correlation between education and income generations activities as a risk factors in developing preeclampsia in rural areas because majority of the preeclamptic women have not attended any kind of school both western and Islamic, like wise those that lack any sources of income and totally depend on husband for medical bills. Family history of hypertension and preeclampsia which is a risk factor in developing preeclampsia has
been observed in these research as majority of preeclamptic women mention either one of their family members of being hypertensive or having preeclampsia in their course of life, there is an inheritance tendency for a female child to inherit these condition from maternal chromosomes as almost all the preeclamptic group mentioned mother having the history of either been hypertensive during her pregnancy or preeclamptic. Family history of hypertension reflects genetic and behavioral factors whereby women may be predisposed to an increased preeclampsia risk.

Conclusion and Recommendation for Research

Pre-eclampsia is common in rural areas of Northern Nigeria due to presence of high risk factors in the study areas, this can be explained by the presence of high maternal mortality in the three states respectively. Risk factors for pre-eclampsia among women leaving in rural areas of Northern Nigeria with the exception of increase BMI are not much different from those that have been reported in other studies, good control of chronic hypertension, and reduction of stressful conditions at home and in pregnancy could be steps towards the primary prevention of this disorder; this study also found that seclusion and polygamy are not risk factors for developing preeclampsia.

In spite of there diet in rural areas lipid alteration plays a role in pathophysiology of pre-eclampsia this can partly be explained by the hormonal variations during pregnancy which affect lipid metabolism, there exists a consistent positive association between elevated maternal Tryglyceride and the risk of pre-eclampsia, increased triglycerides play a part to decreases the HDL-cholesterol. HDL particles carry cholesterol from peripheral tissues to liver. Impaired transport of cholesterol from peripheral tissues to the target area of utilization may cause the decrease in HDL-cholesterol in serum. According to Pizaro et al., (1999) there is a direct correlation between adipose tissue lipoprotein lipase activity and plasma HDL cholesterol. This direct correlation may be responsible for low levels of HDL cholesterol. Hypertriglyceridermia, leading to low HDL cholesterol is due mainly to the actions of Cholesteryl Easter Transfer Protein (CETP).

In hypertriglyceridermia there is also a chance to have that larger triglyceride-enriched VLDL (very low density lipoproteins) particles, which do not increase in number therefore LDL number is not increased. In summary, the findings reported in this research suggest that the women who develop pre-eclampsia had disturbed lipid profile due to abnormal lipid metabolism. Increased triglycerides levels and delayed triglycerides clearance, decrease High density lipoprotein, severe proteinuria of greater than 500mg in 24hrs urine or 3+ using dipstick and high blood pressure are the reasons for the development of preeclampsia. Our findings may be relevant for understanding the pathophysiology of Pre-eclampsia and the future treatment by lipid modifying regimens of this life-threatening condition, for example, by drug therapy or lipoprotein apheresis, and may help in developing strategies for prevention and early diagnosis of pre-eclampsia.

There is need of conducting rigorously designed genetic studies of adequate size to provide precise genetic risks with narrow confidence intervals, if over reporting of false-positive results are to be avoided. In efforts to identify women with at risk of developing pre-eclampsia during pregnancy, a question about family history of pre-eclampsia should be included during antenatal clinics.

Rigorous evaluation is required of tests with modest cost whose initial assessments suggest that they may have high levels of both sensitivity and specificity, there is a need for systematic reviews to map the aetiopathogenesis of pre-eclampsia in order to better develop new tests and treatments.

Screening and early detection are key given that there are no known cures for preeclampsia, and the only treatment available to date is to deliver the baby and placenta at any stage of gestation at which the disease is diagnosed.

Similarly, there is a need for systematic reviews to evaluate prognostic/predictive features that are associated with maternal and fetal complications once pre-eclampsia has started; there is a need for investigation whether lifestyle interventions such as rest at home and exercise are actually effective in reducing pre-eclampsia.

References


55. Jaremo P., Lindahl TL., Lennmarken C., Forsgren V.95no5 P.757.


86. Pirzado, Z.A., Sangi, S.A., Malik, R. (1999). High density lipoprotein cholesterol (HDL) metabolism and...
Illustrations

Illustration 1

Tables

Table 1: Demographic and Clinical Characteristics of Non pregnant non Hypertensive, Pregnant non Hypertensive and Pre-eclamptic women

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Non Pregnant Non Hypertensive N=50</th>
<th>Pregnant Non Hypertensive N=50</th>
<th>Non Pre-eclamptic N=50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>25.18±0.86</td>
<td>24.52±0.53</td>
<td>24.03±0.65</td>
</tr>
<tr>
<td>Age at Marriage</td>
<td>22.21±0.34</td>
<td>23.19±0.23</td>
<td>18.23±0.21**</td>
</tr>
<tr>
<td>Primigravida</td>
<td>23</td>
<td>24</td>
<td>27</td>
</tr>
<tr>
<td>Multiparagvida</td>
<td>27</td>
<td>26</td>
<td>23</td>
</tr>
<tr>
<td>Gestation age (weeks)</td>
<td>NA</td>
<td>23.12±1.43</td>
<td>23.22±0.24</td>
</tr>
<tr>
<td>Systolic BP mmHg</td>
<td>116.70±0.98</td>
<td>116.40±0.73</td>
<td>167.60±2.75**</td>
</tr>
<tr>
<td>Diastolic BP mmHg</td>
<td>74.97±5.63</td>
<td>76.80±8.67</td>
<td>107.48±8.01**</td>
</tr>
<tr>
<td>Fat Mass</td>
<td>25.93±0.66</td>
<td>26.95±0.54</td>
<td>28.05±1.74*</td>
</tr>
<tr>
<td>% Fat</td>
<td>28.48±0.96</td>
<td>28.86±1.02</td>
<td>29.07±1.22</td>
</tr>
<tr>
<td>BMI</td>
<td>25.93±0.66</td>
<td>26.95±0.54</td>
<td>27.05±0.74*</td>
</tr>
</tbody>
</table>

P<0.05 *= indicate significant difference with Group A only
** = indicate significant different with group A& B

Note: the values are means of ±SEM F value of ANOVA and Scheffe post hoc test.
Table 2: Lipid profile, Urinalysis and Platelets Counts of Non pregnant non Hypertensive, Pregnant non Hypertensive and Pre-eclamptic Subjects

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Non Pregnant Non Hypertensive N=50</th>
<th>Pregnant Non Hypertensive N=50</th>
<th>Pre-eclamptic N=50</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL-Cholesterol (mmol/L)</td>
<td>3.22±0.16</td>
<td>3.38±0.21</td>
<td>1.00±0.33**</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>1.36±0.41</td>
<td>0.83±0.68</td>
<td>4.21±0.89*</td>
</tr>
<tr>
<td>LDL-Cholesterol (mmol/L)</td>
<td>2.73±0.25</td>
<td>2.72±0.34</td>
<td>3.02±0.69</td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>1.80±0.91</td>
<td>3.55±0.09</td>
<td>4.08±0.07*</td>
</tr>
<tr>
<td>Urine PH</td>
<td>6.32±0.03</td>
<td>6.76±0.06</td>
<td>9.32±0.06**</td>
</tr>
<tr>
<td>Glucose</td>
<td>165.3±0.60</td>
<td>175.6±0.70</td>
<td>1.81±2.15**</td>
</tr>
<tr>
<td>Specific Gravity (NR 1.01-1.030)</td>
<td>1.012±0.003</td>
<td>1.016±0.005</td>
<td>1.127±0.007**</td>
</tr>
<tr>
<td>Hemoglobin (NR 1.0-1.4g/dl)</td>
<td>1.190±0.001</td>
<td>1.196±0.001</td>
<td>1.345±0.001**</td>
</tr>
<tr>
<td>Protein</td>
<td>Trace</td>
<td>Trace</td>
<td>+2-+3</td>
</tr>
<tr>
<td>Platelets (NR 1.5-3.0 x 10^5 MM^3)</td>
<td>1.74±0.29 x 10^5</td>
<td>1.69±0.45x10^5</td>
<td>0.46±0.34x10^5**</td>
</tr>
</tbody>
</table>

P<0.05 *= indicate ** = indicate Significant Difference with Group A only significant different with group A& B

Note: the values are means of ±SEM F value of ANOVA and Scheffe post hoc test.
+=300mg/2hr Kuo et al., 1992
Table 3: Pearson correlations coefficient of Pre-eclamptic demographic and Clinical data, significance (2 tailed) N=50

<table>
<thead>
<tr>
<th>Variables</th>
<th>Age</th>
<th>Systolic BP</th>
<th>Diastolic BP</th>
<th>WT(Kg)</th>
<th>HT(M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP</td>
<td>1</td>
<td>-0.21</td>
<td>0.471**</td>
<td>0.105</td>
<td>-0.177</td>
</tr>
<tr>
<td>Diastolic</td>
<td>-0.021</td>
<td>1</td>
<td>0.471**</td>
<td>0.189</td>
<td>0.69</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.093</td>
<td>0.297*</td>
<td>0.074</td>
<td>0.773**</td>
<td>-0.678**</td>
</tr>
<tr>
<td>HDL</td>
<td>0.075</td>
<td>-0.188</td>
<td>-0.003</td>
<td>0.325*</td>
<td>-0.67</td>
</tr>
<tr>
<td>TRIG</td>
<td>-0.043</td>
<td>0.638**</td>
<td>0.431**</td>
<td>0.145</td>
<td>0.160</td>
</tr>
<tr>
<td>Parity</td>
<td>0.485**</td>
<td>0.116</td>
<td>-0.171</td>
<td>-0.173</td>
<td>0.17</td>
</tr>
<tr>
<td>History of BP</td>
<td>0.432**</td>
<td>0.254</td>
<td>0.221</td>
<td>0.223</td>
<td>0.76</td>
</tr>
</tbody>
</table>

** Correlation is significant at the level 0.01 level (2-tailed)
* Correlation is significant at the level 0.05 level (2-tailed)

Table 4: Pearson Correlation of Socio-Cultural Background of Pre-eclamptic women

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Age at 1st Marriage</th>
<th>Parity</th>
<th>HX of HTN</th>
<th>No of wives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.330**</td>
<td>0.495**</td>
<td>0.309*</td>
<td>0.244</td>
</tr>
<tr>
<td>Age at marriage</td>
<td>-0.289*</td>
<td>-0.287*</td>
<td>-0.287*</td>
<td>-0.352*</td>
</tr>
<tr>
<td>Parity</td>
<td>-0.289*</td>
<td>1</td>
<td>0.599**</td>
<td>-0.301*</td>
</tr>
</tbody>
</table>

** Correlation is significant at the 0.01 level (2-tailed)
* Correlation is significant at the 0.05 level (2-tailed)
**Table 5: Pearson Correlation of Socio-Cultural Background of Pre-eclamptic women**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Age at 1st Marriage</th>
<th>Parity</th>
<th>HX of HTN</th>
<th>No of wives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.330**</td>
<td>0.495**</td>
<td>0.309*</td>
<td>0.244</td>
</tr>
<tr>
<td>Age at 1st marriage</td>
<td>1</td>
<td>-0.289*</td>
<td>-0.287*</td>
<td>-0.352*</td>
</tr>
<tr>
<td>Parity</td>
<td>-0.289*</td>
<td>1</td>
<td>0.599**</td>
<td>-0.301*</td>
</tr>
</tbody>
</table>

**Correlation is significant at the 0.01 level (2-tailed)**

**Correlation is significant at 0.05 levels (2 tailed)**

**Table 6: History of BP in Pregnancy**

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
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</thead>
<tbody>
<tr>
<td>Non Pregnant</td>
<td>11</td>
<td>39</td>
</tr>
<tr>
<td>PREGNANT</td>
<td>17</td>
<td>33</td>
</tr>
<tr>
<td>PREECLAMPTIC</td>
<td>8</td>
<td>42</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
<td>114</td>
</tr>
<tr>
<td>%</td>
<td>24</td>
<td>76</td>
</tr>
</tbody>
</table>
Table 7: Family History of Hypertension, Diabetic and Kidney Diseases

<table>
<thead>
<tr>
<th></th>
<th>Non Hypertension</th>
<th>Diabetes</th>
<th>Kidney Disease</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Pregnant</td>
<td>23</td>
<td>6</td>
<td>6</td>
<td>50</td>
</tr>
<tr>
<td>PREGNANT</td>
<td>15</td>
<td>22</td>
<td>4</td>
<td>50</td>
</tr>
<tr>
<td>PRE-ECLAMPTIC</td>
<td>5</td>
<td>30</td>
<td>7</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>66</td>
<td>17</td>
<td>150</td>
</tr>
<tr>
<td>%</td>
<td>31</td>
<td>44</td>
<td>11</td>
<td>37</td>
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Table 8: Educational status

<table>
<thead>
<tr>
<th></th>
<th>Islamiyya</th>
<th>Primary</th>
<th>JSS</th>
<th>Secondary</th>
<th>Tertiary</th>
<th>Non</th>
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</thead>
<tbody>
<tr>
<td>Non Pregnant</td>
<td>6</td>
<td>1</td>
<td>3</td>
<td>13</td>
<td>7</td>
<td>21</td>
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<tr>
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<td>3</td>
<td>4</td>
<td>17</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>PRE-ECLAMPTIC</td>
<td>11</td>
<td>4</td>
<td>8</td>
<td>0</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>8</td>
<td>15</td>
<td>30</td>
<td>16</td>
<td>56</td>
</tr>
<tr>
<td>%</td>
<td>17</td>
<td>5</td>
<td>10</td>
<td>20</td>
<td>11</td>
<td>37</td>
</tr>
</tbody>
</table>
Table 9: Family History of Hypertension, Diabetic and Kidney Diseases

<table>
<thead>
<tr>
<th></th>
<th>Non Hypertension</th>
<th>Diabetes</th>
<th>Kidney Disease</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Pregnant</td>
<td>23</td>
<td>6</td>
<td>6</td>
<td>50</td>
</tr>
<tr>
<td>PREGNANT</td>
<td>15</td>
<td>4</td>
<td>6</td>
<td>50</td>
</tr>
<tr>
<td>PRE-ECLAMPTIC</td>
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<td>7</td>
<td>8</td>
<td>50</td>
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<tr>
<td>Total</td>
<td>47</td>
<td>17</td>
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<tr>
<td>%</td>
<td>31</td>
<td>11</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

Table 10: If yes who?

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Mother</th>
<th>Father</th>
<th>Relatives</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Pregnant</td>
<td>11</td>
<td>3</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>PREGNANT</td>
<td>14</td>
<td>5</td>
<td>3</td>
<td>22</td>
</tr>
<tr>
<td>PRE-ECLAMPTIC</td>
<td>19</td>
<td>6</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>14</td>
<td>10</td>
<td>66</td>
</tr>
<tr>
<td>%</td>
<td>66</td>
<td>20</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>
Table 11: History of Pre-eclampsia or Eclampsia among family members or relative

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Pregnant</td>
<td>14</td>
<td>36</td>
</tr>
<tr>
<td>PREGNANT</td>
<td>18</td>
<td>32</td>
</tr>
<tr>
<td>PRE-ECLAMPTIC</td>
<td>39</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>71</td>
<td>79</td>
</tr>
<tr>
<td>%</td>
<td>47</td>
<td>53</td>
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</table>

Table 12: Are you totally secluded?

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>Partially</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Pregnant</td>
<td>5</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>PREGNANT</td>
<td>8</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>PRE-ECLAMPTIC</td>
<td>7</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>114</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>13</td>
<td>76</td>
<td></td>
</tr>
</tbody>
</table>
### Table 13: what kind of Income Generating Activities (n=79)

<table>
<thead>
<tr>
<th></th>
<th>Home Trade</th>
<th>Civil Servants</th>
<th>Islamiyya Teacher</th>
<th>Market woman</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Pregnant</td>
<td>17</td>
<td>5</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>PREGNANT</td>
<td>6</td>
<td>8</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>PRE-ECLAMPTIC</td>
<td>7</td>
<td>5</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>18</td>
<td>18</td>
<td>13</td>
</tr>
<tr>
<td>%</td>
<td>39</td>
<td>22.</td>
<td>22</td>
<td>17</td>
</tr>
</tbody>
</table>

### Table 14: Do you totally depend on Husband for Hospital bills? N=150

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>Partially</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Pregnant</td>
<td>21</td>
<td>11</td>
<td>16</td>
</tr>
<tr>
<td>PREGNANT</td>
<td>19</td>
<td>23</td>
<td>10</td>
</tr>
<tr>
<td>PRE-ECLAMPTIC</td>
<td>36</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>76</td>
<td>42</td>
<td>32</td>
</tr>
<tr>
<td>%</td>
<td>51</td>
<td>28</td>
<td>21</td>
</tr>
</tbody>
</table>
Table 15: Are you from polygamous family? If yes which position do you occupy?

<table>
<thead>
<tr>
<th></th>
<th>1st wife</th>
<th>2nd wife</th>
<th>3rd wife</th>
<th>4th wife</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Pregnant</td>
<td>31</td>
<td>13</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>PREGNANT</td>
<td>33</td>
<td>10</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>PRE-ECLAMPTIC</td>
<td>43</td>
<td>6</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>107</td>
<td>29</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>%</td>
<td>71</td>
<td>19</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 16: Are you attending ANC?

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Pregnant</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>PREGNANT</td>
<td>46</td>
<td>4</td>
</tr>
<tr>
<td>PRE-ECLAMPTIC</td>
<td>15</td>
<td>35</td>
</tr>
<tr>
<td>Total</td>
<td>61</td>
<td>39</td>
</tr>
<tr>
<td>%</td>
<td>61</td>
<td>39</td>
</tr>
</tbody>
</table>
Illustration 2

Questionnaire

1. Age ()
2. Age at marriage ()
3. Parity ()
4. History of Hypertension in pregnancy: Yes / No
5. If yes how many times?
   - 1
   - 2
   - 3
   - <4
6. Educational Status
   - Islamiyya
   - JSS
   - Secondary
   - Tertiary
   - None
7. Do you have family history of any of the following diseased conditions?
   - Hypertension
   - Diabetes
   - Kidney disease

8. If yes who among your family members
   - Father
   - Mother
   - Grand mother

9. Can you remember if any of your close relatives ever developed Pre-eclampsia/Eclampsia during the course of her pregnancy?
   If yes who?
   - Mother
   - Aunties
   - Maternal Cousins Females
   - Paternal cousins

10. Are you totally secluded?
    - Yes
    - No
11. Do you have any income generating activities at home?
   - Yes
   - No

12. If yes, what kind of income generating activities do you do for yourself?
   - Market woman
   - Islamiyya teacher
   - Civil servants
   - Others

13. Do you totally depend on your husband for treatment of minor ailment?
   - Yes
   - No

14. Have you been attending antenatal clinics during the course of your pregnancy?
   - Yes
   - No
15. How many wives’ did your husband has?
   - You only
   - Two
   - Three
   - Four

16. Which position do you occupy?
   - First wife
   - Second wife
   - Third wife
   - Fourth wife
Illustration 3

Figures

Figure 1 shows the percentage history of BP during previous pregnancy among the three groups. 22% of the non-pregnant non-hypertensive, 34% of pregnant non-hypertensive, and 16% of the pre-eclamptic women had experienced hypertension during the previous pregnancy. Figure 2 shows the percentage of various tribes that participated in the research. Though only three tribes were captured, i.e., Hausa, Kanuri, and Fulani, in the pregnant group, 58% are Hausa, 20% and 28% are Kanuri and Fulani, respectively. In the pregnant non-hypertensive group, 52% are Hausa, 24% and 18% are Kanuri and Fulani, respectively. In the pre-eclamptic group, 22% are Hausa, 15% and 13% are Kanuri and Fulani. In the whole groups, Hausa accounts for 51%, followed by Kanuri 25% and Fulani 24% respectively.
Figure 2 shows the educational status of the groups. 56% of the respondents are not educated, the remainder 44% have attended ranges of education from Islamiyya 17%, Primary school up to Primary 6 5%, JSS up to JSS3 10%, Secondary up to SS3 20% and tertiary 11% among the pre-eclamptic group. The highest educational status was Islamiyya, while the pregnant non hypertensive has the highest number of tertiary and secondary schools. Figure 3 shows the history of Hypertension (HTN), Diabetes, and Kidney Disease among family members of the three groups. 45% of the respondents have a family history of hypertension, 35% diabetes, and 20% kidney disease, while 31% have neither. Among the pre-eclamptic group, 30% have a history of BP, 7% Diabetes, and 8% kidney diseases.

In Figure 4, the percentage of family and relatives who had one of the aforementioned diseases was observed. 44% say their mother is hypertensive, 14% their father, and 10% other relatives. In the pre-eclamptic group, 63% say their mother is hypertensive. In the pregnant non hypertensive group, 20% say father and 17% other relatives. In the non hypertensive non pregnant group, mothers have the highest percentage of 73%.
Fig: 4.3 History of HTN, DM and KID Diseases in family.
Fig 4.4 History of Hypertension in Family
The preeclamptic group has the highest percentage of family history of pre-eclampsia/eclampsia with a score of 55% followed by pregnant non hypertensive 25% and non pregnant non hypertensive 20% as shown in fig 4.5. There is no much difference among all the three groups regarding seclusion as 76% are not, 13% are secluded and 11% partially, even among the pre-eclamptic women only 7% were secluded and partially secluded the remaining 86% are not.
Fig: 4. 6 Seclusion

- Non-Pregnant
- PREGNANT
- PREECLAMPTIC

Activities

- Home Trade
- Civil Servants
- Islamiyya Teacher
- Market Woman
Fig: 4. 7 Income Generation Activities

The above figure shows the various income generation activities of the groups non pregnant non hypertensive has the highest percentage generally 39% have some kind of home trade, 22% are civil servants and Islamiyaa teachers and 17% are market women while the preeclamptic has the lowest percentage 23% home trade, 5% civil servants and Islamiyaa teachers the remaining are market women.
Figure 8 above shows the percentage of the groups based on paying hospital bills, the preeclamptic group has the highest percentage of 47% out of the total 76% that depends on husband for medical bills while 46% of the pregnant women do not depend on there husband for medical bills.
Fig: 4. 11 Pre-eclamptic group Age/Age of Marriage based on tribes
Fig: 4.12 Parity

- Non Pregnant Non Hypertensive
- Pregnant Non Hypertensive
- Preeclamptic

Groups

Percentage

- Primigravida
- Multigravida
Fig: 4.13 Gestation age (WKS)

Fig: 4.14 BP (mmHg)
Fig: 4.15 BMI, %Fat and Fat Mass
Fig: 4.16 Lipid Profile

![Lipid Profile Graph](image-url)
Fig: 4.17
Fig 4: 18 Hemoglobin and Platelets Counts
Fig: 4. Pre-eclamptic group Blood Pressure based on Tribe
Fig. 4.21 Pre-eclamptic group Lipid profile based on tribe

Fig. 4.22 PH of Non Pregnant non Hypertensive
Fig: 4.23 PH of pregnant non hypertensive
Fig: 4. Glucose of non pregnant non hypertensive
Fig: 4.25 Glucose of Pregnant non Hypertensive GRP

Urine Glucose of Pregnant Non Hypertensive GRP
Fig: 4.26 Urine Glucose of Pre-eclamptic
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