Review of Risk Factors, Diagnosis condition and Management Procedure of Preeclamsia in industrial and non-industrial areaof Bangladesh

A thesis report, submitted to the Department of Pharmacy, East West University, in partial fulfillment of the requirements for the degree of Masters of Pharmacy

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CERTIFICATE BY THE SUPERVISOR

This is to certify that the dissertation entitled**"Review of risk factors, diagnosis condition and management procedure of preeclampsia in industrial and non-industrial area of Bangladesh"**research work done by **KamrunNaher Shelly,** ID NO: 2013-1-79-004 in partial fulfillment of the requirement for the Degree of Masters of Pharmacy.

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"Review of risk factors, diagnosis condition and management procedure of preeclampsia in industrial and non-industrial area of Bangladesh"**is an authentic and genuine research work carried out by me under the guidance of**Dr. ShamsunNahar Khan,**Chairperson and Associate Professor**,** Department ofPharmacy, East West University, Dhaka, Bangladesh.

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CERTIFICATE

This is to certify that, the research work on**"Review of risk factors, diagnosis condition and management procedure of preeclampsia in industrial and non-industrial area of Bangladesh"** submitted to the department of pharmacy, East West University, Dhaka, Bangladesh, in partial fulfillment of the requirement for the degree of Masters of pharmacy (M. Pharm) was carried out by **KamrunNaher Shelly**, ID: 2013-1-79-004, under our guidance and supervision and that no part of the thesis has been submitted for any other degree. We further certify that all the resources of the information in thus connection are duly acknowledged.

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Dedicated

To

My Loving Parents

ACKNOWLEDGMENT

Above all, I express my gratitude to Almighty for giving me the strength and energy to carry out completing this research work.

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Statement of Purpose

The research was carried out in order toidentify the risk factors, diagnosis and management facilities of preeclamsia.

The specific objectives are as follows:

- To review existing literature and conducted statistical analysis to establish the prevalence and determinants of preeclampsia during pregnancy
- To assess the individuals sign and symptoms, diagnosis reports, treatment pattern and their impact of pregnancy.
- To propose a conceptual framework for research and interventions to prevent preeclampsia during pregnancy.

Abstract

Preeclampsia (PE) is a major cause of maternal and fetal mortality and morbidity. The purpose of the study was to identify the risk factors, diagnosis condition and management procedure of pre eclampsia patients in industrial and non-industrial area in Bangladesh.This descriptive type of cross sectional hospital based study was conducted in the 22 Health care centers for a period of 6 months of pre-eclampsia patients by interview. A thorough history and presenting vital signs, presence or absence of known signs and symptoms of preeclampsia, laboratory tests, treatment and all the information were recorded in a predesigned data collection sheet.In this study 38.34% patients were from 21-25 years of age, 26.22% patients were from 25-30 years of age and 15.04% patients were > 30 years of age. Majority of the sample population lives in industrial area(60%). Among the studied patients highest percentage had complaints of abdominal pain (39.80%) and edema (38.34 %). In this study 12.62% Patients had pre-existing hypertension, 1.45% patients had history of stroke, 42.23% had family history of hypertension, 27.84% patients had Gestational diabetes, 35.43% patients had obesity, 5.84% twin pregnancy, 60.19% patients had first time conceive. Among the study population OCP user are 74.27%. Hypertension, glucose intolerance, multiple pregnancy and cardio vascular disease are all known risk factors of pre eclampsia.In the study population intrauterine growth retardation was present in 27.66% babies, Intra uterine death was in 2.42% cases, and abortion was 2.91%.The findings of the study showed that the teenager and age above 30 years are at higher risk. The management facilities of preeclampsia are also available in Bangladesh.Among the study population 90.77% patients were treated with Methyldopa, 84.95% with Labetalol, 40.29% with Nifedipine and 31.55% with phenobarbital.These drugs are effective and safe for the management of preeclampsia and also cost effective.Multidisciplinary management is carried out with consideration of the maternal risks due to continued pregnancy and the fetal risks associated with induced preterm delivery. Screening women at high risk and preventing recurrences are key issues in the management of Preeclampsia.

Keywords: Pre-Eclampsia, Risk-Factors, Diagnosis, Therapeutic management.

Chapter One

Introduction

1.1 Preeclampsia

Pregnancy and child birth are a reason to celebrate but for half a million women worldwide childbirth turns fatal every year because of complications of pregnancy. Almost of these death occurring in the developing countries(Singh S et al., 2012).

Preeclampsia is a multisystem disorder pregnancy complication that is characterized new onset hypertension (systolic and diastolic pressure of ≥ 140 and 90 mmHg) and proteinuria (protein excretion of ≥ 300 mg in a 24 hours urine collection) that develop after 20 weeks of gestation and affects both mother and fetus(Redman CW et al., 2005) . Dependent on the systemic involvement, several other symptoms, such as edema, disturbance of homeostasis, renal or liver failure, and HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet counts). Preeclamsia can have an early onset (starting before 34 weeks of gestation) or late onset (starting after 34 weeks of gestation) can mild to severe symptoms (systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 110 mmHg, proteinuria > 5g / 24 hours, oliguria, neurological symptoms, and other clinical symptoms such as deranged liver function, thrombocytopenia) and can evolve in eclampsia in the most severe case. In addition, it can manifest as a maternal disorder only, with an appropriate fetal growing, or it can present itself with a growth restricted fetus (in utero growth restriction (IUGR)) or sudden fetal distress.

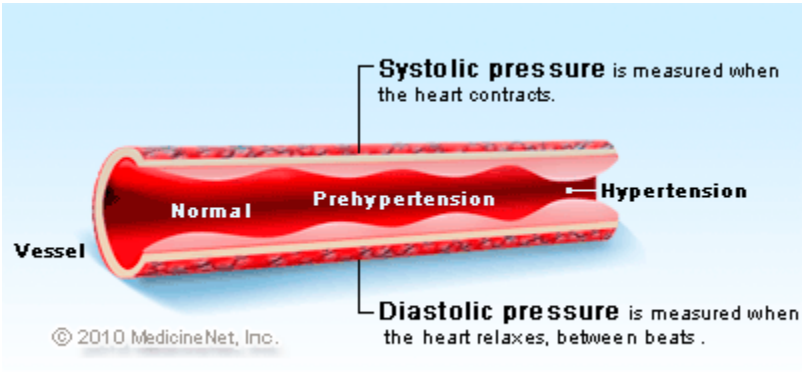

Figure1.1: High Blood Pressure

1.2 current condition

Accurate incidence figures are difficult to obtain and the incidence varies between countries, but it is believed that worldwide 3-8% of pregnant women are affectet (Hutcheon JA et al., 2011).

In economically poor regions, where there is often only very limited antenatal and intrapartum care, preeclampsia is a severely life-threatening condition, reflected by the fact that it is one of the leading causes of maternal mortality (Say L et al., 2014). Pre-eclampsia is also a leading cause (23.6 %) of perinatal death in economically poor countries. In economically rich countries, pre eclampsia is less lethal in an absolute sense, although the condition is responsible for around 13 % of maternal deaths; enhanced surveillance and diagnostic possibilities enable more timely and better detection, which, in turn, leads to higher rates of iatrogenic preterm birth, and pre-eclampsia is responsible for occupancy of up to 20 % of neonatal intensive care unit cots (National Advisory Body, 2001)

Although there is no proven effective method to prevent pre-eclampsia, screening and early identification of women at risk of pre-eclampsia could enable appropriate application of antenatal care, management and treatment. Screening includes testing, usually in the first half of pregnancy, to identify women at increased risk of pre-eclampsia (Hyde C et al., 2013) .At present, preeclampsia screening consists of assessing clinical risk factors such as age, body mass index (BMI) and family history, in combination with an ultrasound scan at 20 weeks. However, an international cohort project determined that the predictive power of clinical risk factors was modest. Recently, several maternal serum markers have been assessed as novel candidates for predicting preeclampsia (North RA et al., 2011)

1.3 Classification of preeclampsia

Preeclampsia is a pregnancy-specific syndrome that affects many organ systems and is recognized by new onset of hypertension and proteinuria that occur after 20 weeks' gestation. It is estimated to complicate 2 to 8% of all pregnancies (Duley L et al., 2009). Although the precise cause is unknown, the pathophysiologic processes underlying this

disorder are described in two stages (Roberts JM et al., 1999). The first stage is characterized by reduced placental perfusion possibly related to abnormal placentation with impaired trophoblast invasion and inadequate remodeling of the uterine spiral arteries. The second stage refers to the maternal systemic manifestations with inflammatory, metabolic, and thrombotic responses converging to alter vascular function which can result in multi-organ damage (Gammill HS et al., 2005). Precise classification of the various hypertensive disorders of pregnancy has remained challenging due to the changing nomenclature as well as the geographic variation in accepted diagnostic criteria. For example, terms such as "toxemia" and "pregnancy-induced hypertension" are now considered outdated. Furthermore, varying diagnostic criteria are used in different regions of the world with disagreement regarding the degree of hypertension, presence/absence of proteinuria, and classification of disease severity (Steegers EAP et al., 2010). These inconsistencies have led to challenges in comparing and generalizing epidemiologic and other research findings.

The classification system based on the Working Group Report on High Blood Pressure in Pregnancy is most commonly used in the United States in which four major categories are defined: gestational hypertension, preeclampsia- eclampsia, chronic hypertension, and superimposed preeclampsia on chronic hypertension. Preeclampsia is defined as new onset of sustained elevated blood pressure (≥140mmHg systolic or ≥ 90mmHg diastolic on at least two occasions 6 hours apart) and proteinuria (≥300mg in a 24 hour urine collection) first occurring after 20 weeks of gestation. Although the symptoms and signs of preeclampsia occur along a continuum, the syndrome is often categorized as mild or severe to communicate the severity of disease and management approach.

Preeclampsia is considered severe when any of the following is present in addition to the defining blood pressure and proteinuria criteria:

- Blood pressure ≥160 mmHg systolic or ≥110 mmHg diastolic
- Urine protein excretion of greater than five grams in a 24 hour collection
- Neurologic disturbances (visual changes, headache, seizures, coma)
- Pulmonary edema
- Hepatic dysfunction (elevated liver transaminases or epigastric pain)

• Renal compromise (oliguria or elevated serum creatinine concentration; creatinine ≥ 1.2 is considered abnormal in women without a history of renal disease)
• Thrombocytopenia
• Placental abruption, fetal growth restriction, or oligohydramnios

Eclampsia refers to seizures that occur in a preeclamptic woman which cannot be attributed to other causes. HELLP syndrome is defined by the presence of hemolysis, elevated liver transaminases, and low platelets. This may or may not occur in the presence of hypertension or proteinuria, but is considered to be along the spectrum of preeclampsia.

The diagnosis of preeclampsia can be particularly challenging in women with pre-existing hypertension and/or renal disease since both blood pressure and urinary protein excretion increase towards the end of pregnancy. Thus, the diagnosis is made based on a sudden increase in blood pressure or proteinuria and/or evidence of end-organ damage (Gifford RW et al., 2000). A major criticism of the various classification systems is that none have been independently evaluated for the ability to identify the subgroup of women who are at increased risk of adverse pregnancy outcomes. Recent studies have sought to develop clinically relevant definitions guided by the evidence and based on predictors of adverse outcomes (von Dadelszen P et al., 2011).

1.4 Epidemiology of preeclampsia

A systematic review by the World Health Organization indicates that hypertensive disorders account for 16% of all maternal deaths in developed countries, 9% of maternal deaths in Africa and Asia, and as high as 26% in Latin America and the Caribbean. Where maternal mortality is high, most of the deaths are attributable to eclampsia, rather than preeclampsia. Based on data from the United States National Hospital Discharge Survey, the rate of preeclampsia during admission for labor and delivery increased by 25% from 1987 to 2004, while the rate of eclampsia decreased by 22%, albeit not statistically significant. Severe morbidity associated with preeclampsia and eclampsia

include renal failure, stroke, cardiac dysfunction or arrest, respiratory compromise, coagulopathy, and liver failure . In a study of hospitals managed by Health Care America Corporation, preeclampsia was the second leading cause of pregnancy-related intensive care unit admissions after obstetric hemorrhage (Porreco RP et al., 2010).

1.4.1 Fetal and Neonatal effects

Fetal and neonatal outcomes related to preeclampsia vary around the world. Approximately 12 to 25% of fetal growth restriction and small for gestational age infants as well as 15 to 20% of all preterm births are attributable to preeclampsia. The associated complications of prematurity are substantial including neonatal deaths and serious long-term neonatal morbidity (Goldenberg RL et al., 1998). One quarter of stillbirths and neonatal deaths in developing countries are associated with preeclampsia/eclampsia. Infant mortality associated with preeclampsia is three times higher in low resource settings compared to high income countries, largely due to the lack of neonatal intensive care facilities.

1.4.2 Recurrence subsequent pregnancies

Studies have reported a 7-20% chance of preeclampsia recurrence in a subsequent pregnancy (Caritis S et al., 1998). This risk is further increased if a woman has had two prior preeclamptıcn pregnancies and is also influenced by gestational age of onset (Sibai BM et al., 1991). Estimates of the recurrence of preeclampsia vary widely based on the quality of the diagnostic criteria used. In a study done in Iceland using strict diagnostic criteria for preeclampsia and other hypertensive disorders, the estimated recurrence of preeclampsia or superimposed preeclampsia in a second pregnancy was 13% (Hjartardottir S et al., 2006)

1.4.3 Preclampsia and later life cardiovascular disease

Women who had eclampsia in any pregnancy after their first had a mortality risk that was two- to five-fold higher over the next 35 years compared to controls (Chesley SC et al., 1976). Following this early report, others have demonstrated an association between preeclampsia and later life cardiovascular disease and related mortality. Cardiovascular

disease risk was increased eight-fold in a Scandinavian population of healthy nulliparous women who developed preeclampsia severe enough to necessitate a preterm delivery (Irgens Hu et al., 2001). In a cohort of women delivering in Jerusalem, there was a two-fold higher risk of mortality at 24-36 year follow up in women with prior preeclampsia compared to women who did not have this diagnosis (Funai EF et al., 2005). The deaths were largely related to cardiovascular causes. These findings have also been confirmed in other populations (Smith GC et al., 2001). Hypertension, dyslipidemia, insulin resistance, endothelial dysfunction and vascular impairment have all been observed months to years after preeclampsia, further supporting the link between preeclampsia and subsequent cardiovascular disease (McDonald SD et al., 2008). It remains unresolved as to whether these common risk factors lead to the development of preeclampsia and later life cardiovascular disease or whether preeclampsia itself may contribute to this future risk.

1.5 Risk factors for pre-eclampsia

The epidemiology of preeclampsia reflects a wide range of risk factors as well as the complexity and heterogeneity of the disease. Risk factors can be classified into pregnancy specific characteristics and maternal pre-existing features. The incidence of preeclampsia is increasing may be related to the higher prevalence of predisposing disorders such as hypertension, diabetes, obesity, delay in child-bearing, and the use of artificial reproductive technologies with associated increase in multi-fetal gestation (Berg CJ et al., 1993)

The risk factors for preeclampsia are varied and unique to this condition. Genetic factors are at least partially responsible, as both a maternal and paternal family history of the disease predisposes to preeclampsia. There is a 7-fold risk of recurrence for women who have had the disease in a previous pregnancy (Duckitt K et al., 2005). Multiple gestations are an additional risk factor, and triplet gestation carries a greater risk than twin, suggesting that increased placental mass plays some role. Associations between preeclampsia and nulliparity, change in paternity from a previous pregnancy, increased interpregnancy interval, use of barrier contraception, and conception by intracytoplasmic sperm injection, implicate limited recent exposure to paternal antigen as a predisposing

factor. Notably, classic cardiovascular risk factors are associated with preeclampsia: maternal age greater than 40, insulin resistance, obesity, systemic inflammation, and preexisting hypertension, diabetes, or renal disease all increase the risk. Consistent with this, women with a history of preeclampsia have an elevated risk for cardiovascular disease later in life.

Surprisingly, smoking during pregnancy protects against preeclampsia.

1.5.1 Pregnancy-specific features

1.5.1.1 Parity—Nulliparity is a strong risk factor, almost tripling the risk of preeclampsia. It is estimated that two-thirds of cases occur in first pregnancies that progress beyond the first trimester.

New paternity also increases the risk of preeclampsia in a subsequent pregnancy. The association between primiparity and preeclampsia suggests an immunological mechanism such that later pregnancies are protected against those paternal antigens (Redman CW et al., 1991). Supporting this concept, previous pregnancy loss, increased duration of sexual activity prior to pregnancy, or prolonged pre- pregnancy cohabitation confers a lower risk of preeclampsia. Conversely, the risk of preeclampsia is increased with the use of barrier contraceptives, new paternity, and with donor sperm insemination (Robillart PY et al., 1999).

1.5.1.2 Placental factors—Excess placental volume as with hydatidiform moles and multi-fetal gestations is also associated with the development of preeclampsia (Day MC et al., 2005). The disease process may occur earlier and have more severe manifestations in these cases. The risk progressively increases with each additional fetus.

1.5.2 Maternal characteristics

1.5.2.1Age—Extremes of child bearing age have been associated with preeclampsia. However, once adjustments for parity are made in the younger age group (since most first

pregnancies occur at a younger age), the association between younger age and preeclampsia is lost (Roberts JM et al., 2009).

Multiple studies demonstrate a higher incidence of preeclampsia among older women independent of parity; however, many of these do not control for pre-existing medical conditions. After controlling for baseline differences, women who were 40 years of age or older had almost twice the risk of developing preeclampsia (Bianco A et al., 1996).

1.5.2.2 Race— The association between African-American Mexican race and preeclampsia has been confounded by the higher prevalence of chronic hypertension, often undiagnosed, in this group. While some studies demonstrate a higher risk of preeclampsia among African-American women(Eskenazi B et al., 1991) , larger prospective studies which controlled for other risk factors and rigorously defined preeclampsia did not find a significant association between preeclampsia and African-American race (Knuist M et al., 1998). More severe forms of preeclampsia may be associated with maternal non-white race.

1.5.2.3 Pre-existing conditions— Many of the maternal risk factors for preeclampsia are similar to those for cardiovascular disease. Pre-existing hypertension, diabetes, obesity, and vascular disorders (renal disease, autoimmune conditions) are associated with preeclampsia(Ness RB et al., 2009). Risk is correlated with the severity of the underlying disorder. Women with underlying chronic hypertension have a 10-25% risk of developing preeclampsia compared to the general population (Rey E et al., 1994). This risk is increased to 31% in women with a longer duration of hypertension of at least four years or more severe hypertension at baseline. With pre-gestational diabetes, the overall risk of developing preeclampsia is approximately 21% (Hanson U et al., 1993). However, the risk is 11-12% with diabetes of less than 10 years duration, which increases to 36 to 54% among women with longer-standing diabetes associated with microvascular disease. For mild renal disease (serum creatinine of less than 1.5mg/dL), the risk of preeclampsia is estimated at 20 to 25% but greater than 50% for pregnant women with severe renal disease (Sibai BM et al., 2000). Preeclampsia also occurs more frequently among

pregnant women with autoimmune conditions such as systemic lupus erythematosus and antiphospholipid antibody syndrome.

Hypertension--- Hypertension, complicating 6% to 11% of all pregnancies, is a leading cause of maternal and fetal morbidity, particularly when elevated blood pressure is due to pre-eclampsia. Undiagnosed chronic hypertension may be masked in early pregnancy because of the initial decrease in pressure, then misdiagnosed as a gestation specific disorder when abnormal values appear later in pregnancy. Hypertension is defined as levels that are ≥ 140 mm Hg systolic and ≥ 90 mm Hg diastolic blood pressure. Pregnancy may diminish kaliuresis and BP rise associated with primary aldosteronism.

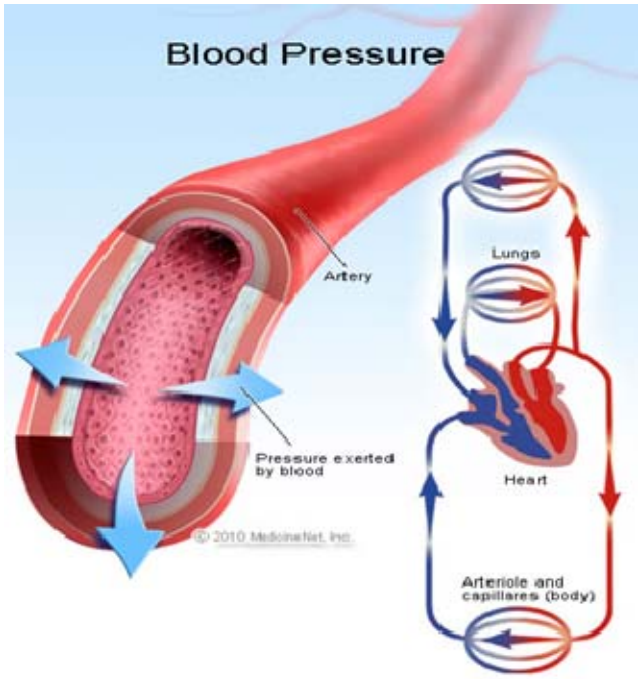

Figure1.2: Hypertension in Pregnancy

Obesity—Elevated body mass index (BMI, kg/m2) is also associated with preeclampsia. Given the obesity epidemic in the around the world, this is one of the largest attributable and potentially modifiable risk factors for preeclampsia. The high prevalence of obesity and projected increase have substantial implications for pregnancy since obesity is associated with infertility, spontaneous miscarriage, fetal malformations, thromboembolic complications, gestational diabetes, stillbirth, preterm delivery, cesarean section, fetal overgrowth and hypertensive complications (WHO Global infobase 2011).

Obesity increases the overall risk of preeclampsia by approximately 2- to 3-fold (Bodnar LM et al., 2007). The risk of preeclampsia progressively increases with increasing BMI, even within the normal range. Importantly, it is not only the late or mild forms of preeclampsia that are increased, but also early and severe preeclampsia, which are associated with greater perinatal morbidity and mortality (Catov JM et al., 2007). The association between preeclampsia risk and obesity has also been demonstrated in varying populations across the globe. Supporting the concept that obesity may play a causal role is the finding that weight loss reduces the risk of preeclampsia. Some studies suggest that excessive maternal weight gain is associated with the risk of preeclampsia, although these may be confounded by the increase in fluid retention with preeclampsia contributing to the higher weight. Although weight loss is discouraged in pregnancy, obesity is a potential modifiable risk factor for preeclampsia. Weight loss prior to pregnancy is encouraged in overweight and obese women to decrease the risk of adverse outcomes. It is estimated that 30% of the preeclampsia risk is attributable to obesity.

Family history of preeclampsia— A family history of preeclampsia nearly triples the risk of preeclampsia (Bodnar LM et al., 2005).

Smoking— Paradoxically, cigarette smoking during pregnancy is associated with a reduced risk of preeclampsia, possibly due to modulation of angiogenic factors (Jeyabalan A et all 2008)

1.6 Sign and Symptoms

Typically the pregnant woman develops hypertension and proteinuria before onset of convulsion. Other cerebral sings may immediately precede (kane SC et al., 2013), such as

- Nausea
- Vomiting
- Headaches and
- Cortical blindness
- Neck pain

If the complication of multi organ failure ensues, sing symptoms of those failure organs will appear, such as

- Abdominal pain
- Jaundice
- Shortness of breath and
- Diminished urine output

The fetus may develop intrauterine growth retardation and with maternal convulsions, bradycardia and fetal distress (Cunningham FG et al., 1997).
Placental bleeding and placental abruption may also occur.
Sometimes the pregnant woman becomes comatose without preceding convulsions

1.7 Pathophysiology of Preeclamsia

During normal pregnancy, the villous cytotrophoblast invades into the inner third of the myometrium, and spiral arteries lose their endothelium and most of their muscle fibers. These structural modifications are associated with alterations, such that spiral arteries

become low resistance vessels, and thus less sensitive, or even insensitive, to vasoconstrictive substances.

Pre-eclampsia has a complex pathophysiology, the primary cause being abnormal placentation. Defective invasion of the spiral arteries by cytotrophoblast cells is observed during pre-eclampsia. Recent studies have shown that cytotrophoblast invasion of the uterus is actually a unique differentiation pathway in which the fetal cells adopt certain attributes of the maternal endothelium they normally replace. In pre-eclampsia, this differentiation process goes awry (Fisher SJ et al., 2009). The abnormalities may be related to the nitric oxide pathway, which contributes substantially to the control of vascular tone. Moreover, inhibition of maternal synthesis of nitric oxide prevents embryo implantation (Duran-Reyas G et al., 1999). Increased uterine arterial resistance induces higher sensitivity to vasoconstriction and thus chronic placental ischemia and oxidative stress. This chronic placental ischemia causes fetal complications, including intrauterine growth retardation and intrauterine death. In parallel, oxidative stress induces release into the maternal circulation of substances such as free radicals, oxidized lipids, cytokines, and serum soluble vascular endothelial growth factor. These abnormalities are responsible for endothelial dysfunction with vascular hyperpermeability, thrombophilia, and hypertension, so as to compensate for the decreased flow in the uterine arteries due to peripheral vasoconstriction.

Endothelial dysfunction is responsible for the clinical signs observed in the mother, i.e., impairment of the hepatic endothelium contributing to onset of the HELLP (Hemolysis, Elevated Liver enzymes and Low Platelet count) syndrome, impairment of the cerebral endothelium inducing refractory neurological disorders, or even eclampsia (Robers JM et al., 1998). Depletion of vascular endothelial growth factor in the podocytes makes the endotheliosis more able to block the slit diaphragms in the basement membrane, adding to decreased glomerular filtration and causing proteinuria. Finally, endothelial dysfunction promotes microangiopathic hemolytic anemia, and vascular hyperpermeability associated with low serum albumin causes edema, particularly in the lower limbs or lungs.

The crucial issue to understand is that the prime mover of pre-eclampsia is abnormal placentation. Two common theories appear to be interlinked, i.e., a genetic theory, and an

immunological theory (Genbacev O et al., 1999). Several susceptibility genes may exist for pre-eclampsia (Nilsson E et al., 2004). These genes probably interact in the haemostatic and cardiovascular systems, as well as in the inflammatory response.

Pre-eclampsia can be perceived as an impairment of the maternal immune system that prevents it from recognizing the fetoplacental unit. Excessive production of immune cells causes secretion of tumor necrosis factor alpha which induces apoptosis of the extravillous cytotrophoblast. The human leukocyte antigen (HLA) system also appears to play a role in the defective invasion of the spiral arteries, in that women with pre-eclampsia show reduced levels of HLA-G and HLA-E (Colbern GT et al., 1994). During normal pregnancies, the interaction between these cells and the trophoblast is due to secretion of vascular endothelial growth factor and placental growth factor by natural killer cells. High levels of soluble fms-like tyrosine kinase 1 (sFlt-1), an antagonist of vascular endothelial growth factor and placental growth factor, have been found in women with pre-eclampsia.

Accordingly, assays of sFlt-1, placental growth factor, endoglin, and vascular endothelial growth factor, all of which increase 4–8 weeks before onset of the disease, may be useful predictors of pre-eclampsia. Recent data show the protective role of heme oxygenase 1 and its metabolite, carbon monoxide, in pregnancy, and identify this as a potential target in the treatment of pre-eclampsia (Ahmed A, 2011).

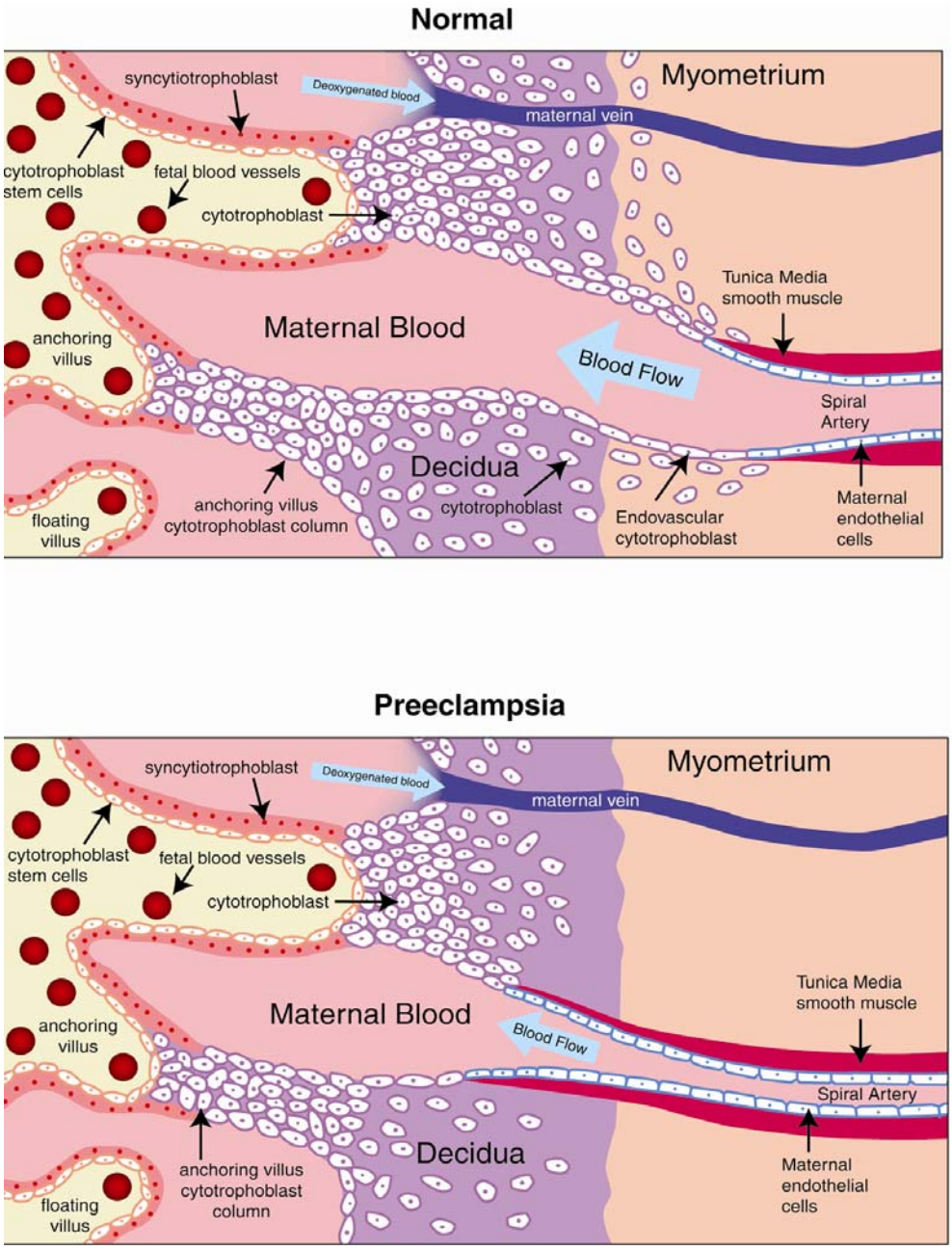

Figure1.3: Abnormal Placentation in Preeclampsia

In normal placental development, invasive cytotrophoblasts of fetal origin invade thematernal spiral arteries, transforming them from small-caliber resistance vessels to highcaliber capacitance vessels capable of providing placental perfusion adequate to

sustain the growing fetus. During the process of vascular invasion, the cytotrophoblasts differentiate from an epithelial phenotype to an endothelial phenotype, a process referred to as "pseudovasculogenesis" or "vascular mimicry" (Upper Panel). In preeclampsia, cytotrophoblasts fail to adopt an invasive endothelial phenotype. Instead, invasion of the spiral arteries is shallow and they remain small caliber, resistance vessels (Lower Panel).

1.7.1 Placental pathophysiology in preeclampsia

The precise origin of preeclampsia remains elusive, but it is believed to be likely multifactorial. A certainty is the central role played by the placenta in its pathology (Hahn S et al., 2006). A long standing hypothesis has been that preeclampsia develops as a consequence of some kind of immune mal adaptation between the mother and the fetus during the very first weeks of pregnancy, leading to a 2-step disorder progression that can be summarized as following: in a first – asymptomatic – step, local aberrant feto-maternal immune interactions within the uterine wall lead to impaired tissue and arterial invasion by trophoblast cells. This results in failed transformation of the uterine spiral arteries and subsequently worsened placental perfusion. Chronic hypoxia or alternate periods of hypoxia/re-oxygenation within the intervillous space is expected to trigger tissue oxidative stress and increase placental apoptosis and necrosis (Soleymanlou N et al., 2005) The clinical disorder arises, in a second step, when the maternal vascular and immune systems cannot handle any longer the increased shedding of placentally-produced debris and the aberrant expression of pro-inflammatory, anti-angiogenic and angiogenic factors, leading to a systemic endothelial cell dysfunction and an exaggerated inflammatory response (Maynart SE et al., 2003). Recently, this hypothesis has been challenged (Huppertz B, 2008). It was proposed instead that intrinsic failure in trophoblast differentiation at different time points of ontogeny may lead, to either a mild disorder with late-onset appearance, or IUGR complicated or not with the maternal symptoms. However, the origin of preeclampsia might not be restricted to an alteration of trophoblast differentiation, but may also in some cases depend on underlying maternal constitutional factors such as genetic, obesity, dysfunctional maternal clearance or inflammatory systems

1.8 Diagnosis of preeclampsia

The diagnosis of preeclampsia is clinical. As defined by the American College of Obstetrics and Gynecology, the diagnosis requires blood pressures greater than 140/90 on two occasions, combined with urine protein excretion greater than 300 mg per day. Edema, a classic feature of the disease, is no longer considered a diagnostic feature, given its lack of sensitivity or specificity. Importantly, in 20% of cases, eclampsia may present without preceding hypertension or proteinuria, suggesting that the currently employed diagnostic criteria are imperfect (Stella CL et al., 2009). Laboratory tests such as liver function tests, quantification of urine protein, and serum creatinine may be helpful in characterizing the degree of end organ damage, but none is specific for preeclampsia Hyperuricemia, more likely to be present in women with preeclampsia than in normotensive pregnant women, has been used as a diagnostic aid and to predict adverse outcomes in preeclampsia, but its predictive value is generally modest (Lim KH et al., 1998). Imbalance of pro- and antiangiogenic proteins as a key factor in the pathogenesis of the preeclampsia.

Clinical and laboratory tests are intended to define and determine the severity of pre-eclampsia. Headaches, visual disorders, brisk tendon reflexes, and vigilance disorders are related to cerebral edema; oliguria to acute renal failure; uterine contraction, vaginal bleeding to placental abruption; vomiting to HELLP syndrome; bandlike epigastric pain to subcapsular hepatic hematoma; and dyspnea to cardiac failure.

Eclampsia, the major neurological complication of pre-eclampsia, is defined as a convulsive episode or any other sign of altered consciousness arising in a setting of pre-eclampsia, and which cannot be attributed to a pre-existing neurological condition.

Clinical examination should include resting blood pressure measurement using an appropriate cuff, and screening for weight gain, edema (including signs of acute pulmonary edema and cerebral edema), cardiomyopathy, and acute renal failure. The fetus should be assessed by electrocardiotocography.

Laboratory tests include: a complete blood count with platelets, haptoglobin, and lactate dehydrogenase; a blood smear to test for schistocytes; bilirubin, aspartate transaminase, and alanine transaminase in order to identify potential HELPP syndrome; electrolyte,

urea, and creatinine assessment to check for acute renal failure or uremia; 24-hour proteinuria; prothrombin, activated thrombin time, and fibrinogen (microangiopathic hemolytic anemia); blood group; and irregular antibody screening. Other examinations include fetal ultrasound with Doppler velocimetry of the umbilical, cerebral, and uterine arteries, estimation of fetal weight, assessment of fetal well-being by Manning score, and examination of the placenta.

Although the definition of severe pre-eclampsia varies , several components of this definition are usually accepted: maternal systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg; maternal neurological disorders such as persistent headaches, phosphene signals, tinnitus, and brisk, diffuse, polykinetic tendon reflexes, eclampsia, acute pulmonary edema, proteinuria ≥ 5 g/day, oliguria, 500 cc/day, creatinine 120 μmol/L, HELLP syndrome, thrombocytopenia, 100,000/mm3, and fetal criteria, especially intrauterine growth retardation, oligohydramnios, or fetal death in utero. Mild pre-eclampsia is defined as diastolic blood pressure ≥ 90 mmHg measured on two occasions at least 6 hours apart, combined with proteinuria (300 mg total protein in a 24-hour urine collection, or a protein creatinine ratio .30 mg/mmol).

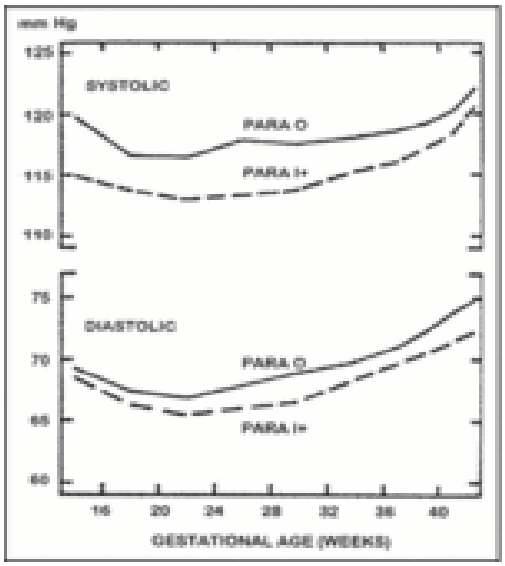

Table: 1.1. Preeclampsia: Judging Severity

	Less Severe	**More Severe**
Presentation	≥ gestational week 34	≥gestational week 35
Diastolic BP	<100 mm Hg	>110 mm Hg
Headache	Absent	Present
Visual disturbance	Absent	Present
Abdominal pain	Absent	Present
Oliguria	Absent	Present
Creatinine (GFR)	Normal	Elevated
LDH AST proteinuria	Mild to moderate	Elevated nephrotic range
No reassuring fetal testing	Absent	Present

1.9 Management of Preeclampsia

1.9.1 Immediate emergency Management

Delivery is the only curative treatment for pre-eclampsia. Management is multidisciplinary, involving an obstetrician, an anesthetist, and a pediatrician. In some cases consultation of maternal fetal medicine and hypertension or nephrology subspecialists may be required. Management decisions must balance the maternal risks of continued pregnancy against the fetal risks associated with induced preterm delivery. The criteria for delivery are based on two often interrelated factors, i.e., gestational age at diagnosis (estimated fetal weight) and severity of pre-eclampsia. Severe pre-eclampsia requires treatment with a dual aim, i.e., preventing the harmful effects of elevated maternal blood pressure and preventing eclampsia. Management of severe pre-eclampsia begins with transfer of the mother in a fully equipped ambulance to a maternity ward providing an appropriate level of care for both mother and child. At admission and daily

thereafter, clinical, cardiotocographic, laboratory, and ultrasound testing are required to detect the severity of pre-eclampsia and tailor management accordingly. Regardless of the severity of pre-eclampsia, there is no advantage in continuing the pregnancy when pre-eclampsia is discovered after 36–37 weeks (Haddad B et al., 2007). Nor is expectant management justified for severe pre-eclampsia before 24 weeks, in view of the high risk of maternal complications and the poor neonatal prognosis.26–28 The obstetric team must then discuss with the parents the possibility of a medical interruption of pregnancy. Prolongation of pregnancy in the event of mild pre-eclampsia can be discussed and reevaluated on a regular basis. At 34 –37 weeks, management depends on the severity of the pre-eclampsia. Expectant management is possible for mild pre-eclampsia to limit the risk of induced preterm delivery, but for severe pre-eclampsia, delivery remains the rule due to the increased risk of maternal and fetal complications

Similarly, at 24-34 weeks, management depends on the severiy of preeclamsia. The presence of one or more of the following signs indicates the need for immediate delivery: uncontrolled severe hypertension (not responsive to dual therapy), eclampsia, acute pulmonary edema, abruption placentae, subcapsular hepatic hematoma, or thrombocytopenia <50,000/mm3. Delivery after corticosteroid therapy for pulmonary maturation is necessary if any of the following criteria is present: persistent epigastric pain, signs of imminent eclampsia (headaches or persistent visual disorders), de novo creatinine >120 μmol/L, oliguria below 20 mL/hour, progressive HELLP syndrome, prolonged or severe variable decelerations with short-term variability less than 3 milliseconds. When emergency delivery is not required, labor can be induced by cervical ripening. Antihypertensive treatment is useful only in severe pre- eclampsia because the sole proven benefit of such management is to diminish the risk of maternal complications (cerebral hemorrhage, eclampsia, or acute pulmonary edema) (Duley L et al., 2006)

There is no international consensus concerning antihypertensive treatment in pre-eclampsia. The four drugs authorized for the treatment of hypertension in severe pre-eclampsia in world wide are nifedipine, labetalol, methyldopa, and dihydralazine.

There is no ideal target blood pressure value, and too aggressive a reduction in blood pressure is harmful to the fetus (Olsem KS et al., 1992). Therapy with a single agent is advised as first-line treatment, followed by combination treatment when appropriate.

Pulmonary maturation using corticosteroids must be considered, taking gestational age into account. Betamethasone remains the gold standard at a dosage of two injections of 12 mg 24 hours (Pryde PG et al., 2009) apart; this treatment reduces the risk of intraventricular hemorrhage, and neonatal mortality.

Magnesium sulfate ($MgSO_4$) may be part of the therapeutic armamentarium for severe pre-eclampsia. It is indicated in the treatment of eclamptic convulsions as well as for secondary prevention of eclampsia, thus replacing treatment by diazepam, phenytoin, or the combination of chlorpromazine, promethazine, and pethidine. The efficacy of $MgSO_4$ in the reduction of maternal and neonatal complications of eclampsia is well established. It is administered intravenously, first at a loading dose of 4g over 15–20 minutes, which can be repeated at a half dose (2 g) if convulsion recurs, and then at a maintenance dose of 1 g/hour for 24 hours. $MgSO_4$ treatment must be monitored in the intensive care unit because organ failure may occur. This monitoring is based on repeated checking. Any manifestation of overdose requires stopping the infusion, considering injection of calcium gluconate, and measuring blood magnesium levels. Eclampsia is generally considered an indication for emergency cesarean section. Nonetheless, a decision to delay a cesarean, albeit rare, may be based on fetal status and justified if the mother's condition is stable and reassuring after treatment.

1.9.2 Management following delivery

Although delivery is the only effective treatment for pre- eclampsia, and despite the fact that clinical symptoms and laboratory abnormalities usually regress in the hours afterwards, the risk of complications persists for some time following delivery (Barton JR et al., 2008). Pre-eclampsia is associated with long term morbidity and mortality. Approximately 20% of women with pre-eclampsia develop hypertension or microalbuminuria during long-term follow-up, and the risk of subsequent cardiovascular and cerebrovascular disease is doubled in women with pre-eclampsia and gestational

hypertension compared with age-matched controls . A recent prospective epidemiological study with a median follow-up duration of 30 years provides evidence that pre-eclampsia is a marker of increased mortality from cardiovascular disease. Hemodynamic, neurological, and laboratory monitoring is necessary following delivery for patients with severe preeclampsia Tan LK et all 2002. Hemodynamic monitoring includes frequent blood pressure measurements to enable adjustment of antihypertensive treatment and frequent monitoring of diuresis and weight according to intake (oliguria should prompt progressive fluid resuscitation and sometimes diuretic use). Neurological monitoring consists of checking for signs of imminent eclampsia, including headaches, phosphene signals, tinnitus, and brisk tendon reflexes. Clinical monitoring must be done several times daily during the week after delivery, a period considered at high risk for complications. If necessary, monitoring can be performed in an intensive care unit.

Laboratory monitoring should be done several times daily in the first 72 hours after delivery and thereafter adapted according to progress of the indices. It must include a complete blood count, liver function tests, and measurement of lactate dehydrogenase. Discharge from hospital cannot be considered until all clinical and laboratory indices have returned to normal, and regular monitoring by the patient's general practitioner as necessary if treatment for hypertension is to be continued after discharge.

The risk of recurrence of pre-eclampsia during a subsequent pregnancy has to be considered. This risk is estimated to be less than 10% for all cases of pre-eclampsia, but is greater when pre-eclampsia is discovered before 28 weeks. The relative risk is 15 if pre-eclampsia occurs at 20–33 weeks, 10 at 33–36 weeks, and 8 after 37 weeks.

Three months after delivery, screening for underlying renal or hypertensive disease may be requested by them patient's primary physician. Such screening is intended to check for normalization of blood pressure values and disappearance of proteinuria, and if abnormalities persist, a referral should be made to a nephrologists or a hypertension expert to determine the cause. This examination is important because pre-eclampsia may unmask previously undiagnosed systemic or kidney disease or thrombophilia. It should include a specific set of questions, blood pressure measurement, a clinical examination looking for signs of autoimmune conditions, and a urinary dipstick test. Testing for antiphospholipid antibodies is recommended after severe pre-eclampsia. The search for

hereditary thrombophilia by assays for protein C and S, antithrombin III, and a test for resistance to activated protein C is recommended in the case of personal or family history of venous thromboembolic disease, early pre-eclampsia, or pre-eclampsia with any intrauterine growth retardation, abruption placentae, or in utero death Percutaneous needle biopsy of the kidney should be performed only if kidney failure persists at three months postpartum or if signs of a systemic underlying condition or proteinuria persist at 6 months. Patients who have had severe pre-eclampsia may share predispositions with nonpregnant patients who have cardiovascular risk factors (Irgens HU et al., 2001). Accordingly, long-term monitoring of cardiovascular, renal, and metabolic risk factors is recommended after severe pre-eclampsia

1.10 Prevention of preeclampsia

Primary prevention of pre-eclampsia is based on the detection of modifiable risk factors. The literature is plentiful regarding the risk factors for pre-eclampsia, but should be interpreted with caution. Women at high risk are those with a personal history of severe pre-eclampsia, while those at low risk are defined as those who have never had pre-eclampsia but have at least one risk factor. There are numerous risk factors, including genetic risk factors, family history of pre- eclampsia, immunologic factors, a new partner, and demographic factors such as a maternal age >35 years, the woman's own gestational age and birth weight (with elevated risks for women born before 34 weeks or weighing less than 2500 g at birth), factors related to the pregnancy, such as multiple pregnancy, congenital or chromosomal anomalies, a hydatidiform mole, or urinary infection, risk factors associated with maternal disease, including chronic hypertension, kidney disease, obesity, insulin resistance, and diabetes, as well as thrombophilia, and environmental factors such as living at a high altitude and stress. Although the search for these risk factors is important, they may not effectively predict this pre-eclampsia by themselves.
However, accurate prediction of pre-eclampsia would enable early and optimal management of women at high risk.

Several predictive tests are being assessed currently. These include clinical tests, such as blood pressure measurement during the second trimester or 24-hour ambulatory blood pressure monitoring, but these lack sensitivity and specificity.

Laboratory tests for oxidative response have been assessed, including assays for uric acid, urinary kallikrein, and fibronectin, but no evidence of their relevance has so far been found. Among the markers used to screen for trisomy during the second trimester (beta human chorionic gonadotropin, alpha fetoprotein, and unconjugated estriol), elevated alpha fetoprotein is associated with a higher risk of pre-eclampsia (unless there are neural tube abnormalities, as when beta human chorionic gonadotropin is elevated).

Frequent monitoring of women with elevated levels could be useful, but these tests may not be carried out for screening purposes due to their low negative predictive value. Serum markers for trisomy in the first trimester (pregnancy- associated plasma protein, inhibin, corticotropinreleasing hormone, and activin) have been tested, but their likelihood ratios seem to be insufficient.

Imaging tests have been evaluated, including uterine artery Doppler ultrasound. Uterine artery Doppler ultrasound is not advised during the first or second trimester in low-risk populations due to the excessive variability of likelihood ratios in this population, which allows for the prediction of only one-third of pre-eclampsia cases (Maynard SE et al., 2003). In a high-risk population, the definition of which is often imprecise, uterine artery Doppler can be performed during the second trimester morphologic ultrasound examination and checked 1 month later in case of abnormal results (resistance index .0.58 or 90–95th percentile, unilateral or bilateral notch). The combination of a uterine artery Doppler examination during the first trimester and a three-dimensional ultrasound assessing placental volume may predict the risk of pre-eclampsia as early as the first trimester (Romero R et al., 2007).

In clinical practice, because no single marker effectively predicts the risk of pre-eclampsia, the current trend is to test a combination of markers. The most commonly used combination of markers assesses sFlt-1, placental growth factor, endoglin, and vascular endothelial growth factor during the first or second trimester. Increased vascular endothelial growth and endoglin levels, combined with increased sFlt-1 and decreased

placental growth factor during the first trimester, is associated with a significantly increased risk of pre-eclampsia.

Improved prediction of pre-eclampsia has been noticed when serum markers combined with Doppler indices. In a recent nested case-control study, second trimester maternal serum cystatin C, C-reactive protein, and uterineartery mean resistance index were observed to be independent predictors of pre-eclampsia.

Secondary prevention is based on antiplatelet aspirin therapy, which reduces the risk of pre-eclampsia by 10% in women who have at least one risk factor (Askie LM et all 2007). No study currently allows determination of the exact dosage or the best time for initiation of aspirin. However, aspirin should be initiated as early as possible, i.e., before 12–14 weeks, which corresponds to the beginning of the first phase of trophoblast invasion. The efficacy of aspirin has been shown only in women with previous pre-eclampsia associated with intrauterine growth retardation and without thrombophilia. Low molecular weight heparin is indicated only in cases of complicated thrombophilia (history of thromboembolic complications or of pre-eclampsia).

Calcium supplementation at a dosage of 1.5 g/day, beginning at 15 weeks and continued throughout the pregnancy, is recommended for prevention of pre- eclampsia in women with a daily calcium intake ,600 mg/day(Villar J et al., 2006).48 The statins, which stimulate HO-1 expression and inhibit sFlt-1 release, could have the potential to ameliorate early-onset pre-eclampsia.

Other treatments, such as antioxidant treatment by vitamins C and E, oligoelements, and nitric oxide have no proven efficacy.

1.11 Preeclamsia in Perspective of Bangladesh

Bangladesh is one of the most densely populated country with a land mass of 147,570 sq. km and a population of more than 149.8 million, 70% of whom live in rural areas. The

population growth rate is 1.374% per annual. According to UNDP, around 83% of the population lives on less than US$ 2 a day and 36% on less than US$ 1 a day. Through continuous effort of the government and the non-government sectors, income poverty has declined from an estimated 58% of the population during 1983-84 to just below 50% in 2000 with one percent reduction every year (NIPORT , 2013) .

Although there has been considerable improvement in the health indicators, still more than 60% of the population has very little access to basic healthcare (MOHFW 2003). The number of qualified physicians and nurses in Bangladesh is quite low, compared to other low-income counties. Around 26% of professional posts in rural areas remain vacant (Chaudhury N et al., 2003). Despite modestly declining poverty and inadequate health services, Bangladesh has achieved substantial gains in the field of health in the three decades since independence in the '70s, as evidenced in mortality and fertility declines in this low income country compared to other South Asian countries (Nasreen et al., 2010).

About a quarter of the population consists of adolescents and youths. Some of the problems concerning adolescents include early age at marriage, high fertility and low levels of secondary and tertiary education. The higher death rate among girls compared to boys aged 15- 19 (1.81 as against 1.55 per 1,000 population) is mainly due to maternal causes. Access to appropriate reproductive health information and services for this group is inadequate.

Maternal death is caused by direct, indirect and other related factors. The major direct causes of maternal deaths in Bangladesh are postpartum haemorrhage, eclampsia, complications of unsafe abortion, obstructed labour, postpartum sepsis, and violence and injuries. About one-fourth of the total maternal death in Bangladesh is complications. As per a study by BRAC, Bangladesh has achieved substantial gains in the field of health during the last three decades despite modestly declining poverty and inadequate health services. However, Infant Mortality Rate (IMR) and maternal mortality ratio (MMR)

continue to be unacceptably high compared to many other developing countries, with persisting socioeconomic differentials.

As per BMMS (Bangladesh Maternal Mortality survey) 2010, the 2 major causes of maternal death were haemorrhage (30%) and ecalmpsia (21%). Both of these complications require management at a facility by a trained provider (BMMS , 2010).

After persisting at very low levels, the proportion of pregnancy healthcare facility has begun to rise in the past decade, from 9% in 2001 to 23% in 2010. Much of that increase has come through the private sector (2.7% to 11.3%). NGOs (Non-governmental organizations).

Even after the increases in facility delivery has happened, it still leaves 2.4 million births at home annually. Some haemorrhage cases can be avoided by proper management of the placenta. However, while managing preeclampsia with drugs to prevent fatal death and maternal death. The Three drugs authorized for the treatment of hypertension in severe pre- eclampsia in Bangladesh are nifedipine, labetalol, and methyldopa (Shamsuddin L et al., 1998).

Based on the above facts it can be seen that the pregnancy related complications are still a major problems in Bangladesh even though Bangladesh is well on its way towards achieving the millennium Development goal 5 (Improving maternal Health). Due to lack of proper facilities, awareness and education on these complications are extremely important to improving maternal health further.

As a result this survey has been conducted to analyze the awareness as well as the facilities of pregnant women within the study population in ensuring safe pregnancy. The purpose of the study is to risk factors, diagnosis and management facilities of preeclampsia patients.

Chapter Two

Literature Review

Literature Review

2.1 Effect of preeclampsia on perinatal outcome: A study done in the specialized urban hospital setup in Bangladesh

A study was conducted from August 2005 to June 2006 on 60 Bangladeshi women in the Department of obstetrics and gynaecology, Dhaka Medical college hospital and Midford hospital.

Information on maternal age, gestational, parity, level of education, risk factors and residence were collected for each women were selected 35 to 40 weeks of gestation on the basis of diagnosis by a registered physician or from the hospital record.

35% had pre-existing risk factors. Maternal age 19-25 were 20%, neonatal age 34-38 weeks, neonatal weight 2.6 gm to 2.8 gm were found which was under weight.(Kishwara.S et al.,2006)

2.2 Prevalence and risk factors for preeclampsia in Indian women: A national cross sectional study.

This survey was conducted by National Family Health Survey(NFHS) during 2005-2006 was designed on the lines of the Demographic and health surveys on 124385 women aged 15-49 years focused on 39,657 married women considered education, category, employment status wealth index geographic region, risk factors birth interval, antenatal care,BP, proteinuria type of pregnancy BMI previous risk factors and food habit.

Rural 56%, Urban 54% , twin pregnancy 67% ,terminated pregnancy 63%,Severe anemia 58%, diabetes 67%,Asthma 72%, non working 62%, first order 58% were found in this study.

Age and parity not associated with preeclamsia which is contrast with other studies(Gagandeep K et al.,2007).

2.3 Preeclamsia rates in the United States,1980-2010: Age, period cohort analysis.

This survey was conducted by National Hospital from 1980-2010 period on 120 million women admitted to hospital.

The rate of Preeclamsia was 3.4%. In comparison women delivering risk factors of severe preeclamsia increased, from 1980(3.4%) to 2010(3.8%) that was increased 6-7 fold.

In age group 15-19 years evidence of preeclamsia was dropped, in 1980 that was 4% and in 2010 was 2.8%. But in age group 30-34 years it was increased, from 1980 was 1.7% to 2010 was 2%.(Cande V et al.,2012)

2.4 Public Health perspective of preeclampsia in developing countries.

The study was conducted from 2001-2010 in African countries, considered preeclamsia, eclampsia, developing countries.

Severity of preeclampsia is seven times higher in developing countries (2.8%) than developed countries (0.4%). In Africa, Egypt, Tanzania it was 1.8% to 7.1% and in Nigeria 2% to 16%.

Multiple gestation is the major risk factor associated with others.

Aspirin therapy is beneficial for pre management of preeclamsia.(Kayode O et al., 2012)

Chapter Three

Method & Methodology

METHODS

3.1 Study design

This is a community and hospital-based cross sectional (descriptive study), where data was collected through interviews with a structured questionnaire as well as recorded data of each patient. The study protocol was reviewed and approved.

3.2 Study Area

We used multistage and non-probability sampling to select districts. Villages were selected randomly for community-level survey. Public health staff members were automatically selected from the study facilities for interview.
Four districts were selected on the basis of heterogeneity. The selected districts were:
Dhaka, Gazipur, Mymensing, Tangail.
In these districts, we conducted a survey of pregnant and recently-delivering women.

3.3 Study Population

A total of 206 pregnant women were included in the study and interviewed as per the questionnaire. The patients were within 15-40 years of age.

3.4Collection of data

We studied 22 secondary- and tertiary-care centre— 4 district hospitals, 6 Upzilla health complex, and 12 Community Health Center in the four selected districts. Observations

and record reviews were used for collecting data. We surveyed each facility, using a standard form.

The data collection from health facilities was undertaken from July to December 2015. Each facility was visited once without prior notice.

3.5Methods of Measurement

A standardized data collection tool was utilized to extract demographic data, presenting vital signs, presence or absence of known signs and symptoms of preeclampsia, laboratory tests, treatment. In addition, when available, delivery records were reviewed for evidence of prior diagnosis of preeclampsia/eclampsia during this or previous pregnancies. If the signs or symptoms of interest were documented during the presenting visit or initial history and physical by either an emergency physician or obstetrical consultant, they were considered positive. If none of those records documented the historical data, they were considered negative.

Laboratory findings were defined as follows: proteinuria as presence of trace protein or higher; elevated liver function tests (LFT) as AST > 47 U/L, ALT > 47 U/L, or alkaline phosphatase > 117 U/L; hyperuricemia as uric acid > 5.7 mg/dL, thrombocytopenia as platelets < 150,000 per 109/L, and anemia.

3.6 Data Analysis

Data were organized, tabulated and aggregated using Microsoft excel. Means proportions of the epidemiological, social, sings, symptoms and clinical parameters were compared amongst the study population.

Chapter Four
Results

Results

Table: 4.1 Summary descriptive statistics, percentage (%) of pregnant women risk with preeclampsia.

Baseline characteristics	**Cases(n=206)**
Age in years	**n, %**
16-20	42 (20.38)
21-25	79 (38.34)
26-30	54 (26.21)
31-35	31 (15.04)
Religion	**n, %**
Muslim	138 (66.99)
Hindu	64 (31.06)
Others	4 (1.94)
Education	**n, %**
No education	5 (2.42)
Up to primary	26 (12.62)
Secondary	82 (39.80)
Higher secondary	60 (29.12)
Above higher secondary	32 (15.53)
Socioeconomic status	**n, %**
Low	89 (43.20)
Middle	85 (41.26)
High	32 (15.53)
Profession	**n, %**
Housewife	113(54.85)
Service, business, others	93 (45.14)
Parity	**n, %**
No child	124 (60.19)
1child	59 (28.64)
2 children	16 (7.76)
3 or more children	7 (3.39)

Distribution of the study population according to their age

During the study period 206 patients were interviewed. The age of the patients ranged from 16 to 35 years. Majority of the patients were within 21-25 years age group (38.34%), while 20.38% of the patients are teenagers.

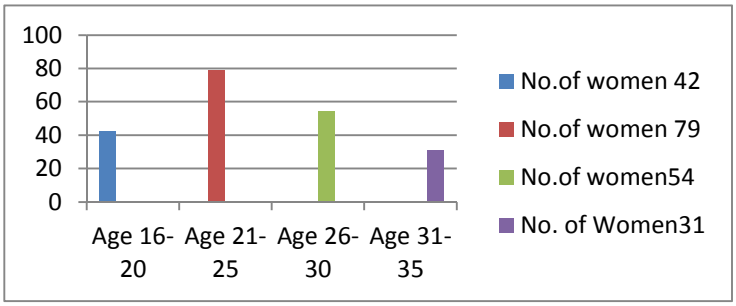

Figure 4.1: Bar diagram illustrating the different age group within the sample population

Levels of educational qualification of the patients:

Level of education of the patients were classified as no education, primary (any education up to class 5), secondary (any education from class 6 to S.S.C exams), Higher Secondary (up to H.S.C exams),Above Higher Secondary .Majority of the Patients (39.8%) where within secondary group,29.12% has done Higher Secondary education and 15.53% has done above Higher Secondary, while 2.42% did no schooling

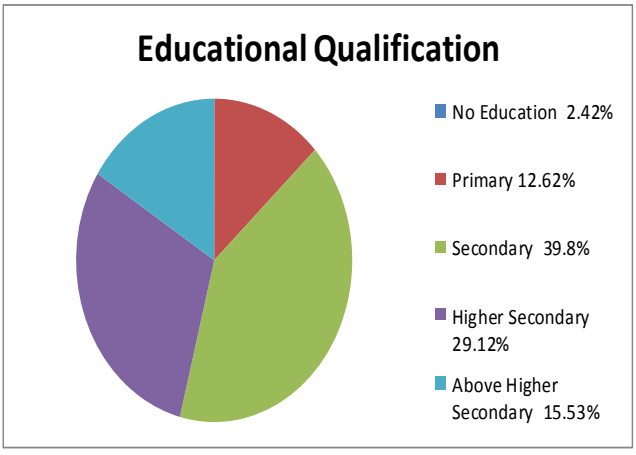

Figure 4.2: Pie chart illustrating the different level of education within the sample population.

Distribution of the sample population according to their occupation.

Majority of the sample population were housewives(54.85%), 25% were service holder and 15.5% did business.

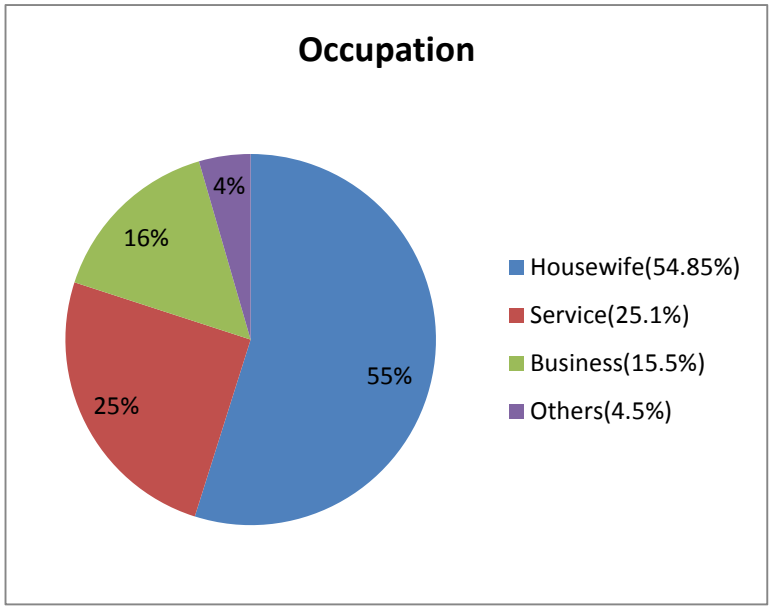

Figure 4.3: Pie chart illustrating the different level of occupation within the sample population.

Comparison of the sample population according to their educational qualification

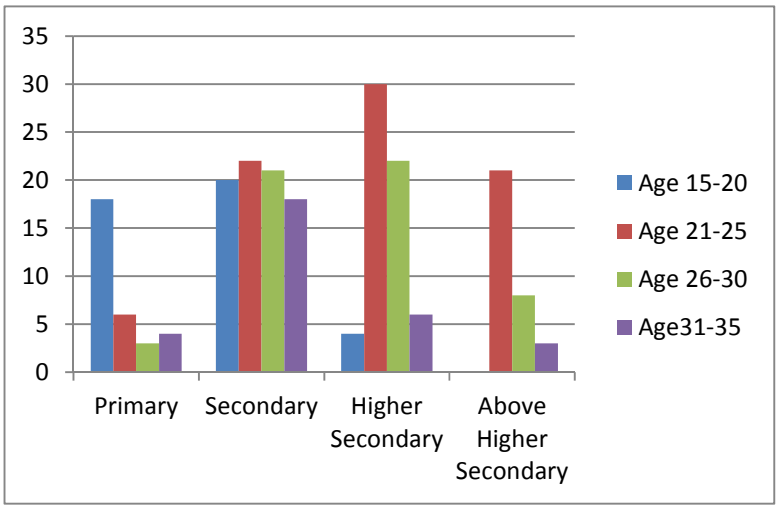

Figure 4.4: Bar diagram illustrating the different age group within the sample population comparing their education level

Distribution of the sample population according to their socioeconomic status.

Majority of the sample population were within low economic status(43.20%)

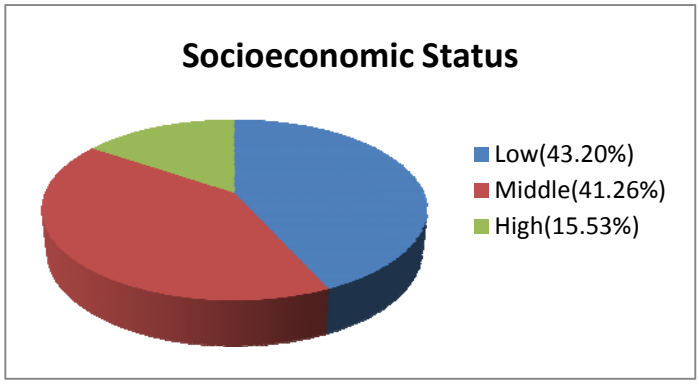

Figure 4.5: Pie chart illustrating the different level of socioeconomic status within the sample population.

Distribution of the sample population according to their present living address

Majority of the sample population were Urban(51.94%)

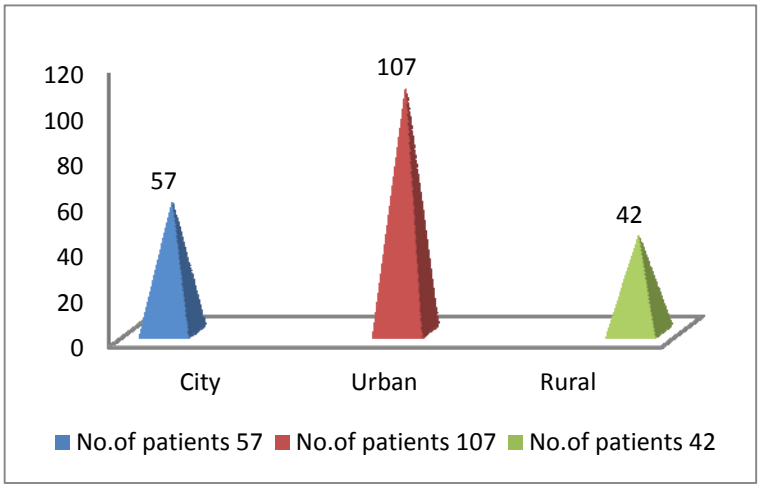

Figure 4.6: Bar diagram illustrating the sample population according to their living address

Comparison of the sample population according to their present living address

Majority of the sample population were living industrial area (60.19%)

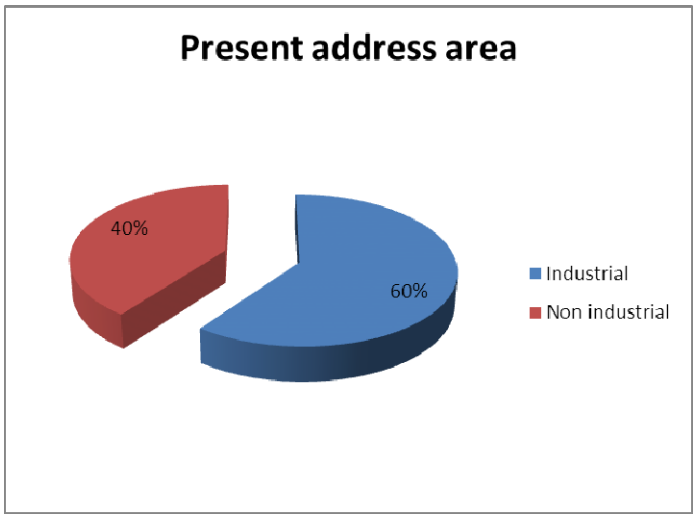

Figure 4.7: Pie chart illustrating the sample population according to their present address

Distribution of the sample population according to their age of marriage

Majority of the sample population got married within 15-20 years age

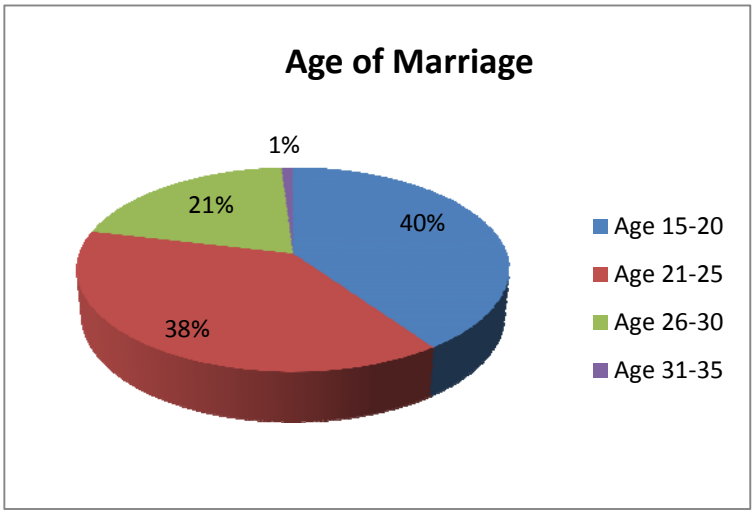

Figure 4.8: Pie chart illustrating the sample population according to their marriage age

Distribution of patient according to OCP use

Majority of the sample population use OCP(74.27%)

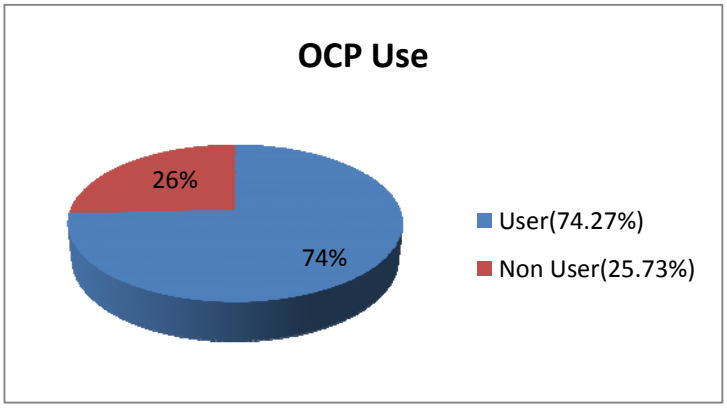

Figure 4.9: Pie chart illustrating the sample population according to the use of OCP

Distribution of the sample population according to their parity

Majority of the sample population(60.19%) had no child, 28.64% had one child, while only 3.39% had more than two children

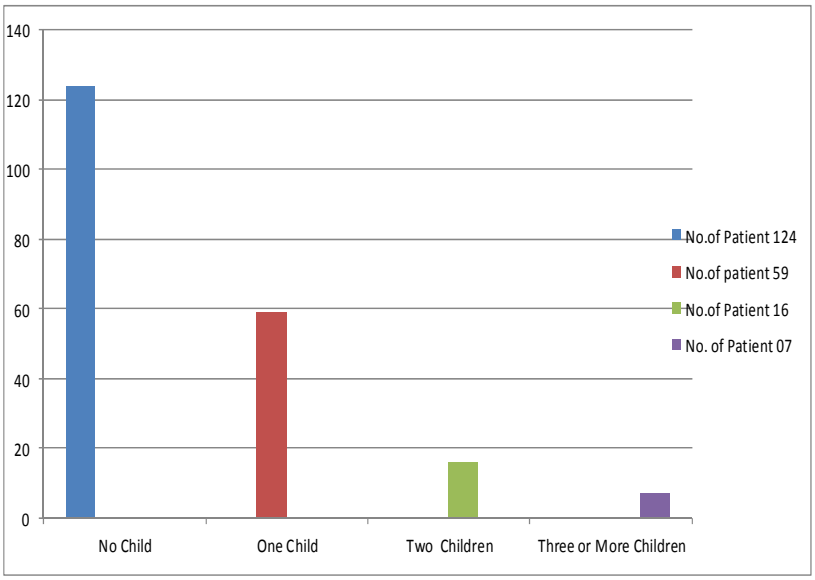

Figure 4.10: Bar diagram illustrating the sample population according to their parity

Comparison of the sample population according to their age between OCP uses, first conceive and maternal death

Majority of the sample population use OCP(90%) at 21-25 years age group and first time conceive at 16-20 years age group(90%) while maternal death found highly at 31-35 age group(3%)

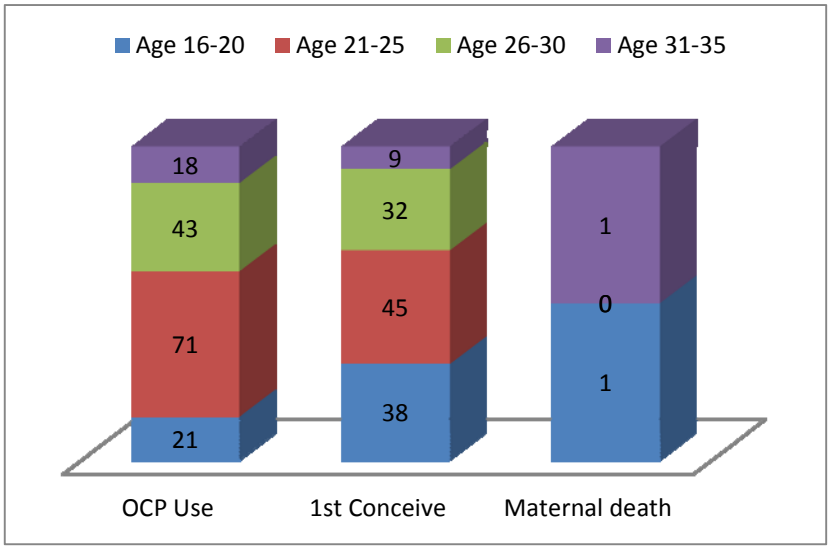

Figure 4.11: Bar diagram illustrating comparison of the sample population according to their age between OCP uses, first conceive and maternal death

Distribution of the sample population according to pre-existing risk factors

Majority of the sample population had no pre-exiting risk factors(15.54%)

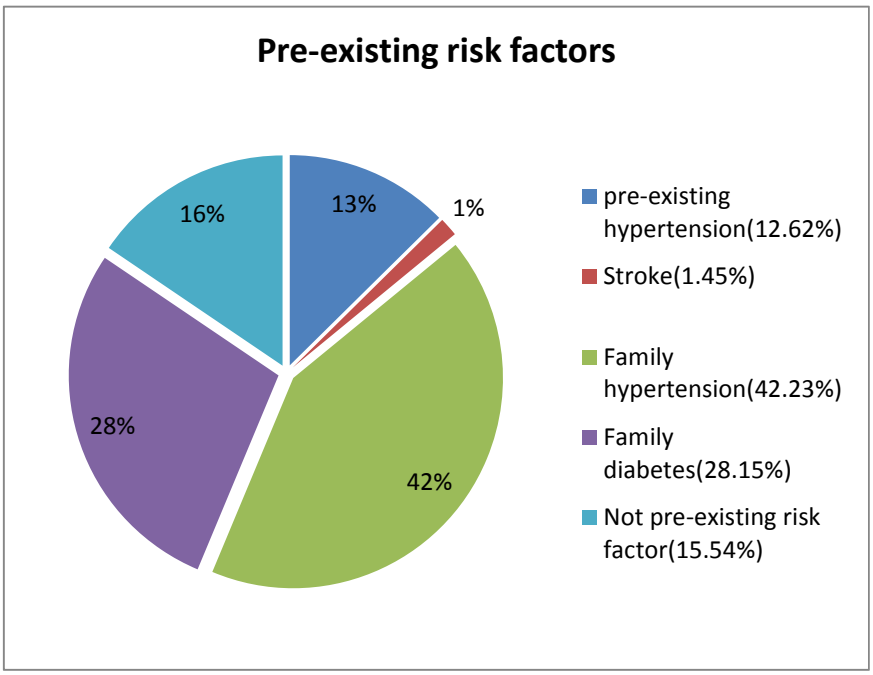

Figure 4.12: Pie chart illustrating the sample population according to their pre-existing risk factors

Table 4.2: Presenting complain of the Patient

Presenting complain	**n (=206)**	**%**
Headache	29	14.07
Nausea	49	23.78
Vomiting	21	10.19
Abdominal pain	82	39.80
Edema	79	38.34
Neck pain	21	10.19
Blurred vision	25	12.13

Distribution of the sample population according to their sings

Majority of the sample population had complain about abdominal pain(39.80%) and edema(38.34%)

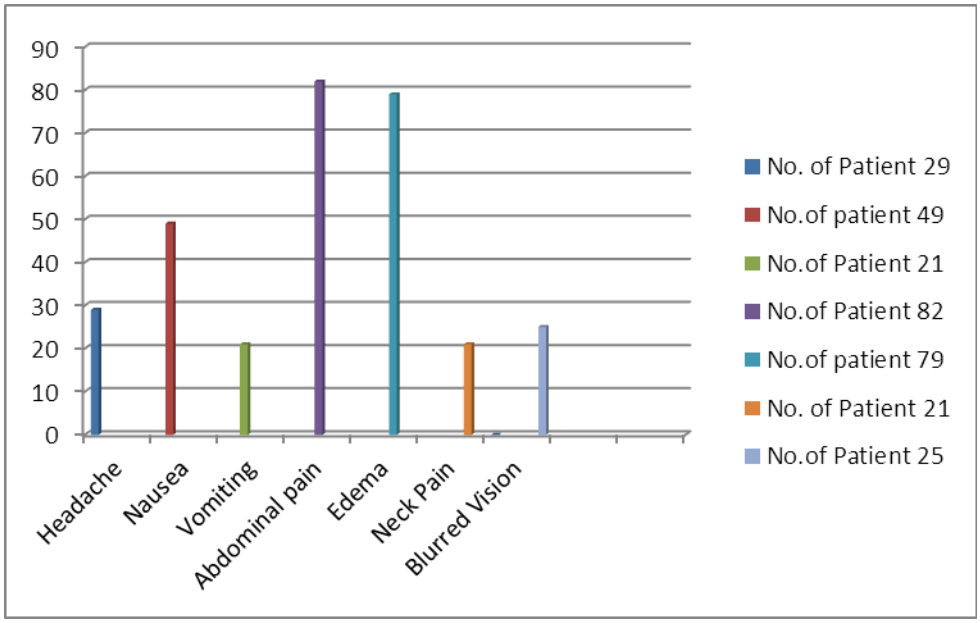

Figure 4.13: Bar diagram illustrating the sample population according to their presenting complain

Comparison of the sample population between their age and presenting sings

Presenting complains are compared with the age group of the study population.

In the study population abdominal pain were mostly seen in 31-35 years age group (62%) and lowest 26-30 age group (23%)

Headache were mostly seen in 31-35 years age group (33%) and lowest 21-25 age group (9%)

Neck pain were mostly seen in 31-35 years age group (23%) and lowest 16-20 age group (5%)

Blurred vision were mostly seen in 26-30 years age group (15%) and lowest 31-35 age group (7%)

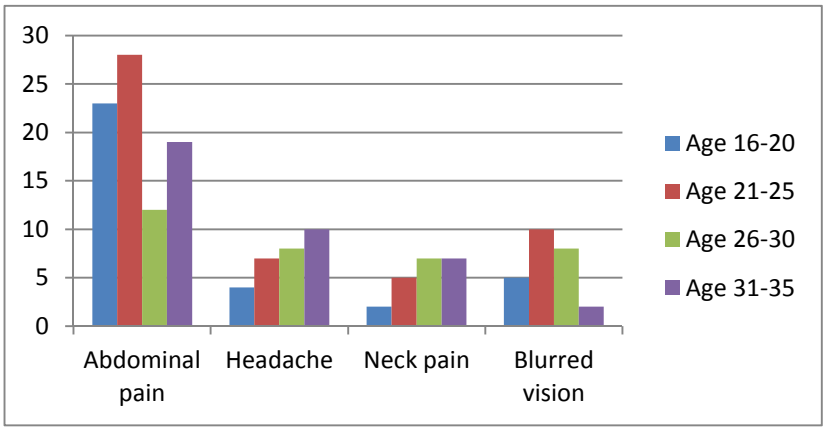

Figure 4.14: Bar diagram illustrating the comparison of the sample population between their age group and presenting complain.

Distribution of sample Population according to Neurological Disturbance

In the study population only 26% were affected by neurological disturbance.

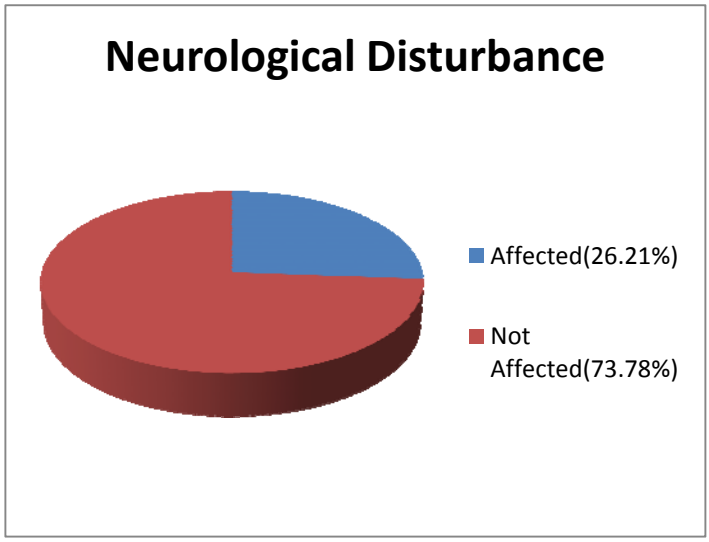

Figure 4.15: Pie chart illustrating the sample population according to the neurological disturbance.

Table 4.3: Symptoms of the Patients

Presenting sings	**n (=206)**	**%**
SBP ≥ 140 mmHg	201	97.5
DBP ≥ 90 mmHg	165	80.09
Edema	171	83.49
Seizure	5	2.42
Obesity	73	35.43

Table 4.4: Risk factors of the Patients

Ancillary data	**n (=206)**	**%**
Proteinuria	114	55.33
Anemia	113	54.85
Gestational diabetes	56	27.84
Thyroid dysfunction	27	13.10
Elevated LFTs	18	8.73
Hyperuricemia	21	10.19
Respiratory distress	38	18.44
UTI	29	14.07

Distribution of sample population according to the risk factors

In the study population 56% had proteinurea, 55% had anemia, 28% had gestational diabetes while only 13% had thyroid dysfunction.

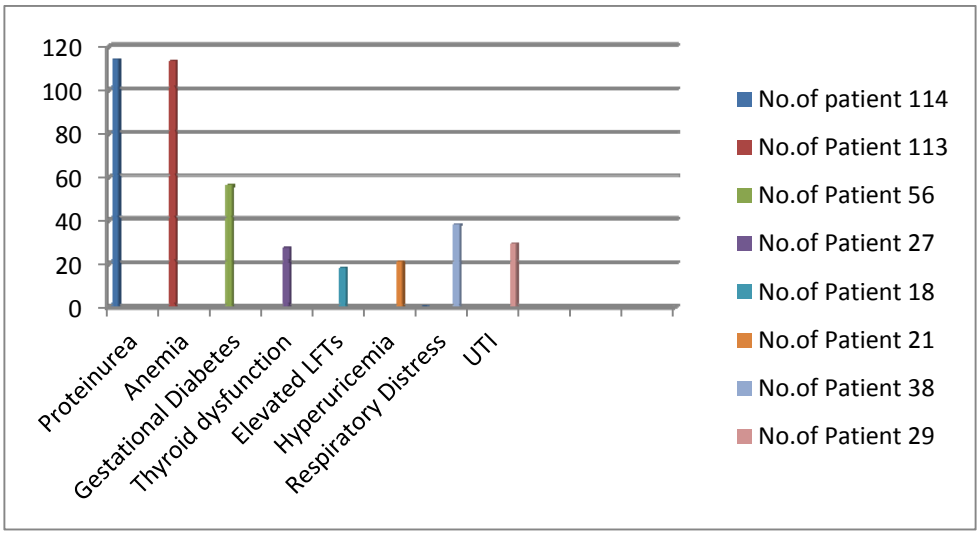

Figure 4.16: Bar diagram illustrating the sample population according to the risk factors.

Comparison of the sample population between age and presenting signs

Presenting signs are compared with the age group of the study population.

In the study population proteinurea were mostly seen in 31-35 years age group (84%) and lowest 21-30 age group (46%)

Edema were mostly seen in 21-25 years age group (87%) and lowest 26-30 age group (78%)

Elevated LFTs were mostly seen in 31-35 years age group (13%) and lowest 16-20 age group (5%)

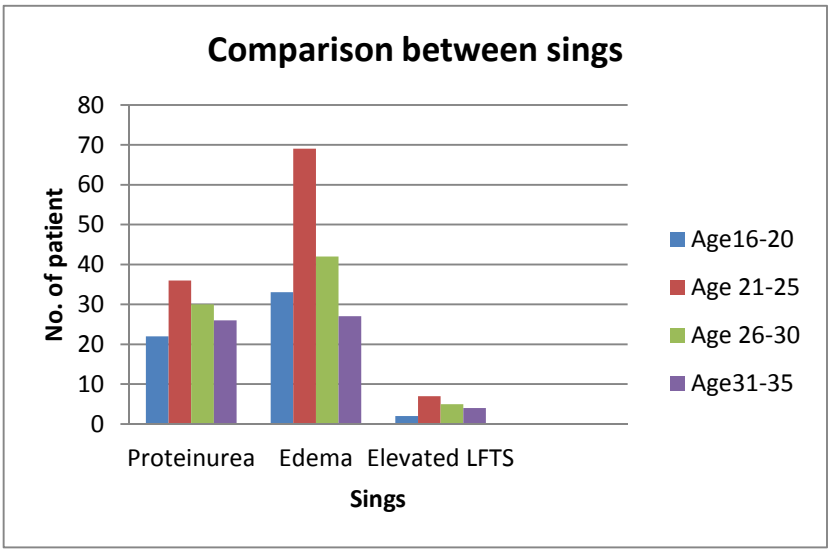

Figure 4.17: Bar diagram illustrating the comparison of the sample population between their age and presenting signs.

Comparison of the sample population between their age and risk factors

Risk factors are compared with the age group of the study population.

In the study population obesity were mostly seen in 31-35 years age group (90%) and lowest 16-20 age group (10%)

Diabetes were mostly seen in 31-35 years age group (74%) and lowest 16-20 age group (5%)

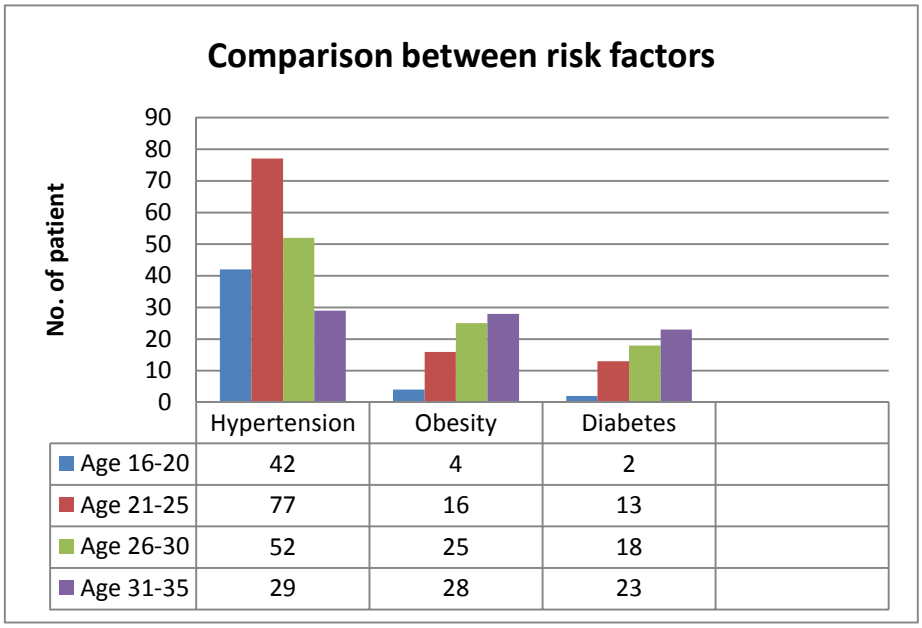

Figure 4.18: Bar diagram illustrating the comparison of the sample population between their age and risk factors.

Table4. 5: Fetal and Maternal health condition

Parameters	**n (=206)**	**%**
No complain	91	44.46
Breech	33	16.01
No fetal movement	11	5.33
IUGR	57	27.66
IUD	5	2.42
Abortion	6	2.91
Maternal death	2	0.97

Fetal health condition

In the study population 45% had no complain about their fetal health, 28% had IUGR, 2.4% IUD and 3% abortion.

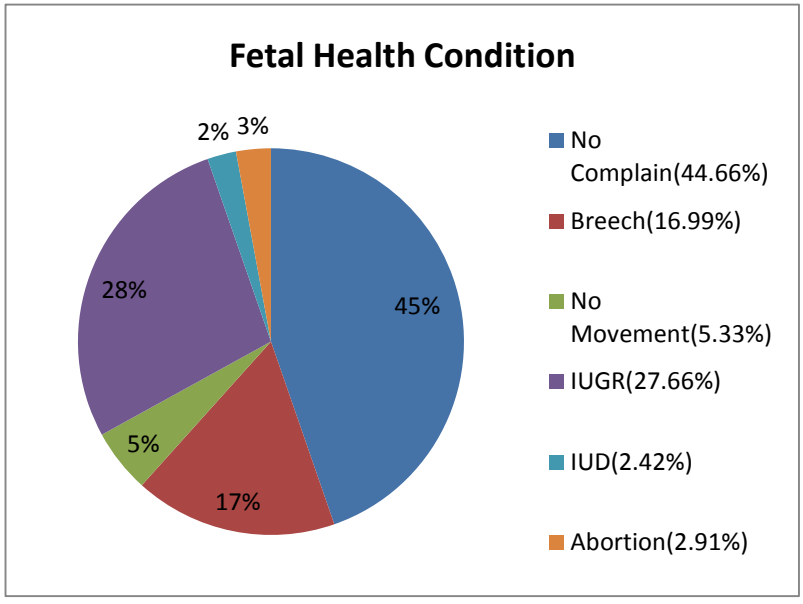

Fig 4.19: Pie chart illustrating the fetal health condition

Comparison of the sample population between their age and fetal health condition

Presenting signs are compared with the age group of the study population.

In the study population IUGR were mostly seen in 31-35 years age group (26%) and lowest 21-30 age group (46%)

IUD were mostly seen in 31-35 years age group (6%) and lowest 21-25 age group (1%)

Abortion were mostly seen in 16-20 years age group (7%) and lowest 26-30 age group (0%)

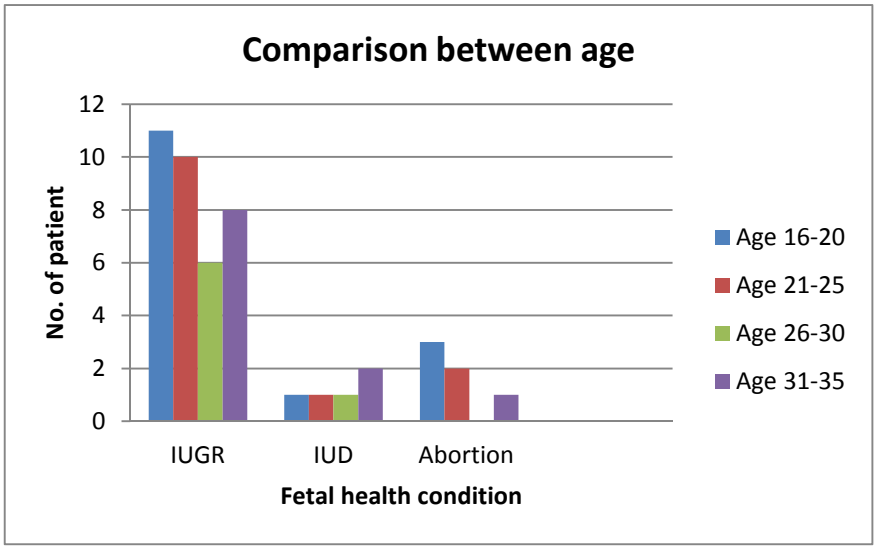

Figure 4.20: Bar diagram illustrating the comparison of the sample population between their age group and fetal health condition.

Table 4.6. Drugs use for management of preeclampsia

Drug use	**n (=206)**	**%**
Methyldopa	187	90.77
Lebetelol	172	84.95
Nifedipine	83	40.29
Phenobarbital	65	31.55

Distribution of the sample population according to the prescribed drugs

In the study population 91% were prescribed methyldopa, 85% labetalol while 32% were prescribed phenobarbital.

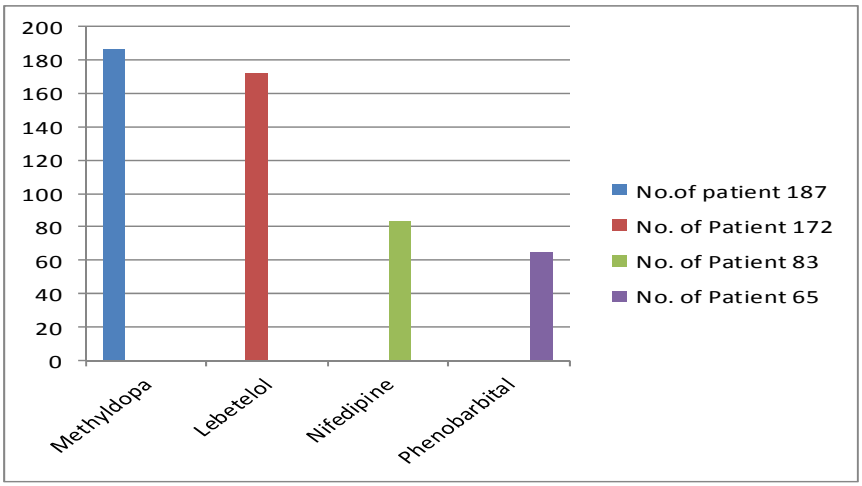

Figure 4.21: Bar diagram illustrating the sample population according to the prescribed drugs.

Distribution of the sample population according to the use of drugs

In the study population 72% are prescribed multiple drugs and only 28% are prescribed Single drugs

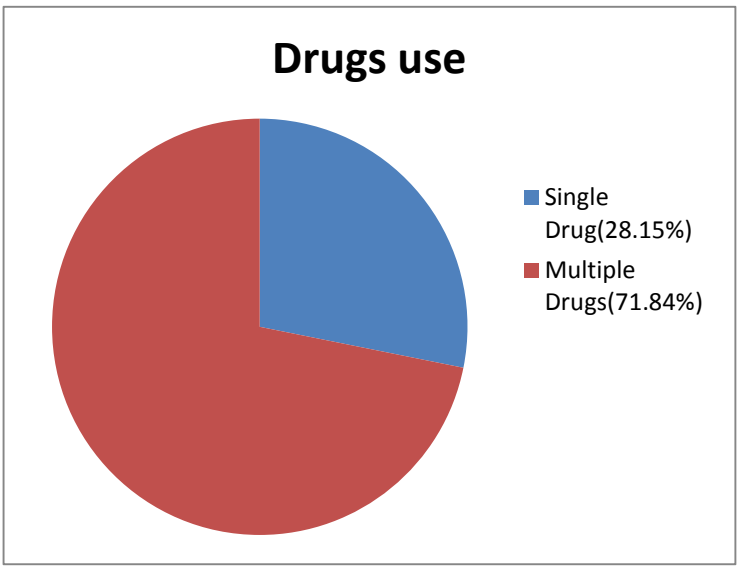

Fig:4.22: Pie chart illustrating the sample population according to the use of drugs

Comparison of the sample population between risk factors and prescribed drugs

Presenting risk factors are compared with prescribed drugs among the study population. In the study population 78% were prescribed single drugs who had 2 risk factors and 22% had 3 risk factors.53% were prescribed 2 drugs who had 2 risk factors, 36% had 3 risk factors and 11% had 4 or more risk factors.20% patients were prescribed 3 or more drugs who had 2 risk factors while 36% had 4 or more risk factors.

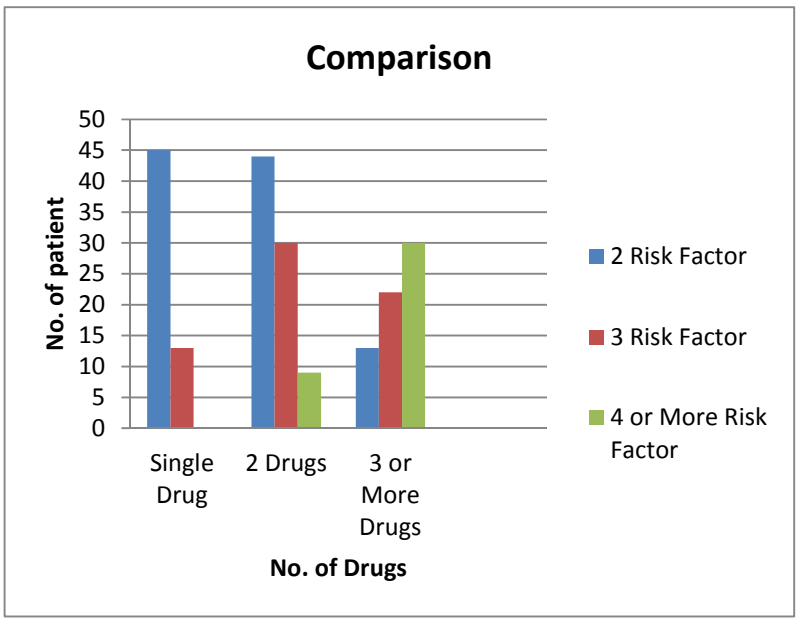

Figure 4.23: Bar diagram illustrating the comparison of the sample population between the risk factors and prescribed drugs.

Chapter Five
Discussion

Discussion

Even though the study was carried out from one center only, the permanent address of all the participants are widely distributed throughout Bangladesh. In Bangladeshi perspective the population is gradually shifting towards the urban areas from rural areas due to better job opportunities and utilities. Therefore, the study population can be used to draw an inference on preeclamsia amongst Bangladeshi women.

Pre-eclampsia complicates about 2-8% of all pregnancies. Pre eclampsia remains a major cause of maternal and preinatal mortality and morbidity and is particularly devastating in developing countries. Despite recent progress towards under standing the cause of pre eclampsia and/or its phenotypes, the aetiology of this serious disorder remains elusive.
Our study provides a novel insight into understanding the etiology of risk, diagnosis and management facilities of preeclampsia in pregnant women living in Bangladesh.

The study found 20% of the patients were in 16-20 years age group, 38.34% patients were from 21-25 years of age, 26.22% patients were from 26-30 years of age and 14.56% patients were > 30 years of age.

Level of education of the patients were found that majority of the Patients (39.8%) where within secondary group,29.12% has done Higher Secondary education and 15.53% has done above Higher Secondary, while 2.42% did no schooling
Majority of the sample population were within low economic status(43.20%) and living industrial area(60.19%)
In this study 12.62% Patients had pre-existing hypertension, 1.45% patients had history of stroke, 42.23% had family history of hypertension.

Among the studied patients highest percentage had complaints of abdominal pain (39.80%) and edema (38.34 %). Then headache (14.07%), vomiting (10.19%), nausea (23.78 %) and neck pain (10.19 %).

Alarmingly 27.84% patients had Gestational diabetes, 35.43% patients had obesity, 83% had edema and 55% had proteinurea.

Presenting complains and risk factors are compared with the age group of the study population. In the study population abdominal pain were mostly seen in 31-35 years age group (62%) and lowest 26-30 age group (23%). Headache were mostly seen in 31-35 years age group (33%) and lowest 21-25 age group (9%). Neck pain were mostly seen in 31-35 years age group (23%) and lowest 16-20 age group (5%). Blurred vision were mostly seen in 26-30 years age group (15%) and lowest 31-35 age group (7%).
In the study population obesity were mostly seen in 31-35 years age group (90%) and lowest 16-20 age group (10%). Diabetes were mostly seen in 31-35 years age group (74%) and lowest 16-20 age group (5%)

Majority of the sample population got married within 15-20 years age, 74.27% are OCP user and 60.19% patients had first conceive.

Hypertension, glucose intolerance, multiple pregnancy and cardio vascular disease are all known risk factors of pre eclampsia.
However addition risks factors are also play important role for the causation of pre-eclapmsia like obesity, teen age and late pregnancies, cardiovascular disease, renal disease, thrombophilia, pregnancies complicated by trisomy or multiple pregnancies.

In the study population intrauterine growth retardation was present in 27.66% babies, Intra uterine death was in 2.42% cases, and abortion was 2.91%. Presenting signs are compared with the age group of the study population.
In the study population IUGR were mostly seen in 31-35 years age group (26%) and lowest 21-30 age group (46%). IUD were mostly seen in 31-35 years age group (6%) and lowest 21-25 age group (1%). Abortion were mostly seen in 16-20 years age group (7%) and lowest 26-30 age group (0%)

The comparison shows that the marriage in teenage and the women got married at an older age, conceive for the first time and had any family history are at higher risk for preeclampsia.

Developing country like Bangladesh is still fighting against these serious conditions. The findings of the study showed that there are management facilities of preeclampsia and eclampasia remain in our country; it is a positive fact that the treatment of preeclampsia is available in Bangladesh.

Among the study population 90.77% patients were treated with Methyldopa, 84.95% with Labetalol, 40.29% with Nifedipine and 31.55% with Phenobarbital. In the study population 72% are prescribed multiple drugs and only 28% are prescribed Single drugs

These drugs are effective and safe for the management of eclampsia and also cost effective.

Lake of knowledge about preeclampsia is also seen to the study population. Some women mentioned that swelling on body during pregnancy is considered a normal sing.

Therefore it is highly probable that they will not be able to proactively understand the different symptoms that may require them to immediate seek medical care and place then in increased risk of preeclampsia.

Chapter Six
Conclusion

Conclusion

Pre-eclampsia is a rare pregnancy-related disease with an unpredictable course that can have serious consequences for both the mother and the fetus. The treatment is simple, i.e., delivery. Nonetheless, induced preterm delivery requires careful weighing of both maternal and fetal risk– benefit. Accordingly, identifying delivery criteria in case of pre-eclampsia is crucial to optimal management. Current research focuses on the prediction of onset of pre-eclampsia or even severe pre-eclampsia so as to allow early management and improve the morbidity and mortality associated with this disease. Government programmes as well as NGOs need to ensure increased campaign and training in helping the illiterate or low educated pregnant women regarding different risk factors that they need to be aware of in order to prevent the eclampsia. These steps should help improve maternal health considerably reducing maternal as well as fetal mortality. Specific tools for secondary prevention must also be developed for recurrent pre-eclampsia.

Chapter Seven
Reference

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