Pre-eclampsia and its outcome (Maternal and Neonatal Morbidity and Mortality) in the two Referral Hospitals (Windhoek Central and Katutura), Namibia

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A mini-thesis submitted in partial fulfillment of the requirements for the degree of Master of Public Health (MPH) in the School of Public Health, University of the Western Cape

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PREFACE

Medical practice without public health is not complete. Especially in the management of a pregnant woman and her child public health plays a pivotal role in understanding the risk factors and prevention of the occurrence of pregnancy related illness.

In my five years stay in Namibia, I observed many women with pre-eclampsia deliver by means of caesarean section irrespective of the severity of the disease and most pregnancies are terminated at early stage pre-maturely. It was also observed that most of the cases of previous caesarean section ending up with another caesarean delivery leaving an inverted T scar, i.e. if the previous scar was of Pfanestiel incision the second would be sub-umbilical vertical incision or vice versa. It is probable that the introduction of an acceptable guideline on management of pre-eclampsia could lead to normal delivery and hence reduction of undesired maternal morbidity and neonatal pre-maturity.

Presenting all Obstetric related problems in Namibia would be beyond the scope of a mini-thesis. However it is my belief that this preliminary study in outcome of pre-eclampsia could pave the way for further clinical and public health oriented research on other obstetric issues in Namibia. Hopefully such research will contribute to the improvement of the obstetric care in Namibia.

Writing a thesis, with the huge responsibility of being hospital administrator and full time medical officer and many sleepless nights in a busy hospital was not an easy task. However the thesis has come into its completion with great support from my family members, my advisor and friends and cooperation from my workmates.

Berhe Hailemariam

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Key Words:

Pre-eclampsia
Incidence
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Neonatal mortality
Risk factors
Management guideline
Caesarean section
Prematurity
Quality care

ABSTRACT

Pre-eclampsia and its outcome (Maternal and Neonatal Morbidity and mortality) in the two Referral Hospitals (Windhoek Central and Katutura), Namibia.

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Background: Pre-eclampsia is a multi-organ system disorder that occurs after the 20th week of gestation in pregnancy and is characterized by hypertension and proteinuria with or with out oedema. It is a major cause of morbidity and mortality for the woman and her child. Based on surveillance data, pre-eclampsia is one of the leading causes of maternal mortality in Namibia. However, there is no in depth study done in Namibia that looks at the extent of confirmed pre-eclampsia and its contribution to maternal and perinatal morbidity and mortality. There is also no standard management protocol currently recommended in Namibia.

The aim of the study is to evaluate the outcomes and quality of care given to pre-eclamptic patients treated in Windhoek Central and Katutura referral hospitals in Namibia with in the period of January 2003 to December 31, 2004.

Research design/ Research Methodology: The study is a retrospective, hospital based study. One hundred and ninety five records of women were retained for final study sample. A data abstraction tool was designed and information retrieved from the patients' files and record books were transferred to each individual abstraction tool. The data were transferred to an Epi-info 2002 program. Frequency and means for age, hospital stay, birth weight, and laboratory investigation were analyzed. Risk ratio, P-value, and 95% confidence interval were analyzed to compare across groups of variables. Permission to

conduct the study was granted by the ethical committee of Namibia and the Higher Degrees committee of the University of the Western Cape.

Results: The incidence of pre-eclampsia in the two-referral hospitals was 3.4%. The mean ages were 28.9 years, 27.5 and 24.1 years for the mild pre-eclamptic, severe pre-eclamptic and eclamptic women, respectively, P-value 0.0181 with a trend towards increasing severity with younger age. The mean hospital stay was 7 days for the mild pre-eclamptic, 7.3 days for the severe pre-eclamptic and 8.14 days for the eclamptic, P-value 0.5634. The mean gestational age for mild pre-eclamptics was 34.8 weeks, for severe pre-eclamptics 33.1 weeks and for the eclamptics 35.3 weeks, P-value 0.0158. Only 16.9% of the study group received magnesium sulphate. 88.7% gave birth by means of caesarean section. 31.8% of the pre-eclamptic women developed complications. Pre-maturity was observed in 51.5% of the neonates. Birth weight less than 2.5 Kg, gestational age $\leq$34 weeks, caesarean section and non-reactive CTG were risk factors for admission to neonatal ICU. Teenage pregnancy, being a state patient, lack of antenatal care, and living outside Windhoek were risk factors for severity of the disease. 51.5% were managed according to international or South African regional guidelines for pre-eclampsia.

Conclusion: Care given to the pre-eclamptic women was not totally in line with the international or South African regional guidelines of pre-eclampsia management. A guideline on the management and prevention of pre-eclampsia needs to be produced for Namibia, and further research on risk factors and on cost effectiveness of premature termination of pregnancy needs to be seriously looked at.

November 2005

DECLARATION

I declare that ***Pre-eclampsia and its outcome in the two Referral Hospitals (Windhoek Central and Katutura), Namibia*** is my own work, that it has not been submitted before for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged as complete references.

Berhe Hailemariam Woldeselassie November 2005

Signed: ----------

CHAPTER 1

INTRODUCTION

This chapter will introduce the study problem and research objectives, as well as, describe the study setting.

Definition of Pre-eclampsia:

Pre-eclampsia is a multi organ system disorder that occurs after the 20th week of gestation and is characterized by:

- Hypertension i.e. Blood pressure $\geq$ 140/90 mm/Hg
- Proteinuria (urine protein $\geq$ 0.3 g/24 hours) with or without
- Abnormal oedema (1)

When the diastolic blood pressure becomes above 110 mmHg and protein above 3 gm per day the condition is called severe pre-eclampsia (2) and if occurrences of seizures are superimposed on pre-eclampsia the condition is referred to as eclampsia (3).

Background

Pre-eclampsia is a major cause of morbidity and mortality for the woman and her child (4). Globally, each year more than four million women develop pre-eclampsia and approximately 100,000 women will have eclamptic convulsion with over 90% occurring in developing countries (5). It results in 12% of maternal deaths globally, up to 40% of

maternal death in some countries and is responsible for occurrence of up to 13% of still births and 20% of early neonatal deaths (6)

Research Problem:

Based on surveillance data, pre-eclampsia is one of the leading causes of maternal mortality in Namibia (7, 8). Though these surveillance data claim that pre-eclampsia has contributed to maternal mortality, in depth information about the cases was not available.

There is no in-depth study done in Namibia that looks at the extent of "confirmed" pre-eclampsia and its contribution to the maternal and perinatal morbidity and mortality.

In addition, there is no standard management protocol currently recommended in Namibia, which could assist uniformity in the diagnosis and management of pre-eclampsia. There is also no uniformity in referral threshold to higher levels of care.

The Saving Mothers Report on Confidential enquiries in Maternal Deaths in South Africa (1999-2001) noted poor quality of care to be a major contributor to maternal death from pre-eclampsia in South Africa. The deaths were attributed to lack of transport (11-20%), lack of appropriately trained medical staff (up to 55%), and failure to recognize patients' problems (12%) (9). In addition to this, 64% of the pre-eclamptic women who died in 1998 and 55.5% of those who died in 2001 had received sub-standard management (9). A similar study has not been conducted in Namibia. This study will also assess the quality of care received by pre-eclamptic women with in the period of 1, 2003 to

December 31, 2004 in two referral hospitals (Windhoek Central and Katutura) in Namibia

Research on pre-eclampsia is worthy of academic investigation, as there is no baseline information data that describes its incidence and its effect in pregnancy for Namibia. Understanding the incidence and risk factors of pre-eclampsia in Namibia will have an impact on prevention of the adverse effects of pre-eclampsia on the mother and the foetus.

Methodology

The study is retrospective, descriptive and analytical, quantitative hospital based study.

It attempts to answer whether pre-eclamptic women in the two referral hospitals had received care which is adherent to a standard protocol for management of pre-eclampsia. It looks at whether the pre-eclamaptic women received appropriate anti-hypertension drugs, or appropriate anti-convulsion drugs. It also looks at whether termination of pregnancy or delivery was employed at an appropriate time or whether proper mode of delivery was employed for the pre-eclamptic women.

Aim of the study

The aim of the study is to evaluate the quality of the care given to pre-eclamptic patients treated in Windhoek Central and Katutura referral hospitals in Namibia with in the period of January 1, 2003 to December 31, 2004.

Objectives of the Study

1. To establish the rate of confirmed pre-eclampsia in the two referral hospitals
2. To measure the incidence of maternal and perinatal mortality and morbidity in pre-eclamaptic women in the two referral hospitals
3. To assess quality of care including financial implications and risk factors for poor maternal and perinatal outcomes.
4. To use these information to recommend management protocols for pre-eclampsia

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The study will also contribute to the current knowledge by presenting its results and discuss whether the findings concur with findings of other studies or are different from them.

Study Setting

The study was conducted in Namibia at Khomas Region at Windhoek Central and Katutura referral hospitals at the department of Obstetrics and gynaecology maternity units. Khomas region is one of the thirteen regions in Namibia. According to the census indicators, 2001: Khomas region has an area of 37, 007 square kilometres and a population of 250, 262 of this 123, 613(49.4%) are females. The growth rate is 1.9 and is 93% urban. Fertility rate is 4.9 and infant death per 1000 live births is 143. The life expectancy for females is 56 years and for males 54 years (10).

The two hospitals are tertiary care institutions that receive referral of high and low risk pregnancies from district hospitals, general practitioners and specialist obstetricians in addition to their own patients.

Different Senior Medical superintendents lead Windhoek Central hospital and Katutura hospital. Their bed capacity is 552 and 831 respectively. However the specialists and medical officers work in both hospitals in rotation basis. The maternity ward bed capacity of Windhoek central hospital is 59 and that of Katutura 79. The average deliveries of the two hospitals are of 7,500 deliveries per year. There are three-consultant obstetrician and gynaecologists in the department of Obstetrics and Gynaecology but medical officers working in the department perform most of the caesarean sections.

The caesarean section rate for the hospitals is 16% and for Namibia 9%. The maternal mortality ratio for the two hospitals is 30 per 100, 0000 and for Namibia overall 271/ 100, 000 and perinatal mortality 79 per 1000 live births for the two hospitals and 27 per 1000 for Namibia respectively.

Pre-eclampsia is a major public health concern that affects both mothers and neonates worldwide. It is also one of the leading causes of maternal and neonatal morbidity and mortality in Namibia however no in depth study had been conducted so far. Hence, understanding the incidence and risk factors of pre-eclampsia in Namibia is necessary, as this would prevent the adverse effects of the disease to both the mother and the neonate, thus quality of care improves.

CHAPTER 2

LITERATURE REVIEW

Pre-eclampsia has been known since ancient times. In order to present evidence based discussion and conclusions, reviewing a literature that is relevant for the aim of the study was necessary.

The literature review includes, the incidence of pre-eclampsia its consequences and risk factors, pathophysiology of pre-eclampsia, diagnosis, neonatal outcome and its management. Brief discussion on expectant management versus aggressive management of pre-eclampsia, cost for different modes of delivery and prevention of pre-eclampsia is also included.

Detailed review on the mechanism of action of antioxidants in the prevention of pre-eclampsia was not included as it would be beyond the scope of the mini-thesis. However their general use and the promise they have in preventing the disease is highlighted.

PRE-ECLAMPSIA: INCIDENCE, CONSEQUENCES AND RISK FACTORS

Pre-eclampsia complicates 2-8% of pregnancies (3). Women with pre-eclampsia are at increased risk for *abruptio placentae, acute renal failure, cerebral haemorrhage, disseminated intravascular coagulation, pulmonary oedema, circulatory collapse and oedema* (1). In a retrospective cohort study of Murphy and Stirrat (11) on 71 pre-eclamptic women with gestational age less than 30 weeks 21% had developed HELLP

syndrome, 15% had abruptio placenta, 13% had renal failure and 1.4% eclampsia but maternal mortality was not observed. Al-Mulhim et al. also reported that the commonest complication to be abruptio placenta (12.6%) followed by oliguria (7.9%), coagulopathy (6%) and renal failure (4.1%) (12).

Risk Factors

Family history of hypertension, extremes of reproductive age, primi-gravidity, diabetes, renal disease, hypertension prior to pregnancy, and black race are some of the predisposing factor of pre-eclampsia (13,14,15). Women 40 years and above are more than five times likely to die of pre-eclampsia than those between 20 and 24 years older and black women's risk of dying from pre-eclampsia is three times more than white women (3.5 and 1.1 per 100, 000 respectively) (114) Some studies reflected that neither maternal age nor race had a significant effect on the outcome of pre-eclampsia, but suggested that increased severity of disease might be an important determining factor (15, 16).

In a cohort study of 878,680 pregnancies in 700 hospitals in Latin America and Caribbean, the following risks factors were significantly associated with increased risks of pre-eclampsia: Nulliparity (RR = 6.6, 95% CI 5.6-9.8), multiple pregnancy (RR= 2.0; 95%CI 0.9-6.4), history of chronic hypertension (RR=3.9; 95%CI 3.8 – 4.4), gestational diabetes mellitus (RR=3.9; 95% CI 4.6 – 6.6), maternal age $\geq$ 35 years (RR=6.7; 95%CI 5.8 -7.7) and a mother not living with infant's father (RR=2.1; 95% CI 1.5 -2.6). The pattern of risk factors among nulliparous and multiparous in this study was quite similar

(16). Type 1 diabetes (OR =5.58; 95%CI 2.72 - 11.43) and twin births (OR= 3.11, 95%CI 1.61 - 6.00) were also significantly associated with pre-eclampsia according to a study conducted by Ros et al. (18).

Pre-eclampsia occurs mainly in first pregnancies, suggesting that previous exposure to paternal antigen is protective (19, 20). Indeed a previous normal pregnancy is associated with lowered frequency of pre-eclampsia and the protective effect of multiparty is lost with change of partner (19). The idea that paternal antigen is protective is supported by the increased risk of pre-eclampsia in those who carry a pregnancy by a new father. Data based on Norwegian population (1967-1992) confirmed the impact of paternal factor on the risk of developing pre-eclampsia. Men who fathered pre-eclamptic pregnancies were twice as likely to father a pre-eclamptic pregnancy from different women regardless of whether she had a prior pre-eclamptic pregnancy or not (19,20). The protective effect of a long-term sperm exposure might also provide explanation for the high frequency of pre-eclampsia in teenage pregnancy (19).

Another study of Trogstad et al. showed that a change of paternity for the second pregnancy was associated with a reduced risk of pre-eclampsia after controlling for the time since first delivery (AOR = 0.80, 95%CI: 0.72-.90), but the interaction between change in paternity and time between deliveries was significant only for women with no previous pre-eclampsia. This implies that the increase in pre-eclampsia risk ascribed to a new father may be due to insufficient control for inter-pregnancy interval (21). Inter pregnancy interval less than six months and longer than 59 months are associated with an

increased risk of adverse maternal outcome (22). Conde-Agudelo and Belizan (22) in their study found that, compared with women with inter-pregnancy interval of 18 to 23 months, women with inter-pregnancy intervals longer than 59 months had significantly increased risk of pre-eclampsia (OR=1.83; 95% CI 1.72-1.94) and eclampsia (OR= 1.80; 95% CI 1.38-2.32).

Therefore health care providers should realize that the antenatal care of a multiparous patient with a new partner should be the same as in a woman presenting with her first pregnancy as far as the risk of pre-eclampsia is concerned and inter-pregnancy history needs to be taken into consideration.

Obesity is also a definite risk for developing pre-eclampsia. The exact mechanism by which obesity is associated with an increased risk of pre-eclampsia is not completely understood. Possible explanations include increased stress due to the hyper-dynamic circulation associated with obesity and dylipidemia or increased oxidative stress (19).

PATHOPHYSIOLOGY

The best way to cope with human disease is by preventing it from happening. This is only achievable if the cause is understood and if it is feasible to avoid or manipulate those causes (19). Therefore, understanding the pathophysiology of pre-eclampsia is necessary in order to prevent the occurrence of the disease.

Pre-eclampsia occurs only in the presence of a placenta and its resolution begins with the removal of the placenta (20). Even though the mechanisms behind these features are unknown, shallow endovascular cytotrophoblast invasion in the spiral arteries, an exaggerated inflammatory response and inappropriate endothelial cell activity are key features in the pathogenesis of pre-eclampsia (19). This leads to mal-adaptation of the spiral vessels, which interfere with normal villous development. In some cases, compensation can occur, but in others, poor villous development results in placental insufficiency. All women with placental trigger do not develop pre-eclampsia, therefore, the maternal response must be the decisive factor in the development of pre-eclampsia (20, 23).

It is also proposed that pre-eclampsia is a disorder secondary to decreased placental perfusion interacting with maternal constitutional factors that result in oxidative stress. There are increased levels of markers of lipid per-oxidation (including malondi aldhyde and 8-epi-prostaglandin F2alpha) and low concentration of water-soluble and lipid-soluble antioxidants in the plasma and placenta of pre-eclamptic women (4). The administration of antioxidants to women in early pregnancy decreases oxidative stress, endothelial activation and ultimately the frequency of pre-eclampsia (20). This also lends support to the potential role of oxidative stress in pre-eclampsia.

However, current knowledge does not adequately explain the occurrence of pre-eclampsia so it is difficult to determine which women will progress to the disorder. Therefore prevention remains a challenge.

DIAGNOSIS

There are no specific diagnostic investigations for pre-eclampsia, as a result the initial diagnosis of pre-eclampsia remains clinical and the classification of severity is mainly based on the blood pressure value and presence of proteinuria (23).

Measuring mean blood pressure is cumbersome to calculate in a clinical setting (2) and if second trimester mean arterial pressure predicts anything, it is gestational hypertension, not pre-eclampsia which is associated with greater perinatal morbidity and mortality (19). But if raised blood pressure and proteinuria are observed at the antenatal care setting the woman should be referred for evaluation and possible admission to a hospital (23).

Weight gain cannot be used to predicate the development of pre-eclampsia, as excess weight gain alone imparts no adverse prognosis to perinatal outcome (19).

The diagnosis of pre-eclampsia can also be based on laboratory tests. A baseline laboratory evaluation should be performed early in pregnancy in women who are at high risk for pre-eclampsia. Tests should include a hepatic enzyme level, a platelet count, a serum creatinine level, 24-hour urine protein and uric acid (19,23)

Uric acid

Uric acid is used as an indicator of disease severity in established pre-eclampsia and has been reported to be better predictor for adverse perinatal outcome than blood pressure (19). In a study conducted by Williams and Galena on 459 pregnant women, significant elevation in serum uric acid levels over normotensive pregnant women (285± 72

micromole/L) was observed in both the gestational hypertension group (341± 83 micro mole/l) and the pre-eclamptic group (384± 93 micro mol/L), P-value being <0.001 and <0.05, respectively (24). In this study however, uric acid levels, although significantly elevated in women with gestational hypertension and pre-eclampsia, were not prognostic indicators of severity of the maternal and foetal outcome (24). Xio et al., in their study stated that hyper-uricaemia and proteinuria were significantly associated with a higher rate of foetal and maternal complications (25). Brown and Buddle (26) also found that hyperuricaemia to be associated with higher rates of all maternal complications and Small for Gestational Age {SGA} babies. With multivariate analysis however, hyperuricaemia was not found to be significant predicator of adverse maternal and foetal out come (26).

Proteinuria

Proteinuria is a late sign of pregnancy-induced hypertensive disorders but HELLP {Haemolysis, Elevated Liver enzyme levels, Low Platelet count} syndrome and eclampsia could occur in the absence of proteinuria. Dipstick proteinuria is the most common screening test for pre-eclampsia. It is easy and cheap to use. The purpose of using dipsticks is to assist in timely diagnosis of pre-eclampsia (not to predict later pre-eclampsia) (19). However, the practitioner using dipsticks should be aware of the high false negative rates as negative dipstick results do not rule out proteinuria, especially if diastolic pressure is greater than 90 mmHg (3).

Haemoglobin

High maternal haemoglobin {HB} concentration and haematocrit are associated with low birth and placental weight, increased frequency of prematurity and perinatal mortality as well as maternal hypertension. Serial measurement of HB and hematocrit are used to monitor pregnancy at high risk of utero-placental insufficiency (19).

Increase in concentration of Haemoglobin in 2nd trimester could predict development of pregnancy induced hypertensive disorders (19). Brown and Buddle in their study also found that high maternal HB level to be a risk factor for SGA in women with pre-eclampsia (OR 3.7; 95% CI 1.1-12.8 and P=0.04) (26). The predictive values of less pronounced Haemoglobin concentration is low (26).

Platelet Count

In normal pregnancy the platelet count falls below 200x10^{9} counts / L because of the normal maternal blood volume expansion. In pre-eclampsia, the platelet count falls further, probably because of increased consumption and intravascular destruction (23). Brown and Buddle in their study also showed that SGA was associated with low platelet counts (OR= 1.4, 95% CI 1.1-1.8; P=0.02) (26).

Liver Enzymes

Measurement of Alanin Amino Transferase (ALT) and Aspartate Amino Transferase (AST) can assess liver involvement in serum; they increase in pre-eclampsia as a result of leakage across the cell membrane (19). If liver enzymes are elevated, i.e., if the ALT >35

u/L, AST> 30 u/L and LDH (lactose dehydrogenase) is > 670 u/L (27) a diagnosis of severe pre-eclampsia or HELLP syndrome can be entertained.

Uterine artery Doppler

Abnormal uterine artery Doppler results increase the likelihood of pre-eclampsia six-fold despite of the limited ability to screen for pre-eclampsia (19).

NEONATAL OUTCOME

Pre-eclampsia accounts for more than 40% of pre-mature deliveries (2) and substantially increases the risk of low birth weight, and SGA births (25,26,27,28). Ananth CV et al. in their study found eclampsia to have substantially greater risk of delivery of very low birth weight infants (birth weight $\leq$ 1, 499 gm; Risk Difference {RD}= 6.7%) and moderate low birth weight infants (1,500-2,499 gm; RD= 14.6%) and very pre-term (Gestational age < 33 weeks RD=7.1%) and moderately pre-term (33-36 gestational age; RD= 9.3%) birth compared with women with out hypertension (28).

A retrospective cohort study performed by Xiong et al. gestation was 0.6 weeks shorter in women with severe pre-eclampsia than in normotensive women (P<0.01). After adjustment for duration of gestation and other confounders their study showed that pre-eclampsia and severe pre-eclampsia increased the risks of intra uterine growth restriction (IUGR) and low birth weight with an adjusted odds ratio (AOR) being 2.65(1.73-4.39) for pre-eclampsia and 2.53 (1.19-4.93) for severe pre-eclampsia (28).

In a study done by Xio et al. pre-eclampsia was associated with 3.8-fold increased risks for low birth weight (95% CI 1.9-7.5) and women with pre-eclampsia were 3.6 times more likely to deliver an SGA newborn as compared with normotensive women (95% CI 2.3-5.7). After adjusting for maternal age, race, smoking, medical status and gestational age the OR for very low birth weight (VLBW) among the pre-eclamptic women was 30.7, (95% CI 7.0 to 134.9) compared to normotensive women (25). In another study of Odegard et al. a study which compared 307 live singleton born to pre-eclamptic women to 619 controls, pre-eclampsia and severe pre-eclampsia were associated with a 5% and 12% reduction in birth weight respectively, and birth weight was 23% lower than expected. The risk of SGA was four times higher (RR=4.2; 95% CI 2.2-8.0) in infants born after pre-eclampsia than in the control groups. Among primiparas pre-eclampsia was associated with nearly three fold higher risk of SGA (RR=2.8; 95%CI 1.2-5.9) (30).

Magee et al. in a multi-centre retrospective cohort study, found that 16.4% of pre-eclamptic pregnancies being complicated by birth weight less than third percentile or with one or more serious perinatal complications and 34.3% by pre-term birth (31); this finding was regardless of hypertension type. Victoria et al. also found an increased risk of SGA among infants born to women with any hypertensive disorder (RR=1.6; 95% CI 1.5-1.6) compared with infants born to women with normotensive pregnancies (27). There was an increased risk of SGA among infants born to women with mild pregnancy induced hypertension (RR 1.3; 95% CI 1.3-1.4), chronic hypertension with pregnancy induced hypertension (RR 2.2; 95% CI 1.8-2.6), severe pregnancy induced hypertension (RR 2.5; 95% CI 2.3-2.8), eclampsia (RR 3.5; 95% CI 2.2-5.7) and HELLP syndrome

(RR 3.8; 95% CI 3.2-4.5) compared with infants born to women with normotensive pregnancy (27).

Even though, pre-eclampsia is one of the risk factors for pre-maturity, the cause of pre-maturity in 50% of cases is iatrogenic, e.g. induction of labour or caesarean section to prevent death or disability in mother or foetus(32).

Very low birth weight (VLBW, less than 1500gms) and extremely low birth weight (ELBW, less than 1000gms) babies more often require re-admission to hospital in the first two years for respiratory infections and have higher incidences of asthma and otitis media (32).

MANAGEMENT OF PRE-ECLAMPSIA

Despite the high cost to families and health service sources, there is no effective management strategy other than elective delivery and no therapeutic intervention has been proven to prevent or delay the onset of the disease (19). Early diagnosis, close medical supervision and timely delivery are the cardinal requirements of the management of pre-eclampsia. Once the diagnosis is established, subsequent management should be based on the initial evaluation of maternal and foetal well-being. On the basis of the results of this evaluation a decision is then made regarding hospitalization, expectant management, or delivery with the following factors taken into account: the severity of the disease process, the status of mother and foetus, and the length of gestation. Irrespective of the management strategy chosen, the ultimate goal must first be the safety of the

mother and, second the delivery of a live infant who will not require intensive and prolonged neonatal care (32).

Even though delivery is the ultimate cure for pre-eclampsia, management aimed at benefiting the mother may be detrimental to the foetus because premature birth is a significant cause of infant morbidity and mortality (23,33,34). Hence the management of pre-eclampsia should be based on a stepwise protocol: Pregnant women should be screened; those at risk should be monitored once a diagnosis is made; the maternal condition should be stabilized; monitoring should be continued and delivery should be initiated at the best time for the mother and the baby (23). During labour, the management goals are to prevent seizures and control hypertension (35).

Mild Pre-eclampsia

Prolonged bed rest or hospitalisation is frequently recommended for mild pre-eclampsia but no randomised controlled trial has validated these approaches (33). The mother and foetus should be carefully monitored. Daily foetal movement counts together with regular non-stress or biophysical profiles need to be considered. Ultrasound determination of foetal weight and volume of amniotic fluid at diagnosis and every three to four weeks after diagnosis may be used to monitor patients. Maternal blood is checked weekly for platelet count, hepatic enzymes and serum creatinin levels (33). There is general agreement that in women at term with mild pre-eclampsia and a cervix favourable for induction at term (Bishop's score>6), delivery should be induced to avoid possible maternal and foetal complications (32). In contrast there is no agreement about the

management of mild pre-eclampsia earlier in pregnancy in particular about the need for bed rest, prolonged hospitalization, and antihypertensive drug therapy or anticonvulsant prophylaxis (32).

Severe Pre-eclampsia

Severe pre-eclampsia may be rapidly progressive resulting in sudden deterioration in the status of both mother and foetus, so that prompt delivery is recommended regardless of the duration of gestation. Prompt delivery is clearly indicated when there is imminent eclampsia, multiorgan dysfunction, or foetal distress or when severe pre-eclampsia develops after 34 weeks (32,33). Earlier in gestation, however, prolongation of pregnancy with close monitoring may be indicated in order to improve neonatal survival and reduce short and long-term neonatal morbidity (32).

Use of anti-hypertension and anticonvulsant drugs

The predominant mode for treating pre-eclampsia includes anti-hypertensive, anti-convulsions and interruption of pregnancy (36). Severe pre-eclampsia and eclampsia, are life threatening, therefore women suspected of having either condition should receive immediate and continuous attention at a hospital (37).

The primary objective of treatment in women with pre-eclampsia is to prevent cerebral complications such as encephalopathy and haemorrhage and the aim of therapy is to keep the mean arterial pressure below 126 mmHg and the diastolic pressure below 105 mmHg (but not less than 90 mmHg) (32).

Anti-hypertensive treatment benefits the mother with mild to moderated pregnancy induced hypertension. Methyldopa was safe in long term follow up of delivered babies. Atenanol is associated with increase in foetal growth restriction and inhibitors of angiotensin converting enzymes (ACE), so is contraindicated because of unacceptable foetal side effects and diuretics are contraindicated because they may cause growth restriction (23). A meta-analysis (38) of 11 trials with 570 participants did not support recommendations favouring hydralazine. These trials compared intravenous hydralazine 5-10 mg bolus; infusion 3-10 mg/hr (maximum dose 15-80 mg) or 20-40 mg intramuscularly with other anti-hypertensive, most commonly intravenous lobetalol 10-20 mg bolus over 2 minutes as needed or oral or sublingual nifidipine 5-10 mg orally every 30 minutes as needed. Compared with hydralazine, other agents were associated with less maternal hypotension, fewer caesarean sections, fewer placental abruptions and fewer low Apgar score. But in another 20 trials (1637 women) hydralazine was found to have less hypotensive effect than diazoxide and more effective than ketanserine (39. Nifedipine has a clinical advantage because it is given by mouth, and may be given by midwifery staff on 'as needed' basis, (every thirty minutes) in the absence of a doctor (38), however, caution should be used as it may also be associated with a dangerous decline in blood pressure.

In a Cochrane review of 11 trials (1,128 women), Magee and Duley observed that beta-blockers reduce the risk of severe pre-eclampsia (RR=0.37; 95% CI 0.26 to 0.53). In seven trials (856 women), the need for additional anti-hypertensive drug was reduced

(RR=0.44; 95% CI 0.31-0.62) (41). In 12 trials (1346 women) beta-blockers seem to be associated with an increase in SGA infants (RR= 1.36, 95% CI 1.02 to 1.82) but there was insufficient data for conclusion about the effect on perinatal mortality or pre-term birth (40). By subgroup analysis, beta-blockers may be less effective antiyhpertensives than calcium channel blockers (Verapamil or NiCad pine, OR= 2.52; 95% CI 1.29-1.52) (38).

Until better evidence is available, the choice of anti-hypertensive should depend on the experience and familiarity of an individual clinician with a particular drug and on what is known about the adverse maternal and foetal side effects (39).

Anti-convulsants/anti-epileptics including magnesium sulphate have been used to prevent eclampsia, with out conclusive scientific evidence that they are effective for this purpose (34,41). The Magpie trial, a large multi-centred double blinded randomised trial carried out in 33 countries and involving nearly 10,000 pregnant women with pre-eclampsia settled the issue for magnesium sulphate (34,41). Four thousand nine hundred sixty eight women in the study who received an injection of magnesium sulphate had a 58% lower risk of eclampsia (95% CI 40-71) than the 4958 given placebo. Maternal mortality was also lower among women allocated magnesium sulphate (RR= 0.55 95% CI 0.26-1.14) (1). Side effects were only minor: neither the mothers nor their babies showed any serious adverse effects from treatment (34,41). This trial showed that giving magnesium sulphate injections could save countless lives across the world if it could be given

routinely to pregnant women with pre-eclampsia. Importantly, it is a very inexpensive treatment, making it especially suitable for use in low-income countries (34).

Magnesium sulphate is substantially more effective than diazepam and phenytoin for treatment of eclampsia (42,43). In six trials (1336 women) magnesium sulphate was associated with a reduction in maternal death when compared to diazepam (RR=0.59; 95% CI 0.37 to 0.94). In seven trials (1441 women) magnesium sulphate was also observed a substantial reduction in the risk of recurrence of further fits (RR= 0.44; 95%CI 0.34-0.57) (42). In five trials involving 895 women, magnesium sulphate was associated with a substantial reduction in the recurrence of convulsion when compared with phenytoin (RR=0.31; 95%CI 0.20-0.47). There was also reduction in admission to intensive care units (RR=0.67; 95% CI 0.5-0.89) associated with the use of magnesium sulphate. In a study done by Dommisse in South Africa, 37% of the phenytoin group had recurrence of convulsion but none of the magnesium group had further convulsion; and was concluded that phenytoin sodium was not as effective as was magnesium sulphate (43). In one trial of 518 babies (RR=0.73; 95%CI 0.58-0.91) magnesium sulphate was associated with fewer admissions of babies to a special care baby unit (SCBU)(44).

DECISION FOR DELIVERY (Termination of pregnancy)

Delivery is the ultimate cure of pre-eclampsia and is always appropriate for the mother but may be responsible for neonatal adverse outcome particularly if it occurs at less than 34 weeks of gestation (23). The timing of delivery could also affect the outcome for

mother as most maternal deaths occur at post-partum (42). A rushed delivery, especially a caesarean section in an unstable patient may add to her risk rather than lowering it (42).

In extremely low birth weight infants who were born by caesarean delivery and after control for other risk factors, labour does not appear to play a significant role in adverse neonatal outcomes and neurodevelopment impairment at 18 to 22 months of correct age (46). Waldhawan R et al however reported that very low birth weight infants who were born by caesarean section had a higher incidence of grade 3 to 4 intraventricular haemorrhage (23.3% vs 12.1% P<0.001), periventiricular leukomalacia (8.5% vs 4.7%, P<0.2) and neurodevelopment impairment (41.7% vs 34.6%, P<0.02)(46). In a study done by Alexander and his colleagues, 145(52%) of the 278 women with severe pre-eclampsia who delivered infants weighing between 750 and 1500 gm had labour induced and 133 (48%) delivered by caesarean with out labour. Vaginal delivery was accomplished by 50(34%) women in the induced group (47) Neonatal outcomes including respiratory distress syndrome, grade 3 to 4 intraventricular haemorrhage, sepsis, seizures and neonatal death were similar in the two groups (47).

Immediate caesarean delivery compared to vaginal delivery confers no benefit to patients with severe pre-eclampsia (48). In a study done by Coppage KH and Polzin WJ, thirty seven of 59 women with severe pre-eclampsia who had been induced delivered vaginally and 22 of the 59 underwent caesarean delivery. Pulmonary complications in the mother and the neonate were more common in caesarean delivery (P<0.05) and no morbidity was decreased by caesarean delivery (48).

Any severe condition of the mother or the foetus should lead to prompt delivery (45). Therefore the indications for delivery in pre-eclampsia should be based on:

1. Foetal indications: severe intrauterine growth restriction, non-reassuring foetal surveillance, oligohydroaminios and
2. Maternal indications: Gestational age of 38 weeks or greater, platelet count below $100X10^9$ per mm^3, progressive deterioration of hepatic function, progressive deterioration of renal function, suspected placental abruption, persistent headache or visual changes, persistent severe epigastric pain, nausea or vomiting and eclampsia (35).

Caesarean section increases the health risks for mothers and babies as well as the costs of health care compared with normal deliveries (49). Even though the caesarean section rate has increased for the past 25 years there was little evidence of improved outcomes for the mother or baby and among the suggested factors for the increase are fear of litigation, the high false positive rate of intrapartum foetal heart monitoring and fear of damage to the maternal pelvic floor during delivery (50).

Obstetricians also need to consider the overall reproductive outcome for an individual woman and should consider future complications that might be incurred, as many women in the Namibian context might not come back to a tertiary level for delivery.

Expectant Management

Expectant management with plasma volume expansion and pharmacological vasodilatation under central haemodynamic monitoring of maternal circulation may delay and enhance foetal maturity and does not appear to be associated with an increased risk of maternal morbidity (51). In woman with severe pre-eclampsia at less than 34 weeks expectant management to improve neonatal mortality and morbidity may be performed under close monitoring of both mother and the foetus. However in women with mild pre-eclampsia, expectant management should be performed until 38 weeks (52).

Visser and Wallenburg (53) in their study of 254 women with severe pre-eclampsia between 20 and 32 weeks gestation reported that the median prolongation of pregnancy was 14 (range 0-62) days after treatment with volume expansion and vasodilatation and their perinatal mortality was only 20%. Hall et al. in a prospective study of 340 women presenting with early onset severe pre-eclampsia, found a mean gain of 11 days in managing the cases expectantly and their perinatal mortality was only 24% with a neonatal survival rate of 94 %(55). And the chief contributors for the neonatal mortality in their study were pulmonary oedema and sepsis (54).

In the Sibia et al. study, which compared immediate delivery to expectant management of women with severe pre-eclampsia, the average length of pregnancy prolongation in the expectant group, was 13.2 days (range of 4-28 days) (51) Compared with the immediate delivery group the expectant management group had significantly higher perinatal survival (76.4% vs. 35%), and lower incidence of neonatal complications. However no

differences were observed in the two groups with regard to maternal complications (51). Churchill and Duley in their review of two trials (133 women) reported that babies whose mothers had been allocated to the interventionist group had more hyaline membrane disease (RR=2.3; 95% CI 1.39-3.81) and more necrotising enterocolitis (RR=1.5 CI 1.13-1.55) than those allocated on expectant policy (55).

In a ten-year cohort study of pre-term pre-eclampsia by Mashiloange and Moodley (6) 46% of 108 patients who embarked on vaginal delivery delivered successfully. They suggest that vaginal delivery for low birth weight baby born to mothers with severe pre-eclampsia remote from term might be a reasonable option. In a retrospective study of Alexander et al., of 278 singletons, who weighed 750-1500gm or who were delivered because of severe pre-eclampsia vaginal delivery was accomplished in 34% of the induced groups (47). However, Regenstein AC et al in their study that they couldn't find difference between those who were delivered by caesarean section and those allowed to labour. They suggested that trial of labour should be considered in carefully selected women who have very low birth weight infants (56).

There is evidence from several randomised studies that an expectant management approach will result in a better perinatal outcome without an increase in maternal risks (19) but there are not sufficient data for any reliable recommendation for which policy of care (interventionist or expectant management for severe pre-eclampsia) to follow (55). Therefore if the expectant management approach is chosen, a perinatal centre with

expertise and facilities for maternal and neonatal intensive care is needed for such treatments (19).

COST FOR DIFFERENT MODES OF DELIVERY:

Both state and private facilities in Namibia procure pharmaceuticals and medical equipment from similar companies and pay similar amount of money, however the fees for state patients is highly subsidized. In the state health facility any patient who is admitted to the hospital pays N$25 (USD 4.00) irrespective of the duration of hospital stay and type of medication or operation provided. For instance a woman who gave birth vaginally and discharged after six hours of hospital stay and another woman who delivered by caesarean section and stayed in the hospital for five days pay four USD. But in a private hospital the fee for normal vertex delivery is a minimum of six thousand nine hundred eighty seven (N$ 6,987), which is equivalent to USD1,075 (one thousand seventy five) and if the woman stayed in the hospital for another two days the bill reaches N$ 10,097 (USD 1,554.00). The minimum bill for caesarean section and five days hospital stay is N$16,625 to N$ 17,092 (USD 2558 to USD 2630). The minimum hospital fee for a premature baby under 37 weeks gestation with respiratory distress syndrome who stayed in a private hospital only for twenty-four hours is N$ 69, 747 (USD 10, 731) and if admitted for two days it reaches up to N$ 104, 000 (USD 16, 000) (Personal communication MEDI CLINIC Swakopmund Branch- see sample annexure A). So although actual costs of care to the system are not available for Namibian hospitals, extrapolating from charge data in private hospitals may reflect the relative magnitude of

increased costs incurred to the public system in particular relation to the costs of neonatal care.

PREVENTION OF PRE-ECLAMPSIA

Prevention of pre-eclampsia should focus on the intervention and correction of patho-physiological changes (19). Currently there are no well-established measures for prevention of pre-eclampsia (35), however low dose aspirin, calcium and anti oxidants are believed to be used as effective and inexpensive preventive measures to reduce the risk of pre-eclampsia (19,35, 57).

Calcium

Calcium supplementation reduces the risk of high blood pressure in pregnancy particularly for women at high risk of gestational hypertension and in communities with low dietary calcium intake (19). Atallah et al. in their study observed reduction in the incidence of high blood pressure with calcium supplementation (RR=0.58, 95% CI 0.43 - 0.79) in 10 trials of 6634 women (58). The effect was greater amongst women at high risk of developing hypertension (four trials, 327 women: RR 0.47, 95% CI 0.22 - 0.97) and those with low baseline dietary calcium (five trials, 1582 women, RR=0.38, 95% CI 0.22 - 0.64). There was also a reduction in the risk of pre-eclampsia with calcium supplementation (11 trials, 6894 women: RR=0.35, 95% CI 0.20 - 0.60). There was no overall effect on the risk of pre-term delivery although there was a reduction in risk amongst women at high risk of developing hypertension (four trials, 568 women: RR =0.45, 95% CI 0.22 to 0.95) (58).

Anti-platelet drugs

Anti-platelet drugs, such as low dose aspirin, have small to moderate benefits when used for prevention of pre-eclampsia (59). Compared to women with normal pregnancies, women with pre-eclampsia have a relative excess thromboxane A2 compared to prostacycline. It has been hypothesized that the correction of thromboxane: prostacycline ratio by aspirin could prevent pre-eclampsia and its complications. In a large standardized controlled trial in 3, 135 low risk nulliparous women, the use of 60 mg aspirin had reduced the incidence of pre-eclampsia from 6.3 % to 4.6% but was associated significant increase in abruptio placenta. The effect of aspirin was also observed only in women whose blood pressure was >120 mmHg (1).

In the Cochrane review study of Duley et al. use of anti-platelet drugs was associated with a 15% reduction in the risk of pre-eclampsia (32 trials, 29331 women; RR= 0.85, 95% CI 0.78 -0.92). There was also an 8% reduction in the risk of pre-term birth (32 trials 28, 268 women, RR= 0.92, 95% CI 0.88 to 0.97) and a 14% reduction in foetal and neonatal death (30 trials, 30093 women; RR= 0.86, 95% CI 0.75 to 0.98) for women allocated to the anti-platelet group (55). SGA babies were reported in 25 trials (20,319 women) with no overall differences between the groups (RR= 0.92 to 1.01). There were no significant differences between treatment and control groups in the frequency of infants who were SGA (RR=0.91; CI=0.83-1.00) placental abruption, and induction of labour or caesarean section. The Cochrane reviewers concluded that, despite the potential benefits overall, it is not possible to make clear recommendations (60). Addition of ketanserin to aspirin is believed to have a substantial effect in decreasing the frequency of

poor pregnancy outcome among patients with mild to moderate mid-trimester hypertension (19).

In a randomised clinical trial conducted on 990 healthy nulliparous women in Tehran (April 1998-March 2001), pre-eclampsia was observed in 4.6% of the aspirin group, in 4% of the calcium group and in 10.1% of the control group. There were significant differences between the aspirin and control group ($P<0.05$) and calcium and control group ($P<0.05$) but there was no significant difference between the aspirin and calcium groups ($P=0.7$) (57).

Fish oil

Intake of Fish oil is also believed to lower the risk of preterm delivery. In a trial which included women with previous preterm delivery, intrauterine growth restriction, pre-eclampsia and twin pregnancies a reduction in the risk of preterm delivery from 33% to 21% (OR=0.54; CI 0.30-0.98) was observed but does not affect any of the other outcomes (19).

Anti Oxidants

The effects of vitamin C and E on markers of oxidative stress, endothelial activation and the frequency of pre-eclampsia have been assessed by Chappell et al (4). Two hundred and eighty three women were identified as being at risk of pre-eclampsia by abnormal two stage uterine artery Doppler and were randomly assigned vitamin C and E or placebo at 16-22 weeks' gestation. In the cohort who completed the study, the OR for pre-

eclampsia was 0.24 (95% CI 0.08-0.70, P=0.002). They concluded that supplementation with vitamin C and E may be beneficial in the prevention of pre-eclampsia in women at increased risk of the disease (4).

Magnesium

For prevention of recurrent seizures in women with eclampsia magnesium is more effective and has fewer risks than phenytoin and diazepam. If prophylaxis anticonvulsant is to be used magnesium is the drug of choice (42).

ANTENATAL CARE

Absence of antenatal care is strongly associated with eclampsia and foetal death (61). The presence of a risk factor, i.e., first pregnancy, previous pre-eclampsia, ≥ 10 years since last baby, age ≥ 40 years, body mass index ≥ 35, family history of pre-eclampsia (mother or sister), booking diastolic blood pressure ≥ 80mmHg, proteinuria at booking ≥ +1 on more than one occasion or (≥ 300 mg/24 h), multiple pregnancy, and pre-existing medical conditions (hypertension, renal disease and diabetes) should be identified during ANC (61).

Although pre-eclampsia is not preventable, deaths and morbidity from this disease can be prevented thorough early detection, careful monitoring and treatment of the disorder. Therefore, in order to decrease pre-eclampsia related mortality and morbidity appropriate prenatal care must be available to all women irrespective of their social and financial background (35). Because pre-eclampsia is also a unique syndrome of pregnancy that is

potentially dangerous for both mother and foetus; close medical supervision and timely delivery should be provided to all pre-eclamptic women (33,35).

SUMMARY, CONCLUSION AND MOTIVATION FOR THE STUDY

Pre-eclampsia complicates about 2-8% of pregnancy and its main predisposing factors are family history of hypertension, extremities of extremes of reproductive age, primi-gravdity, renal disease, hypertension prior to pregnancy black race and obesity. The protective effect of long-term sperm exposure could also provide explanation for the frequency of pre-eclampsia in teenage pregnancy. As all women do not develop pre-eclampsia maternal response is believed to play a decisive factor in the development of pre-eclampsia.

Initial diagnosis is clinical and the severity of the disease is mainly based on blood pressure and proteinuria. However LFT, FBC, platelet count and uric acid levels are important in determining the severity of the disease.

The cardinal requirements for the management of pre-eclampsia are early diagnosis, close supervision and timely delivery and the mode of treating pre-eclampsia includes antihypetension drugs, anticonvulsants drugs and termination of the pregnancy. In early gestation prolongation of pregnancy with close monitoring could be indicated, however in case of imminent eclampsia or multi-organ dysfunction or foetal distress or sever pre-eclampsia after 34 weeks of gestation prompt delivery is indicated. However care needs to be taken, as immediate caesarean delivery might not always benefit the woman and her

baby. Considering expectant management, especially in cases of mild pre-eclampsia would prevent pre-maturity on the neonate.

In the management of severe pre-eclampsia or eclampsia, magnesium sulphate was found to be more effective than diazepam and phenytoin. It is also cost effective and could be used in countries that are resource poor.

The benefit of anti oxidants and anti platelets has also been reported in different studies and was observed that they have decreased the incidence of pre-maturity in the neonate and development of eclampsia in the mother. However substantial evidence is required for their routine use during antenatal care or for the high-risk patients who might develop pre-eclampsia.

Pre-eclampsia is a disease that is not yet fully understood, however, with proper ANC and production of management guidelines suitable for different set-ups, its adverse effect to mothers and their offspring could be curtailed from the outset.

Sub-optimal clinical management of pre-eclampsia can have serious consequences, it is necessary to formulate and implement clinical practice guidelines for Namibia. This study will take the first step by assessing the current quality of care being offered in Namibia for pregnant women experiencing pre-eclampsia and then recommendation can be made for ways to improve that care and the development of appropriate clinical practice guidelines.

CHAPTER 3

RESEARCH DESIGN/ RESEARCH METHODOLOGY

This section will review the methodology employed to address the aim of the study, i.e., to evaluate the quality of the care given to pre-eclamptic patients treated in Windhoek Central and Katutura referral hospitals in Namibia with in the period of January 1, 2003 to December 31, 2004. The methodology includes the design and set-up for the study method employed, sampling technique, and sample size. The methodology further looks in to data collection techniques that included gaining access to the study area, ethical consideration, pilot testing and actual data collecting method used. It will also review the limitations of the study.

METHOD AND TECHNIQUE

This is a retrospective, descriptive and analytical, quantitative, hospital based study.

All women who gave birth within the study period were considered as source population. Those women who had pre-eclampsia were identified from all deliveries. In order to avoid incomplete information, effort was made to gather as much information as possible from different sources (operation notes, operation record books, nurse's reports and others). A record abstraction tool was prepared and data on demographic information, management of cases and outcome was collected in to this tool.

JUSTIFICATION FOR CHOICE OF METHOD

Three fourths of women in Namibia give birth at health institutions. The proportion of births delivered in health facilities has also increased from 67% in 1992 to 75% in 2000(3). This shows that the majority of women in Namibia prefer to deliver in hospitals; hence the hospital data for this study should be reasonably representative of the study population.

One disadvantage of a retrospective study is its potential for information bias. However, retrospective studies are less costly and less time consuming compared to prospective study.

A prospective cohort study, although is more bias free than retrospective studies, was not chosen because of its expensive and time-consuming nature. The student also couldn't get funds from interested organizations, which would enable him to conduct the research, due to the fact he was not a citizen of the country (Namibia). Hence, a prospective cohort study was not feasible due to financial constraints.

Qualitative methods were not also chosen for this study because the information that could be retrieved through interview or questionnaire from the health professionals might be biased as the health professionals were directly involved in the management of the cases, and also substantial recall bias could be expected.

Interviewing the patients would have helped to get more information on how they had been managed but is beyond the capacity of this study, as it requires a huge amount of finance and manpower to reach the subjects.

SAMPLING METHOD & SAMPLE SIZE

From January 2003 to December 2004 there were 15, 815 deliveries in the Windhoek central and Katutura hospitals. Six hundred and ten women were admitted as cases of hypertension in pregnancy, which makes the incidence of hypertension in pregnancy 3.9%.

Three hundred and eighty records of women with a diagnosis or listed complications of pre-eclampsia or eclampsia, or symptoms associated with pre-eclampsia (i.e. hypertension, convulsions, oedema, etc.) were selected from the maternity and theatre register books of the study period. The latter (symptoms) were included to improve complete case finding. These files were systematically retrieved and reviewed for the following inclusion criteria (standard definition for diagnosis of pre-eclampsia): blood pressure $\geq$140/90, proteinuria $\geq$+1, with or without oedema (1).

Due to potential loss or unavailability of older records, cases were selected in backward fashion from two years of hospital maternity and theatre registers and records until the desired sample size was obtained. Those with symptoms but not confirmed diagnosis according to criteria were excluded.

Sample size

Epi info 2000 program was used to calculate the sample size for a descriptive study. The expected frequency of pre-eclampsia was 6.0% and the worst acceptable 2% and confidence interval 99%. The sample size calculated was 230. However, only one hundred and ninety five (85%) records of women were retained for final study sample, as 15% of the files were not complete and diagnosis could not be confirmed.

INFORMATION AND DATA SOURCES

Information on demographic, clinical, laboratory and management of all pre-eclamptic patients and their babies who were admitted to the two referral hospitals during the study period were retrieved from the maternity admission registers, delivery books and operation books. Information on the following were collected:

1. Mother includes, age, parity, gestational age, hospital stay, ANC attendance, interventions during antenatal and perinatal period, mode of deliver and complications.
2. Neonate includes, birth weight, admission to ICU, complications
3. Laboratory data which includes, urine protein, Haemoglobin, Liver function tests (LDH, ALT, AST), platelet count, uric acid and urea and electrolyte levels
4. Management of pre-eclampsia: diagnosis on admission, fluid therapy, commencement of ant-hypertension or anti-convulsion drugs and mode of delivery

Data Abstraction Tool

A data abstraction tool was designed and developed by the researcher (Annexure B) based on existing tools and selected guidelines.

VALIDITY AND RELIABILITY

Reliability is the degree of consistency of a measurement with which it measures the attribute it is supposed to measure and be able to give same results each time it is being tested (62).

Validity is a term for how well an instrument or measurement procedure measures what it purports to measure. Commonly used measures of validity are content, face, criterion, and construct validity. For a questionnaire, content validity indicates the degree to which the items on the instrument are representative of the knowledge or the characteristics being investigated (62).

In order to strengthen its validity and reliability the data abstraction tool was reviewed by an obstetric specialist for content validity. Data was pre-coded to reduce coding error. The tool was pre-tested on ten files of cases of pre-eclampsia in another district hospital and was revised.

The medical records at the two study hospitals were relatively complete and several sources of data were used to reduce potential information bias.

The information retrieved from the patients' files and record books were transferred to each individual abstraction tool.

Record of neonatal birth weight was not found in 15 (8%) of the cases and birth weight of the neonates who were declared dead was not recorded either in ICU or maternity registers.

The researcher completed all the data abstraction. He is a qualified Obstetrician and Gyanaecologist with 14 years of experience, so he is experienced in reviewing and interpreting medical records. He had completed the literature review, and has familiarised himself with the treatment protocols for pre-eclampsia as training for data collection. There was no duplicate record review to assess quality of the abstraction due to limited availability of comparable expertise in the region and the limited scope of a mini-thesis. However, due to the experience of the researcher, quality of data abstracted is expected to be high.

The data were transferred to an Epi-info 2002 program. Data was cleaned by examining frequencies and logical checking was done for percentages. Outliers and other identified data queries were checked and corrected as appropriate.

LIMITATIONS OF THE STUDY

- Because the study is a retrospective hospital based study an information bias could be inevitable.
- The study is a hospital-based study. Even though majority of women in Namibia prefer to give birth in hospitals there could probably be pre-eclamptic women who had given birth at home during the study period, thus not included in the study.
- The study had a small sample size, which may have limited ability to examine rare events.
- The lack of a control group of women without pre-eclampsia restricted ability to examine risk factors for pre-eclampsia in general. This study therefore only focused on risk factors related to severity of illness.

DATA ANALYSIS

Data analysis and presentation

The incidence of confirmed pre-eclampsia is deduced by dividing the number of pre-eclamptic cases who met the standard clinical definition for pre-eclampsia and presented in the inclusion criteria and who delivered with in the study period (January 2003 to December 2004) divided by the total number of the cases who gave birth with in the study period (January 2003 to December 2004).

Frequency and means for age, hospital stay, birth weight, different laboratory investigations for the different stages of pre-eclampsia are analyzed. The care received by

the three groups of women separated by severity/diagnosis (mild pre-eclampsia, severe pre-eclampsia and eclampsia) is also analyzed. The mode of delivery, indications for caesarean section and complication for each diagnostic (severity) group are also analysed.

Statistical inference

Risk Ratio, P-value, 95% confidence interval was analyzed to compare across groups of variables (age, parity, address, status, antenatal care, uric acid level). For this purpose the cases were divided into mild pre-eclampsia and severe pre-eclampsia (which comprises the severe pre-eclamptic and the eclamptic women). The variables were dichotomised as Caesarean section done (Yes) and not done (No), Age≥34(Yes) and Age<34 (No), Antenatal care attended (Yes) and not attended (No), Primipara (Yes) and multipara (No), Windhoek (Yes) and Out side Windhoek (No), State patient (Yes), private (No). Indication for caesarean section was also dichotomised as Caesarean section done only because of pre-eclampsia/eclampsia (Yes) and because of additional maternal or foetal indications (No). In order to measure the rate of those who received quality or contrary care, a variable as comment was included on the abstraction tool and was dichotomised as managed according to protocol guideline (Yes) and not according to protocol (No).

It was also looked into whether the severity of the disease contributed to the high caesarean section rate, or to low birth rate. Relations between neonatal birth weight or gestational age or caesarean section or the three categories of pre-eclampsia to neonatal ICU admission were also analysed in order to look into the general management and possible financial implications.

Quality care

The quality of care was measured based on the technical care that the study subjects received during their stay in the hospitals. The quality of care that has been given to the patients at different levels (during ante partum, stages of labour, and when complication were observed) including appropriateness of medications and mode of delivery was measured against the standard management protocols for pre-eclampsia as recommended by the South African National Department of Health and National Committee for the Confidential Enquiry into Maternal Deaths (63). Copies of these protocols can be found in Annex C. Note that quality is not identical to good outcomes. Poor outcomes occur despite the best possible health care because disease sometimes defeats the best effort of the health care professionals. Conversely patients may do well despite poor quality care (64). Management of cases outside the standard protocol in the study were then considered poor quality care, regardless of the outcome.

FEASIBILITY OF THE STUDY

Permission was granted from the permanent secretary of the Ministry of Health and Social service of Namibia in order to conduct the study in Windhoek central and Katutura Referral hospitals.

ETHICAL ISSUES

It was believed that the study would contribute to the provision of quality care to pre-eclamaptic women. Permission to conduct the study was granted by the Ethical

Committee of Namibia (Annex D) and the Higher Degrees Committee of the University of the Western Cape.

The study provides information that is valuable for devising policy for reduction of maternal and perinatal morbidity. It will also assist in the development of a clinical and preventive management protocol.

As the study consisted entirely of confidential record review, no informed consent was deemed necessary. Precautions were taken to keep personal identifier data separate from data collected using confidential study numbers.

NOTE ON TERMINOLOGY

For simplification the word "pre-eclampsia" is often used in the results and discussion chapters to generically to represent all women and levels of disease severity (mild & severe pre-eclampsia and eclampsia) included in this study, although the author recognises that once a woman progresses to eclampsia she is no longer "pre" - eclamptic.

Maternal mortality: refers to a woman dying in pregnancy, childbirth or within 42 days of the end of pregnancy (65).

Neonatal Mortality: refers to all still births and neonatal deaths in the first week of pregnancy (65).

CHAPTER 4

RESULTS

This chapter includes: Descriptive analysis for socio-demographic data, admission to the hospital, management at the antenatal ward, laboratory investigations, mode of deliveries, birth weight and complication of neonate and neonatal admission to an ICU. It also includes an analytic analysis of risk factors for admission to neonatal ICU and low birth weight and risk factors for severity of pre-eclampsia.

DESCRIPTIVE ANALYSIS

Incidence of Pre-eclampsia

The incidence rate of pre-eclampsia in the two-referral hospitals was 3.4%. Of the 195 women with the diagnosis of pre-eclampsia, 97 (49.7%) had mild pre-eclampsia, 77(39.5%) severe pre-eclampsia and 21(10.8%) eclampsia (Table I).

Socio- Demographic data:

The mean ages were 28.9, 27.5 and 24.1 years for the mild pre-eclamptic, severe pre-eclamptic and eclamptic women respectively. These mean differences were significant (P-value 0.0181 and suggested a trend towards increasing severity with younger age. (Table I). One hundred and eleven (57%) of all pre-eclamptic women were from Windhoek and 88 (43%) from outside Windhoek (Table I). Ethnically 61(31.6%), 42(21.8%), 32(16.6%), 28(14.5%), 13(6.7%), 10(5.2%) were Ovmabo, Damara, Herero, Coloured, White, and Nama respectively (Table I). The majority, 167(85.6%) of all pre-eclamptic women were state patients while 28(14.4%) were private (Table I).

Table I: Socio- Demographic Data

DIAGNOSIS				
	Mild pre-eclampsia	**Severe pre-eclampsia**	**Eclampsia**	**Total #**
AGE (years)*				
<15	1(1.0%)	0(0.0%)	1(4.8%)	2(1.0)%)
16-20	13(13.4%)	12(15.6%)	6(28.6%)	31(16.0%)
21-25	24(24.7%)	22(28.6%)	6(28.6%)	52(26.8%)
26-30	14(14.4%)	16(20.8%)	4(19.0%)	34(17.5%)
31-35	22(22.7%)	16(20.8%)	3(14.3%)	41(21.0%)
36-40	19(19.6%)	6(7.8%)	1(4.8%)	26(13.4%)
41-45	3(3.1%)	4(5.2%)	0(0.0%)	7(3.6%)
46+	0(0.0%)	1(1.3%)	0(0.0%)	1(0.5%)
ADDRESS				
Windhoek	64(66.0%)	43(55.8%)	4(19.0%)	111(56.9%)
Outside Windhoek	33(34.0%)	34(44.2%)	17(81.0%)	84(43.1%)
Ethnic Group				
Ovambo	31(32.0%)	21(27.3%)	9(42.9 %)	61(31.6%)
Damara	15(15.5%)	21(27.3%)	6(28.6%)	42(21.8%)
Herero	17(17.5%)	13(16.9%)	2(9.5%)	32(16.6%)
Coloured	15(15.5%)	11(14.3%)	2(9.5%)	28(14.5%)
White	10(10.3%)	3(3.9%)	0(0.0%)	13(6.7%)
Nama	6(6.2%)	4(5.2%)	0(0.0%)	10(5.2%)
Others	2(2.1%)	3 (3.9%)	2(9.5%)	7(3.6%)
Status				
State	77(79.4%)	70(90.9%)	20(95.2%)	167(85.6%)
Private	20(20.6%)	7(9.1%)	1(9.1%)	28(14.4%)
Total	**97(49.7%)**	**77(39.5%)**	**21(10.8%)**	**195(100.0%)**

*Mean age

Diagnosis	Observed	Total	**Mean**	Variance	Std. Dev
Mild pre-eclampsia	96	2783	**28.9896**	55.5683	7.4544
Severe Pre-eclampsia	77	2115	**27.4675**	52.6206	7.254
Eclampsia	21	507	**24.1429**	36.4286	6.0356

Chi square= 8.021 Degree of freedom= 2 P value= 0.0181

Medical and Pregnancy History

Overall, 112(57.4%) of the pre-eclamptic women were multipara and 83(42.6%) primipara (Table II). Negative past medical history was found in 165(84.6%), while 14(7.2%) of women had history of hypertension, 2(1%) diabetes mellitus, 1(0.5%) renal disease and 1(0.5%) neurological disorder. In 12(6.2%) the status of past medical history was not known (Table II). Past pregnancy history was not applicable in 83(42.6%) of the pre-eclamptic women because they were primiparas. It was negative in 82(42.0%), 7(3.6%) had previous caesarean section, 7(3.6%) had pregnancy induced hypertension and caesarean section, 7(3.6%) had pregnancy induced hypertension, 7(3.6%) had neonatal or intra uterine foetal death, 1(0.5%) had diabetes mellitus and 1(0.5%) had post partum haemorrhage (Table II).

Table II Medical and Pregnancy History

DIAGNOSIS				
	Mild pre-eclampsia	**Severe Pre-eclampsia**	**Eclampsia**	**Total #**
Parity				
Para I	37(38.1%)	34(44.2%)	12(57.1%)	83(42.6%)
Multi-Para	60(61.9%)	43(55.8%)	9(42.9%)	112(57.4%)
Past Medical History				
Negative	81(83.5%)	66(85.7%)	18(85.7%)	165(84.6%)
Hypertension	6(6.2%)	8(10.4%)	0(0.0%)	14(7.2%)
Unknown	8(8.2%)	2(2.6%)	2(9.5%)	12(6.2%)
Diabetes Mellitus	1(1.0%)	1(1.3%)	0(0.0%)	2(1.0%)
Renal Disease	1(1.3%)	0(%)	0(0.0%)	1(0.5%)
Neurological	0(0.0%)	0(%)	1(4.8%)	1(0.5%)
Past pregnancy History				
Not applicable	37(38.1%)	34(44.1%)	12(57.1%)	83(42.6%)
Negative	45(46.4%)	30(39.0%)	7(33.3%)	82(42.0%)
PIH+C.S	4(4.1%)	3(3.9%)	0(0.0%)	7(3.6%)
C.S	4(4.1%)	3(3.9%)	0(0.0%)	7(3.6%)
PIH	2(3.1%)	3(3.9%)	2(9.5%)	7(3.6%)
Neonatal +IUFD	3(3.1%)	4(5.2%)	0(0.0%)	7 (3.4%)
Diabetes (gestational)	1(1.1%)	0(0.0%)	0(0.0%)	1(3.5%)
PPH	1(1.1%)	0(0.0%)	0(0.0%)	1(0.5%)
Total	**97(49.7%)**	**77(39.5**	**21(10.8%)**	**195(100.0%)**

Admission to the Hospital

The length of stay in the hospital was 1-5 days for 76(39.4%), 6-10 days for 80(41.5%), 11-15 days for 28(14.5%), 16-20 days for 7(3.6%) and 21-25 days for 2(1.0%) of all the pre-eclamptic women. The mean hospital stay was 7.0 days for the mild pre-eclamptic, 7.3 days for the severe pre-eclamptic and 8.14 days for the eclamptic. Chi-square was 1.1477 and P- value 0.5634 (Table III).

On admission 101(51.8%) of all the patients had no physical complaints, while 56(28.7%) had a headache, 22(11.3%) epigastric pain, 10(5.1%) convulsion, 4(2.1%) blurred vision and 2(1.0%) vaginal bleeding (Table III).

Table III Admission to Hospital

DIAGNOSIS				
	Mild pre-eclampsia	**Severe Pre-eclampsia**	**Eclampsia**	**Total**
Hospital Stay (Days)*[1]				
1-5	38(40.0%)	30(39.0%)	8(338.1%)	76(39.4%)
6-10	43(45.3%)	32(41.6%)	5(23.8%)	80(41.5%)
11-15	9(9.5%)	12(15.6%)	7(33.3%)	28(14.5%)
16-20	4(4.2%)	2(2.6%)	1(2.6%)	7(3.6%)
21-25	1(1.1%)	1(1.3%)	0(0.0%)	2(1.0%)
Chief Complaint				
No complaint	76(78.4%)	23(29.9%)	2(9.5%)	101(51.8%)
Head ache	14(14.4%)	35(45.5%)	7(33.3%)	56(28.7%)
Epigastric pain	5(5.2%)	16(20.8%)	1(4.8%)	22(11.3%)
Convulsion	0(0.0%)	0(0.0%)	10(47.6%)	10(5.1%)
Blurred vision	0(0.0%)	3(3.9%)	1(4.8%)	4(2.1%)
Vaginal bleeding	2 (2.1%)	0(0.0%)	0(0.0%)	2(1.0%)
Gestational age (Weeks) *[2]				
22-25	2(2.1%)	2(2.6%)	0(0.0%)	4(2.1%)
26-30	16(16.5%)	23(29.9%)	1(4.8%)	40(20.6%)
31-35	24(24.7%)	20(26.0%)	9(42.9%)	53(27.3%)
36-40	52(53.6%)	32(41.6%)	10(47.6%)	94(48.5%)
41+	3(3.1%)	0(0.0%)	0(0.0%)	3(1.5%)
Antenatal Care				
Yes	82(84.5%)	53(68.8%)	4(19.0%)	139(71.3%)
No	15(15.5%)	24(31.2%)	17(81.0%)	56(28.7%)
Total	**97(49.7%)**	**77(39.5%)**	**21(10.8%)**	**195(100.0%)**

***[1]Mean Hospital stays by diagnosis**

Diagnosis	Observed	Total	Mean	Variance	Standard deviation
Mild pre-eclampsia	95	671	7.0632	16.5066	4.0628
Severe pre-eclampsia	77	566	7.3506	16.5066	3.9596
Eclampsia	21	171	8.1429	18.0286	4.2460

Chi Square= 1.1477 df= 2 P value=0.5634

***[2] Mean Gestation age (weeks)**

Diagnosis	Observed	Total	Mean	Variance	Standard deviation
Mild pre-eclampsia	97	3378	**34.8247**	17.4377	4.1758
Severe pre-eclampsia	77	2554	**33.1688**	18.0106	4.2439
Eclampsia	20	706	**35.3000**	5.800	2.4083

Chi Square= 8.2943 df= 2 P value= 0.0158

Gestational age on admission was 4(2.1%) at 22-25 weeks, 40(20.6%) at 26-30 weeks, 53(27.3%) at 31-35 weeks, 94(48.3%) at 36-40 weeks and 3(1.5%) at 41+ weeks. The mean gestational age for the mild pre-eclamptic was 34.8 weeks, 33.1 weeks for the severe pre-eclamptic and 35.3 for the eclamptic. The Chi-square was 8.2943 and P-value 0.0158 (Table III) suggesting a statistically significant difference, which appears to be lower gestational age in the severe pre-eclampsia group, compared with the mild pre-eclampsia and eclampsia groups which appear similar.

Management at Antenatal ward

Liver function tests, uric acid or urea and electrolyte (U&E) or platelet count was checked in 142(72.8%) but not checked in 53(27.2%) of the 195 pre-eclamptic women (Table IV).

One hundred eighty five (95.4%) of all the pre-eclamptic women had been given antihypertensive drugs of which 89 where cases of mild pre-eclampsia (Table IV).

Cardiotocography reading was reactive in 143 (73.3%), deceleration was observed in 31(15.9%) and was not done in 21(10.8%) of the study groups. Deceleration was observed in 14(14.4%) of the mild pre-eclamptic, 15(19.5%) of the severe pre-eclamptic and 2(9.5%) of the eclamptic women (Table IV).

Table IV Management (Antenatal Ward)

DIAGNOSIS				
	Mild pre-eclampsia	**Severe pre-eclampsia**	**Eclampsia**	**Total #**
LFT/Urea &electrolyte/Uric acid/Platelet checked				
Yes	63(64.9%)	68(88.3%)	11(52.4%)	142(72.8%)
No	34(35.1%)	9(11.7%)	10(47.6%)	53(27.2%)
Anti-hypertension given				
Yes	89(91.8%)	75(98.7%)	21(100%)	185(95.4%)
No	8(8.2%)	1(1.3%)	0(0.0%)	9(4.6%)
CTG				
Reactive	68(70.1%)	60(77.9%)	15(71.4%)	143(73.3%)
Deceleration	14(14.4%)	15(19.5%)	2(9.5%)	31(15.9%)
Not done	15(15.5%)	2(2.6%)	4(19.0%)	21(10.8%)
MgSulphate given				
Yes	0(0.0%)	18(23.4%)	15(71.4%)	33(16.9%)
No	0(0.0%)	59(76.6%)	6(28.6%)	65(83.1%)
Not necessary	97(100.0%)	0(0.0%)	0(0.0%)	97(100.0%)
Total	**97(49.7%)**	**77(39.5%)**	**21(10.8%)**	**195**

Administration of Magnesium Sulphate was not necessary in 97(49.7%) as they were cases of mild pre-eclampsia. It was administered in 33 (16.9%) of the study group but was not administered in 65(33.3%) of the study group. Fifty-nine (76.6%) of the severe pre-eclamptic women and 6(28.6%) of the eclamptic didn't receive the treatment (Table IV)

Laboratory results (Liver function tests)

LDH was checked in 132 (67.7%) of the pre-eclamptic women and the normal value for LDH is 91-181 IU/L. Twenty-one (15.9%) of the 132 pre-eclamptic women had normal LDH level. The mean LDH level was 261 IU/L, for the mild pre-eclamptic, 289 IU/L for the severe pre-eclamptic and 291IU/ L for the eclamptic. The chi-square was 5.4610 and P-value 0.0652. These mean differences were marginally significant and suggested a trend towards increasing severity with increasing level of LDH (Table V).

ALT was checked in 132 (67.7%) of the 195 pre-eclamptic women. The normal range of ALT was 10-60 IU/ L. Only 4(3.0%) had an abnormal ALT reading. The mean ALT level was 17.4 IU/L, 22.7 IU/L and 21.7 IU/L for the mild pre-eclamptic, severe pre-eclamptic and eclamptic women, respectively. Chi Square was 1.5812 and P-value 0.4536 (Table V).

AST was checked in 131(67%) of the 195 pre-eclamptic women. The normal range for AST is 10-42 IU/ L. Twenty two (16.8%) of all the pre-eclamptic women had AST level of $\geq$ 43 IU/L. The mean AST levels were 26.5 for the mild pre-eclamptic group, 33.9 for

the severe pre-eclamptic and 34.3 for the eclamptic. Chi-square was 4.1945 and P-value 0.1228 (Table V).

Table V Laboratory Results (Liver Function Tests)

DIAGNOSIS				
	Mild pre-eclampsia	**Severe pre-eclampsia**	**Eclampsia**	**Total**
LDH (IU)				
91-180	16(25.8%)	3(5.1%)	2(18.2%)	21(15.9%)
≥181	46(74.2%)	56(94.9%)	9(81.8%)	111(84.1%)
Total	**62(47.0%)**	**59(44.7%)**	**11(8.3%)**	**132(100.0%)**
ALT (IU)				
0-60	62(100.0%)	55(96.6%)	11(100%)	128(97.0%)
≥61	0(0.0%)	4(3.4%)	0(0.0%)	4(3.0%)
Total	**62(47.0%)**	**59(44.7%)**	**11(8.3%)**	**132(100.0%)**
AST (IU)				
<43	55(88.7%)	47(79.7%)	3(30.0%)	109(83.2%)
≥43	7(11.3%)	12(20.3%)	7(70.0%)	22(16.8%)
Total	**62(47.3%)**	**59(45.0%)**	**10(7.6%)**	**131(100.0%)**

Mean laboratory values

LDH	**Observed**	**Total**	**Mean**	**Variance**	**Std.Dev.**
Mild pre-eclampsia	62	16194.000	261.19	14162.617	119.0
Severe pre-eclampsia	59	17082.0	289.52	14057.6	118.56
Eclampsia	11	3207.00	291.54	15263.27	123.54

Chi-Square= 5.4610 df= 2 P value= 0.0652

ALT					
Mild pre-eclampsia	62	1079.0	17.40	108.60	10.4214
Severe pre-eclampsia	59	1340.0	22.71	390.13	19.7520
Eclampsia	11	239.00	21.72	226.01	15.0339

Chi-square= 1.5812 df= 2 P value= 0.4536

AST					
Mild pre-eclampsia	62	1642.0	26.4839	162.9424	12.7649
Severe Pre-ecalmpsia	59	2003.0	33.9492	570.3939	23.8829
Eclampsia	10	343.00	34.3000	203.5667	14.2677

Chi-square= 4.1945 df. = 2 P value= 0.1228

Laboratory Results (Uric Acid, Platelet count Haemoglobin)

Uric acid level was checked on 126 (65%) of the 195 pre-eclamptic women. The normal range of uric acid is 0.15-0.40 mmol/L. Uric acid level was high (≥0.41 mmol/L) in 38 (30.2%) of all the pre-eclamptic women and the mean uric acid levels were 0.34 mmol/L, 0.35 mmol/L, and 0.46 mmol/L for the mild pre-eclampsia, severe pre-eclampsia and eclampsia groups, respectively. Chi-square was 9.0658 and P-value 0.0107 (Table VI), indicating a clear trend for increasing uric acid with increased disease severity.

Platelet count was checked on 154 (79%) of the pre-eclamptic women. The normal range for platelet count is $150X10^9$/L-$400X10^9$/L. The count was less than $100X10^9$/L in 6(3.9%), 101-$150X10^9$/L in 21(13.6%) and more than $150X10^9$/L in 127(82.5%). The mean platelet counts were 235 $X10^9$/L, $230X10^9$/L and $247X10^9$/L for the mild pre-eclampsia, severe pre-eclampsia and eclampsia groups, respectively. Chi-square was 0.2693 and P-value 0.8740 (Table VI).

Haemoglobin was checked in 184(94%) of the pre-eclamptic women of the study group. Normal HB during pregnancy ranges 11-16gm/dl. The level of HB was 6-10gm/dl in 36(19.6%), 11-15gm/dl in 143(77.7%) and above 16gm/dl in 5(2.7%). The mean HB levels among mild pre-eclamptic, severe pre-eclamptic and eclamptic were 11.8gm/dl, 12.6gm/dl, and 11.3gm/dl, respectively. The chi-square was 13.3470 and P-value 0.0013 (Table VI), with the eclampsia cases showing statistically lower mean haemoglobin compared to mild and severe pre-eclampsia.

Table VI Laboratory Results (Uric Acid, Platelet count, HB)

DIAGNOSIS	Mild Pre-eclampsia	Severe Pre-eclampsia	Eclampsia	Total
Uric Acid (mmol/L)				
< 0.41	46(75.4%)	39(70.9%)	3(30.0%)	88(69.8%)
≥0.41	15(24.6%)	16(29.1%)	7(70%)	38(30.2%)
Total	**61 (%)**	**55 (%)**	**10 (%)**	**126**
Platelet count/ 10^9/L				
≤100	2(2.6%)	2(3.2%)	2(14.3%)	6(3.9%)
<150	9(13.4%)	9(17.6%)	3(21.4%)	21(13.6%)
≥ 150	67(75.9%)	51(82.3%)	9(64.3%)	127(82.5%)
Total	**78(50.6%)**	**62(40.3%)**	**14(9.1%)**	**154(100.0)**
HB (gm/dl)				
≤10	22(23.4%)	7(9.7%)	7(38.9%)	36(19.6%)
>10	72(76.6%)	65(90.3%)	11(61.1%)	148(80.4%)
Total	**94(51.1%)**	**72(39.1%)**	**18(9.8%)**	**184**

MEAN LABORATORY VALUES

Mean Uric acid level for each diagnosis

Diagnosis	Observed	Total	**Mean**	Variance	Std.Dev.
Mild pre-eclampsia	61	21.120	**0.3462**	0.0071	0.0842
Severe pre-eclampsia	55	19.440	**0.3535**	0.0078	0.0884
Eclampsia	10	4.6200	**0.4620**	0.0126	0.1123

Chi-square= 9.0658 df. = 2 P value= 0.0107

Mean Platelet count for each diagnosis

Diagnosis	Observed	Total	**Mean**	Variance	Std.Dev.
Mild pre-eclampsia	78	18347.80	**235.22**	5893.4075	76.76
Severe Pre-eclampsia	62	14297.10	**230.5984**	7436.2821	86.23
Eclampsia	14	3464.900	**247.4929**	19483.3084	139.5826

Chi-square= 0.2693 df. =2 P value= 0.8740

Mean HB level for each diagnosis

Diagnosis	Observed	Total	Mean	Variance	Std.Dev
Mild pre-eclampsia	94	1108.04	11.787	2.9418	1.7152
Severe Pre-eclampsia	72	904.4800	12.562	2.6272	1.6209
Eclampsia	18	203.5400	11.3078	3.6662	1.9147

Chi-square= 13.3470 df. = 2 P value= 0.0013

Mode of delivery, Indications for caesarean section and maternal complication

One hundred seventy three (88.7%) of the pre-eclamptic women of the study group gave birth by means of caesarean section and twenty-two (11.3%) vaginally (Table VII).

The indication for caesarean deliveries were: 52(30.1%) mild pre-eclampsia, 47(27.2%) severe pre-eclampsia, 29(16.8%) foetal distress, 22(12.7%) eclampsia, 15(8.7%) previous caesarean section, 5(2.9%) failed induction, 2(1.2%) abruptio placenta, and 1(0.6%) intra uterine foetal death (IUFD) (Table VII).

Maternal complications were observed in 31.8% of the 195 pre-eclamptic women. There was convulsion in 20(10.3%), severe pre-eclampsia in 16(8.2%), HELLP syndrome in 7(3.6%), abruptio placenta in 5(2.6%), pulmonary oedema in 4(2.1%), renal failure in 3(1.5%), post partum haemorrhage (PPH) in 2(1.0%), paralysis in 2(1.0%) and congestive heart failure (CHF) in 1 (0.5%) (Table VII). Sixteen (16.5%) of the mild pre-eclamptic on admission progressed to severe pre-eclampsia and two (2.6%) of the severe pre-eclamptics developed convulsion (Table VII).

Table VII Mode of delivery, Indications for C-section, Complications (Maternal)

DIAGNOSIS (at time of intervention)				
	Mild pre-eclampsia	**Severe pre-eclampsia**	**Eclampsia**	**Total**
Mode of delivery				
SVD	16(16.5%)	6(7.8%)	0(0.0%)	22(11.3%)
C-section	81(83.5%)	71(92.2%)	21(100.0%)	173(88.7%)
Total	**97(49.7%)**	**77(39.5%)**	**21(10.8%)**	**195(100.0%)**
Indication for C-section				
Fetal Distress	12(14.8%)	16(22.5%)	1(4.8%)	29(16.8%)
Mild pre-eclampsia	48(59.3%)	4(5.6%)	0(0.0%)	52(30.1%)
Severe pre-eclampsia	7(8.6%)	40(56.3%)	0(0.0%)	47(27.2%)
Eclampsia	0(0.0%)	2(2.8%)	20(95.2%)	22(12.7%)
Previous C-section	9(11.1%)	6(8.4%)	0(0.0%)	15(8.7%)
Failed induction	2(2.5%)	3(4.2%)	0(0.0%)	5(2.9%)
Abruptio placenta	2(2.5%)	0(0.0%)	0(0.0%)	2(1.2%)
IUFD	1(1.2%)	0(0.0%)	0(0.0%)	1(0.6%)
Total	**81(46.8%)**	**71(41.0%)**	**21(12.1%)**	**173(100.0%)**
Maternal complications				
No complication	74(76.3%)	61(79.2%)	0(0.0%)	135(69.2%)
Convulsion	0(0.0%)	2(2.6%)	18(85.7%)	20(10.3%)
Severe Pre-eclampsia	16(16.5%)	0(0.0%)	0(0.0%)	16(8.2%)
HELLP syndrome	2(2.1%)	5(6.5%)	0(0.0%)	7(3.6%)
Abruptio-placenta	3(3.1%)	2(2.6%)	0(0.0%)	5(2.6%)
Pulmonary oedema	1(1.0%)	2(2.6%)	1(4.8%)	4(2.1%)
Renal Failure	0(%)	2(2.6%)	1(4.8%)	3(1.5%)
PPH	1(1.0%)	1(1.3%)	0(0.0%)	2(1.0%)
Paralysis	0(0.0%)	1(1.3%)	1(4.8%)	2(1.0%)
CHF	0(0.0%)	1(1.3%)	0(0.0%)	1(0.5%)
Total	**97(49.7%)**	**77(39.5%)**	**21(10.8%)**	**195(100.0%)**

Birth Weight, Neonatal Complications

Only 180 (92.3%) of the birth weights were recorded with 36(20.0%) weighing less than 1500 gm, 72(40.0%) 1500-2499 gm and another 72(40.0%) more than 2500 gm. The mean weights were 2.45 Kg, 2.08 Kg and 2.2 Kg for mild pre-eclamptic, severe pre-eclamptic and eclamptic women, respectively. Chi-square was 7.1952 and P-value 0.0274 (Table VIII), with mild pre-eclampsia having higher birth weight than more severe categories.

Neonatal Complication was not observed in 62(32.0%) of 194 births. Prematurity was observed in 100(51.5%), intra uterine growth restriction (IUGR) in 14(7.2%), respiratory distress syndrome (RDS) in 7(3.6%), jaundice in 4(2.1%) and death in 7(3.6%) (Table VIII).

Table VIII Birth weight, Neonatal complications

DIAGNOSIS				
	Mild Pre-eclampsia	**Severe pre-eclampsia**	**Eclampsia**	**Total #**
Birth weight (gm)*[1]				
<1500	11(12.2%)	23 (32.9%)	2 (10.0%)	36(21.0%)
1500-2499	38 (42.2%)	22 (31.4%)	12(60.0%)	72(40.0%)
2500+	41 (45.6%)	25 (35.7%)	6 (30.0%)	72(40.0%)
Total	**90(50.0%)**	**70(38.9%)**	**20(11.1%)**	**180(100.0%)**
Neonatal complications				
No complication	37(38.1%)	21(27.3%)	4(20.0%)	62(32.0%)
Pre-maturity	46(47.4%)	43(55.8%)	11(55.8%)	100(51.5%)
IUGR	7(7.2%)	5(6.5%)	2(10.0%)	4 (7.2%)
RDS	1(1.0%)	3(3.9%)	3(15.5%)	7(3.6%)
Jaundice	4(4.1%)	0(0.0%)	0(0.0%)	4(2.1%)
Death	2(2.1%)	5(6.5%)	0(0.0%)	7(3.6%)
Total	**97(50.0%)**	**77(36.7%)**	**20(10.3%)**	**194(100.0%)**

*[1] **Mean birth weight for each Diagnosis**

Diagnosis	Observed	Total	**Mean**	Variance	Std. Dev.
Mild pre-eclampsia	90	220.1560	**2.4462**	0.6724	0.8200
Severe pre-eclampsia	70	145.7170	**2.0817**	0.6534	0.8083
Eclampsia	20	43.7040	**2.1852**	0.4776	0.6765

Chi-square= 7.1952 df.= 2 P value= 0.0274

Admission to Neonatal ICU

One hundred (51.8%) of all the neonates born to the pre-eclamptic women were admitted to neonatal ICU. Of these 46(46.0%) were born to women with mild pre-eclampsia, 40(40.0%) to women with severe pre-eclampsia and 14(14.0%) to women with eclampsia (P-value=0.2927) (Table IX).

Table IX Admission to Neonatal ICU

	Mild pre-eclampsia	**Severe pre-eclampsia**	**Eclampsia**	**Total**
Admitted	46(46.0%)	40(40.0%)	14(14.0%)	100(51.8%)
Not admitted	50(53.8%)	36(38.7%)	7(7.5%)	93(48.2%)
Total	96(49.7%)	76(39.4%)	21(10.9%)	193(100.0%)*

*X^2= 2.4599 df =2; P=0.2927

RISK FACTOR ANALYSIS

RISK FACTORS FOR ADMISSION TO NEONATAL ICU AND LOW BIRTH WEIGHT

Table X shows that neonatal birth weight less than 2.5Kgm, gestational age ≤ 34 weeks, caesarean section, and non-reactive CTG to be risk factors for admission to neonatal ICU. However there was no significant difference for severity of pre-eclampsia in a mother as reason for admission to ICU.

Eighty one (75.7%) of those with birth weight of less than 2.499Kg and 9(12.5%) of those more than 2.499 kg had been admitted to neonatal ICU (OR=21.8, 95% CI 9.5-49.8, P-value=0.0000) indicating that those who had lesser birth weight had a tendency of being admitted to ICU as would be expected.

Seventy four (87.1%) of those who were born at gestational age less than 34 weeks and 25(23.4%) of those born at gestational age of more than 34 weeks had been admitted to ICU (OR=22.06, 95% CI 10.2-47.9, P-value=0.000).

Ninety four (55.3%) of the neonates who had been delivered by means of caesarean section and 6(26.1%) of those delivered vaginally were admitted to neonatal ICU (OR=3.5, 95% CI 1.3-9.3, P-value=0.0085) indicating that caesarean delivery predisposes to ICU admission.

Sixty eight (47.9%) of those where CTG was reactive and 24 (82.8%) of those where CTG was not reactive prenatally had been admitted to ICU (OR=0.19, 95%CI 0.069-0.53, P-value=0.00059) indicating that CTG non reactive being risk factor for admission to neonatal ICU.

Fifty four (55.7%) of those neonates born to women with severe pre-eclampsia or eclampsia and forty six (47.9%) of those born to women with mild pre-eclampsia had been admitted neonatal ICU (OR=1.4, 95% CI 0.8-2.4, P-value=0.28) indicating that severity of the disease had no significant difference for admission of neonates to ICU.

Severity of pre-eclampsia as risk factor for caesarean delivery and for birth weight was also assessed, with 43(46.7%) of the severe pre-eclamptic and 55(67.9%) of the mild pre-eclamptic cases having caesarean section only because of pre-eclampsia. In 49(53.3%) of the severe pre-eclamptic and 26(32.2%) of the mild pre-eclamptic caesarean section was performed because of additional other obstetric indications (RR=1.6; 95% CI 1.14-2.4; P-value= 0.008.) other than pre-eclampsia.

Table X Risk Factors for admission to Neonatal ICU

	Admitted to Neonatal ICU				
Risk Factor	Yes	No	OR	95% CI	P-value
Weight≤2.499Kg					
Yes	81(75.7%)	26(24.3%)	21.8	9.5-49.8	0.000
No	9(12.5%)	63(87.5%)			
Total	90(50.3%)	89(49.7%)			
Gestational age≤34Weeks					
Yes	74(87.1%)	11(11.8%)	22.06	10.2-47.9	0.00000
No	25(23.4%)	82(76.6%)			
Total	99(51.6%)	93(48.4%)			
Severe pre-eclampsia or Eclampsia					
Yes	54(55.7%)	43(44.3%)	1.4	0.8-2.4	0.28
No	46(47.9%)	50(52.1%)			
Total	100(51.8%)	93(48.2%)			
Caesarean section					
Yes	94(55.3%)	76(44.7%)	3.5	1.3-9.3	0.0085
No	6(26.1%)	17(73.9%)			
Total	100(51.8%)	93(48.2%)			
CTG reactive					
Yes	68(47.9%)	74(52.1%)	0.19	0.069-0.53	0.00059
No	24(82.8%)	5(17.2%)			

RISK FACTORS FOR SEVERITY OF PRE-ECLAMPSIA

Table XI shows that age≥ 34 years, being a state patient, lack of antenatal care and being from outside Windhoek to be strongly associated with severity of pre-eclampsia and age ≤ 20 years old, primiparity, uric acid level ≥ 0.41 to have weaker association to the severity of pre-eclampsia.

Age

Of the one hundred and ninety five pre-eclamptic women who gave birth during the study period, 150(77.3%) were in the age category of < 34 years old and 44 (22.7%) ≥ 34 years old. Ninety-six (49.5%) were mild pre-eclamptic and 98(50.5%) severe pre-eclamptic (OR= 0.4; 95% CI 0.2-0.8, P-value= 0.013) (Table XI) indicating statistically fewer older women in the severe pre-eclampsia and eclampsia groups. But when teens were compared with non-teens there was no significant difference observed with 33(17%) ≤ 20 years and 161(83%) older than 20. Nineteen (57.6%) of the severe pre-eclamptic and fourteen (42.4%) of the mild pre-eclamptic were with the age category ≤ 20 years (OR=1.4; 95% CI 0.67-3.0, P-value= 0.373). However when age as risk factor was considered between the mild pre-eclamptic and eclamptic more teens had suffered from eclampsia (OR=2.92; 95% CI 1.0-8.5, P-value=0.042)(Table XII), hence teenage pregnancy is risk factor for eclampsia when compared to the milder forms of pre-eclampsia.

Parity

There were more primiparas in the severe pre-eclampsia and eclampsia groups. Forty six (55.4%) of the severe pre-eclamptic/eclamptic and 37 (38.1%) of the mild pre-eclamptic women were para I (RR=1.2; 95% CI 0.9-1.5). However, the difference was not statistically significant (P-value=0.2726) (Table XI).

Status

More of the severe pre-eclampsia/eclampsia cases were state patients. Ninety (91.8%) of the severe pre-eclamptic/eclamptics and seventy-seven (79.4%) of the mild pre-eclamptic cases were state patients (RR= 2.9; 95% CI 1.2-7.3; P-value= 0.0133) (Table XI).

Antenatal care

Fifty-seven (58.2%) of the severe pre-eclampsia/eclampsia and eighty two (84.5%) of the mild pre-eclamptics have attended antenatal care (RR= 0.56; 95% CI 0.43-0.72, P-value= 0.00009) (Table XI), suggesting ANC may protect against progression to more severe categories of the disease.

Address

With regard to region of origin, 47(48.0%) of the severe pre-eclamptic/eclamptic and 64 (66.0%) of the mild pre-eclamptic cases were from Windhoek and 51(60.7%) of the severe pre-eclamptic/eclamptic and 33 (39.3%) of the mild pre-eclamptic from outside

Windhoek (RR= 0.7; CI 0.5-0.9; P-value= 0.016) (Table XI), suggesting possibly more referrals of severe pre-eclamptics/eclamptics to these referral hospitals as might be expected.

Uric acid level

Twenty-three (35.4%) of the severe pre-eclampsia/eclampsia and fifteen (24.6%) of the mild pre-eclampsia had uric acid level of $\geq$ 0.41 umol /litre (RR= 1.3; 95% CI 0.9-1.8; P-value= 0.13) (Table XI).

Table XI Risk Factors for Severity of Pre-eclampsia

Diagnosis Severe pre-eclampsia or Eclampsia				
Risk factor	**Yes**	**No**	**Total**	**P-value**
Age ≥ 34 Years				
Yes	15(34.1%)	29(65.9%)	44(100.0%)	0.013
No	83(55.3%)	67(44.7%)	150(100.0%)	
Age <20 Years				
Yes	19(57.6%)	14(42.4%)	33(100.0%)	0.3732
No	79(49.1%)	82(50.9%)	161(100.0%)	
Primipara				
Yes	46(55.4%)	37(44.6%)	83(100.0%)	0.2726
No	52(46.4%)	60(53.6%)	112(100.0%)	
State patient				
Yes	90(53.9%)	77(46.1%)	167(100.0%)	0.0133
No	8(28.6%)	20(71.4%)	28(100.0%)	
Antenatal care				
Yes	57(41.0%)	82(59%)	139(100.0%)	0.00009
No	41(73.2%)	15(26.8%)	56(100.0%)	
Address (Windhoek)				
Yes	47(42.3%)	64(57.7%)	111(100.0%)	0.016
No	51(60.7%)	33(39.3%)	84(100.0%)	
Uric acid ≥ 0.41				
Yes	23(60.5%)	15(39.5%)	38(100.0%)	0.13
No	42(47.7%)	46(52.3%)	88(100.0%)	

Table XII Maternal Age ≤ 20 years as risk factor (mild pre-eclampsia Vs. Eclampsia)

Eclampsia					
Risk factor	**Yes**	**No**	**OR**	**95%CI**	**P-value**
Age≤20					
Yes	7(33.3%)	14(66.7%)	2.92	1.0-8.5	0.042
No	14(17.9%)	82(85.4%)			

Table XIII shows that 48.5% of all the pre-eclamptic cases were not managed according to regional or international guidelines and the 95% CI for those who were not managed accordingly was 41.2%-55.7% and for those who were managed according 43.0%-58.8%.

Table XIII Comment based on Pre-eclampsia management guideline

Admission	**Mild pre-eclampsia**	**Severe pre-eclampsia**	**Eclampsia**	**Total**
Yes	44(44.0%)	41(41.0%)	15(15%)	100(51.5%)
No	52(55.3%)	36(38.3%)	6(6.4%)	94(48.5%)
Total	96(49.5%)	77(39.7%)	21(10.8%)	194(100.0%)

X2=4.67 df=2 P-value= 0.0969

CHAPTER 5

DISCUSSION

The results of this study indicate that there was no maternal mortality with in the study period. However, as this is a retrospective hospital based study the possibility of information bias, which is the potential disadvantage of such study, should be considered. As the sample is also relatively small there could probably be women who died during the study period but not included in the sample. The neonatal mortality rate was also low compared to the neonatal mortality of the Khomas region (10). It was also observed that 95% of the pre-eclamptic women had received anti hypertension drugs. Although these findings are encouraging it was noticed that:

1. There was no difference in the management of the different categories of pre-eclampsia.
2. The use of magnesium sulphate as a prophylaxis was low (only 23.0% of the severe pre-eclampsia cases received magnesium sulphate)
3. The Caesarean section rate was extremely high (89.0%)
4. Birth weight was less than 2500 gm in 60% of the neonates

SOCIO-DEMOGRAPHY

One hundred and sixty one (83.0%) of the 195 women in the study group were with the age range of 14 to 35 years indicating that younger women were more affected by pre-eclampsia. This corresponds with the studies of Moodley and Mashioane where the mean

age was 28 years (9) and also that of Brown MA and Buddle ML (26). In this study was also observed a significant difference in the mean age of the different categories of pre-eclampsia, which suggests a trend towards increasing severity with younger age (the mean age for the eclamptic was 24.1 years and P-value 0.0181). This corresponds to the findings of Hall et al where younger women are at higher risk for developing eclampsia (16).

The decreasing incidence of pre-eclampisa by ethnicity from Oshivambo to Nama could be because of the distribution of the population of Namibia, the Ovambo being highly populated and the Nama least populated. Similarly when ethnicity is considered by colour, 89.7% were Namibians of African origin and 6.7% Namibians of European origin. This compares to 86% Namibians of African origin and 6.6% Namibians of European origin overall in the population of the region/Namibia (77). Other studies findings suggest that being black is a risk factor pre-eclampsia (14).

MEDICAL AND PREGNANCY HISTORY

More than half of the pre-eclamptic women in this study were multiparous. Conde-Aguedelo and Belizam JM also found similar pattern of risk factor among nulliparous and multiparous women (17). Pre-eclampsia is generally considered as a disorder of primi-gravida (19,61), however it does occur in subsequent pregnancies following a change of partner (19). Thus, multiparity should not be taken for granted as protective for pre-eclampsia before history of change of partner is ruled out.

Fourteen (7.2%) of the women in the study group had pregnancy-induced hypertension in their previous pregnancy. The presence of gestational hypertension in previous pregnancy is a known risk factor for gestational hypertension in a subsequent pregnancy (61). Short inter-pregnancy interval has also been associated with higher risk of pre-eclampsia (22), however data on inter-pregnancy interval was not available for this study. There was only one woman who had diabetes mellitus in the study group. Though it was observed only in one-woman in this study, presence of diabetes mellitus was reported to be associated with pre-eclampisa in different studies (17, 18).

QUALITY OF CARE

There was no significant difference (P-value 0.5634) in the mean hospital stay between the three categories of pre-eclampsia in this study. This suggests that there was little distinction in the management of different types of pre-eclampsia.

Management at antenatal ward

A base line laboratory evaluation should be performed in women who are at high risk for pre-eclampsia and once the diagnosis of pre-eclampsia has been made, an expanded set of laboratory tests should be performed (35). The laboratory investigations for the pre-eclamptic women were requested only on admission as a case of pre-eclampsia and in 53 (27.2%) women LFT and U&E were not checked. Presence of base line laboratory investigation would have assisted in the evaluation of the progression and timely management of the disease.

The treatment of hypertension (less than 160/110 mmHg) in woman with mild pre-eclampsia does not improve outcome (68) however 89(48.1%) of those women who received anti hypertensive drug in this study were cases of mild pre-eclampsia. Based on the results of 10 randomised trials evaluating drug treatment in women with mild pre-eclampisa, Sibia BM also commented that there was no clear benefit to drug treatment in women with mild pre-eclampsia (32). However, an inference could not be made on the effect of antihypertensive drugs on the outcome of pre-eclampsia in this study as most of the women were delivered immediately.

In managing pre-eclampsia, antepartum testing with non-stress test should be performed on weekly bases starting at the time of diagnosis (35). Though CTG was done in 88.2% of the study group, none of the women had stayed in the hospital for one week before delivery. Delaying delivery in the absence of maternal complication should be considered if the CTG is reactive.

Magnesium sulphate reduces the risk of eclampsia and it is likely it reduces the risk of maternal death (4). Magnesium sulphate was given to only 23% of the severe pre-eclamptic women in this study, which was very low compared to other studies (4,69). In their study on maternal and perinatal outcomes of eclampsia in Nova Scotia, Lee W, O'Connell CM and Baskett TF reported that 97% of pre-eclamptics had received magnesium sulphate (69). The routine use of magnesium sulphate prophylaxis in all women with pre-eclampsia has been questioned, however if a decision is made to treat

such women prophylactically during labour and delivery it is considered the ideal therapy (32).

Laboratory results

Elevated levels of Lactate Dehydrogenase (LDH), Alanin amino-transferase (ALT) and Aspartate amino-transferase (AST) occurs as a result of periprotal hemorrhagic necrosis (2). LDH level is considered an indicator for seriousness of the disease if its $\geq$ 600UI/L (69). Therefore even though the mean levels of LDH in the three categories of pre-eclampsia in this study were higher than the normal values, they were not high enough to justify for the seriousness of the pre-eclampsia the study group had. Unlike the LDH, the mean levels of AST and ALT were within normal range in the three categories of the study group and also no significant difference was observed. However, this has to be looked at cautiously as there is no single test of clinical usefulness, and no test could be totally predictive of maternal or foetal outcome. Pregnant women with elevated liver enzymes could often be misdiagnosed because they had low diastolic blood pressure (70).

In general liver function tests are reserved for patients with upper abdominal pain (71), however the tests in this study were requested to 72.8% of the study group while epigastric pain was observed only on 11.3%.

The mean uric acid level among the eclamptic women was higher than the mild and the severe pre-eclamptic cases indicating a clear trend for increasing uric acid with increased

disease severity. This corresponds with the studies of Xio et al and Brown and Buddle (24,26).

Platelet level should be less than 100, 000mm^3 in order to be considered as an indicator for the severity of pre-eclampsia (2, 70). Only 3.9% of the women whose platelet was checked had a platelet count of less than 100,000mm^3 and no significant difference was observed in the mean platelet count among the different categories of pre-eclampsia.

Some studies stated that increase in haemoglobin concentration could predict development of pre-eclampsia (19,25), however, such correlation was not observed in this study and the eclampsia cases showed a statistically lower mean haemoglobin compared to mild and severe pre-eclampsia.

Mode of Delivery

Though delivery is the ultimate cure of pre-eclampsia, neonatal outcome should also be considered in the absence of maternal complications (19,23). Almost 90% of the women in this study were delivered by means of Caesarean section and 57% of the indications for the caesarean section were uncomplicated mild and severe pre-eclampsia. This rate of caesarean delivery is higher than that reported by Mashiloane and Moodley (6) and similar to that of Hall et al where 81.5% the pre-eclamptic gave birth by means of caesarean section, with foetal distress being the commonest reason for delivery (54). However, in this study, caesarean section as indication for foetal distress was observed only in 16.8% of the study group. Al-Mulhim et al in their study also reported that

spontaneous vaginal delivery to be less frequent (69%) among pre-eclamptic women compared to normotensive women (86.2%) implying that being pre-eclamptic predisposes to caesarean delivery (12).

The reason for the high caesarean delivery could not certainly be speculated from this study; however, in other studies fear of litigation was one of the suggested indications for caesarean section (50).

Repeat caesarean section was offered for the 15(100.0%) women with previous caesarean scar in this study. This was not uncommon practice in other areas as well. Wilkinson and his colleagues reported that repeat caesarean section accounted for 60% of all caesarean section in Scotland in women with no other recorded complications (72).

Though caesarean delivery could be considered as protective for maternal complications, the financial impact and the short-term and long-term morbidity of the neonates should be taken into consideration (32). Caesarean section is also incriminated for sub-fertility; rupture of the uterus in subsequent pregnancy and placenta prevae (73, 74). Therefore it should be reserved only for absolute maternal and foetal indications.

Morrison JJ, Rennie JM and Milton PJ in their study also reported that the incidence of neonatal respiratory morbidity to be higher for a group delivered by caesarean section before the onset of labour compared with caesarean section during labour and compared with vaginal delivery (OR= 6.8; 95%CI 5.2-8.9, P-value <0.001) (45).

MATERNAL AND NEONATAL OUTCOME

Maternal outcome

Maternal mortality has been used as a measure of the success of obstetric intervention but is now too rare for use in local practice in the modern world hence maternal morbidity has been suggested as an alternative method (66).

The maternal complication rate that was observed in 31.8% of the study group was similar to that of Lee and his colleagues' report where 32% of the pre-eclamptic women in their study had major maternal complications (69). The commonest complications in this study were convulsion, progression to severe pre-eclampsia and HELLP syndrome. These complications were similar to the findings of Murphy DJ and Stirrat GM (11), except that abruptio placenta was observed in 11(15%) of their study group, while it was observed only in 5(2.6%) women in this study. Abruptio placenta was also the commonest maternal complication observed in the study of Al-Mulhim and his colleagues (12).

Despite maternal complications, no maternal mortality was observed during the study period. However, 33 to 37% of maternal deaths between 1998 and 2000 in South Africa were due to pre-eclampsia alone and the major cause of mortality in 55% of the pre-eclamptic women was substandard management (9), so proper management of pre-eclampsia should remain a priority in obstetrics.

Neonatal Outcome

The gestational age observed among the severe pre-eclampsia group in this study corresponds to that of Bechbender A et al, where women with severe pre-eclampsia had a high rate of pre-term delivery at less than 35 weeks gestation (67). The mean gestational age for the eclamptic women observed in this study was also similar to that reported by Anath CV, et al (28).

One hundred and eight (60.0%) neonates had a birth weight of less than 2500gm with mild pre-eclampsia having higher mean birth weight than the more severe categories. These mean birth weights correspond to the mean gestational age of the different categories of pre-eclampsia. The observed trend of birth weight was also similar to those of other studies (27,28,29,67). The lower birth weight among the severe pre-eclampsia cases which was observed in this study corresponds to that of Xiong X and Fraser WD's study where the birth weights were significantly lower in women with severe pre-eclampsia (29).

The intrauterine growth restriction (IUGR) which was observed in 14(7.2%) of the study group was similar to the findings of Odegard RA et al where severe and early onset pre-eclampsia were associated with significant foetal growth restriction (30).

Pre-eclampsia is responsible for the occurrence of more than 40% of premature deliveries around the globe (2). This was also observed in this study where 100(51.1%) of the neonates were delivered prematurely. Although pre-eclampsia is a risk factor for low

birth weight, caesarean delivery especially among mild pre-eclamptic group could contribute to prematurity (32). Heard AR et al in their study also suggested that uncomplicated hypertension was associated with preterm delivery due to elective caesarean section (75).

RISK FACTORS

Admission of the neonates to an ICU in this study didn't show significant difference among the different categories of pre-eclampsia group (P-value 0.29) (Table IX). In the study of Lydakis C and colleagues, pregnancies in women with uncomplicated pre-eclampsia had an increased risk for emergency caesarean section, pre-term delivery (gestational age <37 weeks) and birth weight less than 2.5Kg (76). This was also observed in this study where birth weight less than 2.5Kg, gestational age less than 34 weeks and caesarean section were strongly associated with ICU admission and 47.9% of the neonates who were admitted to ICU were cases born to women with only mild pre-eclampsia.

Age more than 35 years old, not attending ANC follow up, being a state patient and coming outside the capital city were found to be risk factors for pre-eclampsia in this study, but uric acid level had no strong association with severity of pre-eclampsia. Age more than 35 years old as a risk factor has been observed in other studies as well (13,14,15). However, teenage pregnancy in this study was strongly associated with eclampsia than with the other categories of pre-eclampsia. The association of failure to attend ANC with severity of pre-eclampsia that was observed in this study was also

observed in a study done by Milen and his colleagues (61). Even though the socio-economic back ground of the pre-eclamptic women in this study was not assessed, being a state patient was associated with the severity of the disease. Wagner AK also indicated this in his literature review (35).

EXPECTANT MANAGEMENT

Different studies have shown that prolongation of gestation in uncomplicated pre-eclampisa enhances foetal maturity (44,51,52). The similarity of the mean hospital stay and almost universal delivery by caesarean section among the different pre-eclampsia categories in this study indicates that expectant management of pre-eclampsia was not a practice in the two-referral hospitals. Most of the mild pre-eclampsia cases could have been managed expectantly as the frequently recommended management of mild pre-eclampsia (32,33), and this in return might have reduced the ICU admission of neonates. However other studies also has also shown that aggressive management compared with expectant management results in equivalent maternal morbidity, fewer small for gestational age infants and more markers of serious neonatal morbidity (31).

FINANCIAL IMPLICATION

The cost of caesarean delivery and admission of neonates to an ICU should also be considered. Had the caesarean sections been performed at private facility or had the neonates been admitted to a private hospital ICU the cost would have approximately been around USD153, 846 (about one million N$ according to the present rate) more.

CONCLUSION

The absence of maternal mortality during the study period was encouraging. However, important findings that indicate that the care given to the pre-eclamptic women was not totally in line with international or regional guidelines of management of pre-eclampsia. These are:

- Expectant management of mild or severe pre-eclampsia was not followed, as:
    1. Difference was not observed in the management of the different categories of pre-eclampsia.
    2. The caesarean section rate was very high
    3. The rate of pre-maturity and neonatal ICU admission was very high
- All pre-eclamptic women were treated with anti-hypertensive drugs irrespective of severity of the disease
- Magnesium sulphate usage as a prophylaxis during or before delivery for severe pre-eclamptic cases was not practiced.

In general the findings in this study indicated that the management of pre-eclampsia lacks specificity for the different categories. This could be because of lack of a guideline in the management of pre-eclampsia to assist clinicians in making clinical decisions when faced with differing severity of disease.

RECOMMENDATIONS

1. Further research on risk factors and suggest ways to prevent pre-eclampsia.
2. A guideline on the management and prevention of pre-eclampsia needs to be produced for Namibia, with an emphasis on appropriate evidence-based care for each level of disease severity. The guideline should be implemented with training/continuing education of providers, and also an evaluation of the impact of the guideline on care and outcomes.
3. Research on cost effectiveness of premature termination of pregnancy in the context of pre-eclampsia needs to be seriously looked at in the Namibian context.

It is also necessary to note that there were methodological limitations in this study. The study was hospital based retrospective study with a relatively small sample size; as a result sampling and information bias may have occurred and we had limited power to study the more rare outcomes. However it is believed that this study will pave way for further study in pre-eclampsia and other perinatal research.

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ANNEXURE A

COTTAGE MEDI-CLINIC HOSPITAL - Estimated Costs

GENERAL	Medical	Est. stay .....days	@ N$	**1 578.80**
WARD	Surgical	Est. stay .....days	@ N$	**1 578.80**
	High Care	Est. stay.....days	@ N$	**3 543.10**
	Lodger	Est. stay .....days	@ N$	**200,00**
	Day Ward	Est. stay .....days	@ N$	**918.30**
	Paediatric	Est. stay .....days	@ N$	**1 724.40**
MATERNITY	Normal Delivery	First day	N$	**4 635.20**
		Subsequent days	@ N$	**1 596.80**
	Caesarian Section	First day	N$	**7 199.90**
		Subsequent day	@ N$	**1 583.00**
THEATRE	Per minute		N$	**83.10**
CASUALTY	Facility Fee		N$	**307.90**
	Consultation Fee		N$	**58.80**

N.B. The total cost and deposit are only estimated amounts and can be changed depending on the number of days admitted and the type of treatment.

Signature: ..... Date: .....

ANNEXURE B

DATA ABSTRACTION TOOL - Pre-eclampsia and its outcome

Study Number: -------

The following were recorded in the subject medical record, delivery register, theatre register or related records pertaining to the selected delivery.

A. Socio-demographic data

Age (in years) -------

Ethnic group----

1. Ovambo
2. Herero
3. Damara
4. Nama
5. White
6. Coloured
7. Other, Specify _____

Address—

1. Windhoek
2. Outside Windhoek

Status:

1. State
2. Private

B. Medical & Pregnancy History

1. Parity----
   1. Primipara
   2. Multipara

2. Medical History ---- Check all that apply
   1. Chronic hypertension
   2. Chronic Renal Disease (glomerulonephritis, Chronic pyelonephritis)
   3. Diabetes (circle class) A B C D F-R
   4. Heart Disease, Class I (No limitation of activity)
   5. Heart Disease, Class II-IV (any limitation in activity)
   6. Haematological Disorder (Chronic anaemia)
   7. Hepatitis: (Type)
   8. Neurological Disorder (Seizure or epilepsy)
   9. Negative
   10. Unknown

3. Past Pregnancy History ---- Check all that apply

1. Not applicable (this is her first pregnancy)
2. Gestational Diabetes (Class A)
3. Pregnancy Induced Hypertension (PIH){BP≥160/110 or 30/15 elevation &proteinuria 1-2+&or persistent oedema}
4. PIH- Sever (BP≥160/110 & proteinuria>2+ both after 26 weeks gestation)
5. PIH- with Eclampsia (CNS involvement & seizures)
6. Large for Gestation (LGA) infant (> 4000Gms or 9 lbs)
7. Small for Gestation (SGA) infant (<10th percentile for GA)
8. Multiple Gestation
9. Pre-term delivery (<37 weeks gestation)
10. Post- term delivery (>42 Weeks gestation)
11. Instrument Delivery (Forcepts, Vacuum extraction)
12. Caesarea section delivery
13. Postpartum haemorrhage (Blood loss more than 500ml)
14. Still birth or intrauterine Foetal Demise
15. Neonatal Death (First 28 days of life)
16. Negative
17. Unknown

C. Admission to hospital

Date of admission-----
Date of Discharge ----
Hospital stay (# of days) ------

1.Chief complaints (other than pregnancy/labour): -- Check all that apply
    1. Headache
    2. Epigastric pain
    3. Nausea and or vomiting
    4. Blurred vision
    5. Other, Specify _____
2. Blood pressure on admission: ----
3. Oedema: ----
    1. Yes
    2. No
    3. Unknown
4. Proteinuria (++dipstick or 3gm/24hr): ----
    1. Yes
    2. No
    3. Unknown
5. Gestational age (in weeks on admission) -----

6. Attended Antenatal Care ---
   1. Yes
   2. No
7. Pre-eclampsia signs or symptoms noted during Antenatal care and appropriate referral made to hospital?
   1. Yes, signs and symptoms present and referral made
   2. No, signs and symptoms present but NO referral made
   3. No signs or symptoms noted during ANC
8. Diagnosis:
   1. Mild Pre-eclampsia - BP >140/90 and <160/110
   2. Severe pre-eclampsia - BP 160/110 or greater
   3. Pre-eclampsia, unspecified/unknown severity
   3. Eclampsia - experiencing convulsions
9. Presentation:
   1. Cephalic
   2. Breech
   3. Transverse
   4. Other, Specify _____

D. Management

I. If the diagnosis was pre-eclampsia/mild and woman admitted to antenatal ward/not in labour what measures were taken?

1. Was round done daily?
1.**Yes**
2. No

2. Was Blood pressure measured 4 hourly?
1.**Yes**
2.No

3. Was the mother counting foetal movement daily (Kick chart)?
1.**Yes**
2. No

4. Were liver function tests, FBC, Serum urea, creatinine and uric acid checked weekly?
1.**Yes**
2. No

5. Was anti hypertension treatment given when blood pressure become ≥150/100 mmHg?
1.**Yes**
2.No

6. Was CTG done on daily basis?
1. **Yes**
2. **No**

II. If Diagnosis was pre-eclampsia/mild and woman in 1st stage of labour what measures were taken?

1. Was blood pressure measured every ½ hour?
1. **Yes**
2. **No**

2. Was urine output assessed hourly?
1. Yes
2. No

3. Was antihypertensive drug given/continued?
1.Yes
2. No

4. Was magnesium sulphate given/continued?
1.Yes
2. No

5. Was labour pain managed?
1. **Yes**
2. **No**

Specify: Analgesics Epidural Other

6. Was partogram correctly used?
1.Yes
2. No

7. Was mental status monitored/noted?
1.**Yes**
2. No

III. If Diagnosis was pre-eclampsia/mild and woman in 2nd stage of labour what

Measures were taken?

1. Was blood pressure measured every 15 minutes?
1.**Yes**
2. No
2. Fetal heart monitored after every contraction
1. Yes
2. No
3. Delivered within expected time period (2 hours for primipara or 1 hour for multipara)
1. Yes
2. No
4. Was second stage of labour shortened using vacuum extraction?
1. Yes
2. No
5. Ergometrine or Syntrometine **NOT** given
1. Yes
2. No
6. Syntocinon, Pitocin or Oxytocin (5 units IV and IM) given

1. **Yes**
2. **No**

VI. If Diagnosis was pre-eclampsia/mild and woman in 3rd stage of labour what measure was taken?

1. Postpartum blood loss (estimate in cc) --
2. Postpartum haemorrhage diagnosed
   1. **Yes**
   2. **No**
3. Blood pressure taken immediately after delivery
   1. **Yes**
   2. **No**
4. Controlled blood pressure if between 140/0 and 150/100 mmHg
   1. **Yes**
   2. **No**

V. If Diagnosis was Severe pre-eclampsia (BP>160/110) what measures were taken?

1. Was an intravenous drip and pre-load with 300ml Ringer's Lactate started?
   1. **Yes**
   2. **No**
2. Was rapid acting antihypertensive administered/continued?
   1. **Yes**
   2. **No**
3. Was diastolic blood pressure maintained above 90-100 mmHg?
   1. **Yes**
   2. **No**
4. Was magnesium sulphate started (as a prophylaxis)?
   1. **Yes**
   2. **No**
5. Was fetus assessed for fetal distress (clinically or by CTG)?
   1. **Yes**
   2. **No**
6. Was renal function assessed (urea or creatinine)?
   1. **Yes**
   2. **No**
7. Was platelet count assessed?
   1. **Yes**
   2. **No**
8. Was liver function assessed (AST or LFT)?
   1. **Yes**
   2. **No**
9. Was foetal condition assessed by CTG?
   1. **Yes**

2. No

10. Was doctor consulted?

1.**Yes**

2. No

11. Were steroids initiated if gestational age 27-34 weeks?

1.**Yes**

2. No

VI. If the diagnosis was eclampsia, what measures were taken?

1. Woman placed on her side (lateral position)

1. Yes

2. No

2. Was airway cleared?

1. Yes

2. No

3. Was oxygen given?

1.Yes

2. No

4. Was doctor consulted?

1. Yes

2. No

5. Was an intravenous drip started?

1.**Yes**

2. No

6. Was magnesium sulphate given?

1. **Yes**
2. **No**

7. Was blood pressure monitored every 15 minutes?

1. Yes

2. No

8. Was rapid acting antihypertensive administered/continued?

1. Yes

2. No

9. Was diastolic blood pressure maintained above 90-100 mmHg?

1. Yes

2. No

10. Was Central Venous pressure line inserted?

1.**Yes**

2. No

11. Was CTG done to monitor fetal condition?

1.**Yes**

2. No

12. Was indwelling catheter inserted?

1. Yes

2. No

13. Was fluid intake restricted to 80 ml/hr or less?

1. Yes
2. No

14. Was urinary output monitored?
1. Yes
2. No

15. Was woman monitored in high care for at least 24 hours?
1. Yes
2. No

16. Was calcium gluconate (10 ml in 10% solution) given IV in case of magnesium sulphate toxicity?
1. Yes
2. No
3. Not applicable

VII. What drugs were given for control of hypertension?

1. Methyl dopa (500mg six hourly or 750 mg 8 hourly)
1. Yes
2. No
2. Was Nifidipine added (10-30 mg 8 hourly with start 10mg)?
1.Yes
2.No
3. Was Prazosin added (1-7 mg every 8 hourly start with 1 mg)?
1. Yes
2. No
4. None
5. Other drugs given (note name, dose, route, administration)

_____
_____
_____

VIII. How was Magnesium sulphate use, if was given?

1. Was loading dose of 4 gm and 5gm in each buttock given?
1.**Yes**
2. No
2. Was the magnesium sulphate diluted by saline?
1.**Yes**
2. No
3. Was lignocain given during an Intramuscular injection?
1.**Yes**
2. No
4. Was maintenance of 5 gm of magnesium sulphate im given 4 hourly?
1.Yes

2. No

5. Was patellar (Knee) reflex assessed?
   1 Yes
   2 No
6. Was respiratory rate measured?
   1.**Yes**
   2. No

E. Delivery

1. Was labour induced/pregnancy terminated?
   1. Yes
   2. No
2. If yes what was the indication?
   1. Severe pre-eclampsia and gestational age >34 weeks
   2. Severe pre-eclampisa / term pregnancy
   3. Intra uterine fetal death?
   4. Abrupion of the placenta
   5. HELLP syndrome
   6. Other
3. What was mode of delivery?
   1. Spontaneous vaginal delivery (SVD)
   2. Breech extraction
   3. Vacuum extraction
   4. Forceps delivery
   5. Caesarean section
4. If caesarean section? What was the indication?
   1. Foetal distress,
   2. Abruptio placenta
   3. Pre-eclampisa
   4. Eclampsia
   5. Other
5. If pregnancy terminated, were termination criteria met
   1. Eclampsia
   2. Severe pre-eclampsia before 24-26 weeks that does not respond to expectant management
   3. Before 28 weeks on maternal request or doctor's advice
   4. Renal Failure/HELLP

6. If pregnancy NOT induced/terminated, were any termination/induction criteria present

   1. Eclampsia
   2. Severe pre-eclampsia before 24-26 weeks that does nto respond to expectant management
   3. Before 28 weeks on maternal request or doctor's advice
   4. Renal Failure/HELLP

F. Post Partum Care

1. Was the mother kept at least for 24 hours in the hospital after delivery?
1.**Yes**
2. No

2. Was oral anti hypertension continued?
1.**Yes**
2. No

3. Was dihydralazine or nifidipine give if BP was > 160/110 mmHg?
1.**Yes**
2. No

4. Was the blood pressure on discharge less than 160/ 100 mmHg?
1.**Yes**
2. No

5. Was appointment given to the mother to come back after 2 weeks for check up?
1.Yes
2. No

G. Laboratory Results (on admission or 1st done, indicate if never done)

1. What was the level of LDH? ----
2. What was the level of ALT? ----
3. What was the level of uric acid? ----
4. What was the level of platelet? ----
5. What was the level of HB? ----
6. What was the level of creatinine? ----
7. What were the electrolytes? ----
8. What was the blood glucose? ----

H. Maternal Complications

1. Was there maternal complication?
    1. Yes
    2. No
2. If yes what?
    1. Abruptio placenta,
    2. Sever pre-eclampsia
    3. Convulsion
    4. Pulmonary oedema,
    5. Post partum haemorrhage
    6. Death
    7. Other

I. Use of NOT Recommended Treatments

1. Was plasma volume expansion used (other than preloading prior to antihypertensives)?
   1. Yes
   2. No
2. Was central venous pressure used to control plasma volume expansion?
   1. Yes
   2. No
3. Was diazepam used to arrest convulsions?
   1. Yes
   2. No
4. Was Phenobarbitone used?
   1. Yes
   2. No
5. Was HELLP syndrome expectantly managed?
   1. Yes
   2. No

J. Neonate

1. Weight (KG)---
2. Height (Cm.)---
3. Neonatal complication?
   1. Yes
   2. No
4. If yes neonatal complication, what?
   1. Premature,
   2. IUGR
   3. Respiratory distress syndrome,
   4. Jaundice,
   5. Death
   6. Other
5. Was the neonate admitted to ICU?
   1.**Yes**
   2. No
6. What was the outcome for the infant?
   1. Alive
   2. Dead
   3. Other

NOTE: Antenatal care review is limited, and transport and referral items are not included as the study is being conducted in tertiary referral hospitals.

CHAPTER THREE

GUIDELINES FOR THE MANAGEMENT OF HYPERTENSION IN PREGNANCY

Hypertensive disease in pregnancy is one of the 5 major causes of maternal mortality in South Africa. This important fact should always be remembered when pregnant mothers are provided with information and education during visits for antenatal care, during labour or in the puerperium. This important information should also be given to communities and relatives of pregnant mothers.

3.1 DEFINITION

A blood pressure of 140/90 mmHg or more during pregnancy is indicative of any hypertensive disease. The condition is called pre-eclampsia when proteinuria develops for the first time after 20 weeks gestation. Eclampsia is the name of the condition when hypertension and proteinuria in pregnancy is complicated by convulsions.

3.2 HYPERTENSIVE DISEASES IN PREGNANCY AFFECT MANY ORGANS

Although one usually considers blood pressure and proteinuria to define hypertensive diseases, it does not mean that other important organs are not involved. Severe pre-eclampsia affects many organs because the primary pathology involves endothelial cells and they are present in every organ. It is necessary to know how these organs are affected as this will help the health worker to diagnose complications at an early stage.

- **Central nervous system**: Severe headache
  Changes in behaviour, decreased levels of consciousness
  Restlessness
  Hyperreflexia
  Visual disturbance

Convulsions

Coma

- **Cardiovascular system:** Severe hypertension

  Headache

  Oedema

- **Renal system:** Proteinuria

  Poor urinary output (less than 1ml/kg/hr

  Haematuria (from haemolysis)

- **Haematological system:** Petechiae

  Bruising

  Bleeding from puncture sites

  Jaundice (from haemolysis)

- **Liver:** Jaundice

  Upper abdominal pain

- **Placenta:** Poor fetal growth

  Fetal distress

- **Respiratory system:** Pulmonary oedema – shortness of breath

3.3 GENERAL MEASURES TO PREVENT MATERNAL DEATHS FROM HYPERTENSIVE DISEASE

1. See that all pregnant women receive antenatal care.
2. Healthcare workers attending to pregnant women should be aware of the risks of high blood pressure in pregnancy.
3. Healthcare workers should know which pregnant women have a high risk of developing hypertension or its complications.
4. Magnesium sulphate must be freely available at all antenatal clinics and emergency services and personnel should have the knowledge to administer it.

5. Healthcare workers should know how to use drugs for the management of acute hypertension.
6. Proper systems of referral and transport should be in place and known by healthcare workers.

3.4 HOW IS BLOOD PRESSURE TAKEN IN PREGNANCY?

- Use the correct size cuff.
- Patient may sit or lie on her side.
- Cuff should be on the level of the heart.
- Use Korotkoff 5 sound (where the sounds disappear) to determine diastolic value.
- Only use Korotkoff 4 sound (where the sound muffles) when sound 5 approaches zero.

3.5 WHAT IS ABNORMAL?

- Blood pressure of 140/90 mmHg or more at 2 occasions or more at least 6 hours apart.
- Rise in diastolic blood pressure of 15 mmHg or more above values in early pregnancy.
- Rise in systolic blood pressure of 30 mmHg or more above values in early pregnancy.

3.6 WHAT IS DANGEROUSLY ABNORMAL?

- Blood pressure of 160/110 mmHg or more.
- Proteinuria, ++ on dipstix in a clean catch urine specimen.
- Complaints such as severe headache, abdominal pain and blurring of vision.
- Convulsions.
- Coma.

3.7 WHICH PATIENTS ARE MORE AT RISK?

- Hypertension before pregnancy.
- Hypertension early in pregnancy.

MANAGEMENT OF PRE-ECLAMPSIA

ADMISSION OF A WOMAN WITH PRE-ECLAMPSIA

History and examination

A full clinical assessment is performed as for all pregnancy admissions. Special attention should be given to:

- Symptoms of imminent eclampsia
- Vaginal bleeding
- Severity of oedema
- Pallor and jaundice
- Heart and lung examination
- Precise measurement of the BP, to the nearest 2 mmHg
- A repeat BP measurement after 20 minutes
- Uterine tenderness, irritability, fetal size and liquor volume
- Assessment of the cervix for induction of labour

Special investigations

Where possible, the following investigations should always be performed on admission:

- Full blood count (FBC), including platelet count
- Serum urea and creatinine
- Serum uric acid (unless the mother is in labour)
- Liver function tests (in eclampsia and severe pre-eclampsia)
- Urine dipstick test for protein
- Ultrasound assessment of fetal size and liquor volume
- Cardiotocography (CTG)

Further management depends on whether the pre-eclampsia is mild or severe: mild pre-eclampsia can be admitted to an antenatal ward, while severe pre-eclampsia requires emergency management (see under emergencies).

All pre-eclamptic women should be admitted to hospital

FURTHER MANAGEMENT OF MILD PRE-ECLAMPSIA

- Do daily ward rounds and ask for symptoms of imminent eclampsia
- Measure 4 hourly BP
- Perform daily urine dipstick test for protein
- The mother counts fetal movements daily (figure 6.2)
- Repeat FBC, serum urea, creatinine and uric acid weekly
- Perform CTG daily if possible
- Start antihypertensive medication if BP ≥150/100 (box 6.2)
- If less than 34 weeks, give dexamethasone 8 mg IM 8 hourly for 3 doses to accelerate fetal lung maturity

If proteinuria is irregularly observed, request a 24 hour specimen for protein content.

If proteinuria disappears, the mother may be discharged, to attend antenatal clinic weekly.

Delivery is indicated for any of the reasons listed in box 6.3.

FETAL MOVEMENT COUNTING

This is only indicated for high risk pregnancies, e.g. pre-eclampsia, diabetes mellitus, intrauterine growth impairment, previous unexplained still birth.

1. Ask the mother to count fetal movements (not just kicks) for one hour at the same time every day, usually after breakfast
2. The number of movements should be recorded on a fetal movement chart (figure 6.2)
3. If there are 4 or more movements in one hour, the count is repeated at the same time on the next day
4. If there are less than 4 movements in one hour, or less than half of the hourly average (after about a week of counting), the mother should count fetal movements for one more hour
5. In the second hour, if there are still less than 4 movements or less than half of the hourly average, CTG is indicated to assess fetal well-being. Delivery may be considered depending on the clinical situation

Date	Time Started	Movements in first hour	N.B.	Movements in second hour	N.B.
			If less than 4 move-ments in the first hour go on to the second hour and count again		If less than 4 move-ments in the second hour please go to your clinic for a further test

Figure 6.2. Fetal movement chart

SEVERE PRE-ECLAMPSIA

If the diastolic BP is ≥110 mmHg on two occasions at least 20 minutes apart:

1. Start an intravenous drip and preload with 300 mL Ringer-Lactate over 20 minutes
2. Insert an indwelling urinary catheter
3. Control the blood pressure
4. Transfer from a community health centre to hospital by ambulance
5. At hospital, take blood for FBC, urea, creatinine, uric acid, and liver function tests
6. Measure the blood pressure at least hourly
7. Record urine output hourly
8. Assess fetal condition with CTG, and fetal size by ultrasound
9. If <34 weeks or estimated fetal weight <2 kg, give dexamethasone 8 mg IM 8 hourly for 3 doses to accelerate fetal lung maturity
10. Delivery may be delayed for 24 hours to allow dexamethasone to take effect
11. Conservative management is acceptable for pregnancies of 26-33 weeks (or estimated fetal weight of 900-1500 g), if there are no indications for delivery (box 6.3)

CONSERVATIVE MANAGEMENT OF SEVERE PRE-ECLAMPSIA

From 26-33 weeks, after stabilisation of a mother with severe pre-eclampsia (see emergencies below), it may be in the baby's interests to allow the pregnancy to continue. This is permissible as long as there is no indication for delivery (box 6.3), and should take place in hospitals with experience and facilities for managing severe pre-eclampsia, and with facilities for the treatment of very low birth weight infants.

Management is the same as for mild pre-eclampsia with the addition of:

- CTG every 6 hours
- Weekly ultrasound scans of the fetus
- FBC, serum urea, creatinine and uric acid twice weekly
- Liver function tests twice weekly
- Careful daily assessment for indications for delivery (box 6.3)

IMMINENT ECLAMPSIA

Management is the same as for severe pre-eclampsia, with the addition of magnesium sulphate (box 6.4)

At times, the patient's symptoms may resolve, making delivery unnecessary. She should then be treated as for pre-eclampsia (mild or severe, depending on the level of the blood pressure).

HELLP SYNDROME

HELLP (haemolysis, elevated liver enzymes, low platelets) syndrome should be managed as for severe pre-eclampsia, but may require delivery within 24 hours of diagnosis (if dexamethasone needs to be given) or immediately. Transfer to a level 2 or level 3 hospital is essential, as there is a high risk of haemorrhage, renal failure, and pulmonary oedema.

ORGAN DYSFUNCTION IN PRE-ECLAMPSIA

Evidence of organ dysfunction in pre-eclamptic women requires immediate transfer to a level 2 or level 3 hospital. Such patients may show evidence of:

- Acute renal failure – rapid rise of serum urea and creatinine levels, and oliguria (urine output <500 mL/24 hours)
- Liver dysfunction – jaundice or a rise in serum liver enzyme levels
- Coagulation dysfunction – deranged INR and PTT profiles
- Cardiorespiratory dysfunction – acute pulmonary oedema: this should be treated immediately as described for women with cardiac disease
- Cerebral dysfunction – prolonged coma or lateralising signs

CONTROLLING THE BLOOD PRESSURE IN PRE-ECLAMPSIA

Emergency treatment (BP ≥160/110)

- Preload the patient with 300 mL Ringer-Lactate solution over 20 minutes
- Give dihydralazine 6.25 mg in 10 mL water over at least 4 minutes
- Transfer the patient to hospital by ambulance
- Measure the blood pressure every 10 minutes
- Aim for a diastolic BP of 140/90 mmHg
- Repeat dihydralazine dose every 20-30 minutes if necessary

Other regimens of dihydralazine are acceptable (e.g. 6.25 mg IM as a single dose, or continuous infusion 1.25 to 2.5 mg/hour with titration against the blood pressure). Alternative drugs are labetalol (as an infusion at 20 mg/hour, increasing by 20 mg/hour every 20 minutes to a maximum of 300 mg/hour), and nifedipine (5 mg orally, not sublingually).

Maintenance treatment (BP ≥150/100)

The drugs are usually prescribed in a stepwise fashion, depending on response

- Step 1: Methyldopa 500 mg orally twice daily up to a maximum of 750 mg 3 times daily
- Step 2: Add nifedipine 10 mg orally 3 times daily up to a maximum of 30 mg 3 times daily.
- Step 3: Add prazosin starting with 1 mg orally 3 times daily up to a maximum of 7 mg 3 times daily
- Step 4: Consider delivery.

Box 6.2. Controlling the blood pressure in pre-eclampsia

INDICATIONS FOR DELIVERY IN PRE-ECLAMPSIA

Pregnancy ≥38 weeks
Pregnancy ≥32 weeks in severe pre-eclampsia
Estimated fetal weight ≥1.5 kg in severe pre-eclampsia
Pregnancy <26 weeks in severe pre-eclampsia
Eclampsia
Cerebral oedema
HELLP syndrome
Renal dysfunction (serum urea ≥8 mmol/L, creatinine ≥100 mmol/L, urine output <500 mL/24 hours)
Rising uric acid level (persistently ≥0.45 mmol/L)
Thrombocytopaenia (platelet count persistently <100,000/mm^3)
Uncontrollable hypertension (persistently >160/110 mmHg)
Fetal distress
Dead fetus
Suspected abruptio placentae

Box 6.3. Indications for delivery in pre-eclampsia

MANAGEMENT OF ECLAMPSIA

Principles of care are:

- Control of convulsions
- Reduction of blood pressure
- Clinical and laboratory assessment
- Delivery

ECLAMPSIA BOX

An 'eclampsia box' should be kept at all health institutions that manage pregnant women. The box should contain all the necessities for the immediate management of eclampsia: magnesium sulphate, intravenous drip equipment, a urinary catheter and a copy of a protocol for management.

IMMEDIATE MANAGEMENT OF ECLAMPSIA

1. Call for help, including an advanced midwife or doctor
2. Turn the woman onto her side (left lateral)
3. Clear the airway – ensure that it is open and remove secretions or vomitus
4. Give oxygen by mask
5. Prevent injuries, e.g. with cot sides, and remove sharp objects, etc.
6. Insert an oropharyngeal airway if necessary
7. Start an intravenous drip and give magnesium sulphate (box 6.4)
8. With persistent convulsions or restlessness, give additional magnesium sulphate 2 g IV or clonazepam 1 mg IV over 5 minutes
9. Insert an indwelling urinary catheter
10. Transfer from a community health centre to hospital

MANAGEMENT OF ECLAMPSIA AFTER FITS HAVE BEEN CONTROLLED

1. Send blood for FBC and measurement of urea, creatinine, liver functions and clotting profile (INR, PTT)
2. Control the blood pressure if ≥160/110 mmHg (box 6.2)
3. Insert a central venous pressure line using a cubital vein, if feasible
4. Continue intravenous fluids (Ringer-Lactate or normal saline) at 80 mL/hour
5. Monitor BP, urine output and state of consciousness hourly
6. Assess fetal condition with CTG, and fetal size by ultrasound
7. Continue magnesium sulphate 5 g IM 4 hourly using the precautions as listed (box 6.4) until 24 hours after delivery or 24 hours after the last convulsion, whichever is later
8. The baby should be delivered as soon as possible after the first fit:
   - By caesarean section if there is fetal distress or the cervix is unfavourable
   - Vaginally if the mother is in labour or if the cervix is favourable for induction
9. Vacuum extraction may be necessary in the second stage
10. Do not use ergometrine in the third stage (use oxytocin 10 units IM)
11. Expect return to full consciousness within a few hours of the last fit
12. Transfer women with persistent coma or lateralising signs to a level 2 or level 3 hospital
13. Observe the patient for at least 24 hours in a special care or high care unit
14. Take blood for FBC, and serum urea and creatinine on the day after delivery
15. Do not discharge to a lower level of care after delivery
16. Do not discharge from hospital for at least 3 days

ADMINISTRATION OF MAGNESIUM SULPHATE*

Loading dose: Dilute magnesium sulphate 4 g (8 mL 50% solution) with 12 mL normal saline and give slowly intravenously over 4 minutes, with 5 g IM in each buttock with 1 mL 1% lignocaine. A total of 14 g is given

Maintenance dosage: Magnesium sulphate 5 g IM 4 hourly into alternate buttocks with 1 mL 1% lignocaine, subject to precautions below

Precautions before giving maintenance dose injection

A 5 g maintenance dose is only given if:

- Patellar (knee) reflexes are present,
- The respiratory rate is ≥16 breaths/minute, and
- Urine output is ≥100 mL in the last 4 hours (i.e. since the last dose)

Treatment of overdose

- The symptoms and signs of overdose are a feeling of extreme weakness, decreased respiratory rate, and absent tendon reflexes
- Give calcium gluconate 10% 10 mL IV slowly

**Intravenous infusions of magnesium sulphate (1 g/hour) should only be given in a high care situation, usually in a level 2 or level 3 hospital*

Box 6.4. Administration of magnesium sulphate

LABOUR AND DELIVERY

Delivery of pre-eclamptic and eclamptic women requires skill and experience, and neonatal intensive care facilities for small or ill babies. Transfer to level 2 or level 3 hospital may be necessary. Local protocols for transfer should take into account the levels of expertise and facilities in level 1 and level 2 hospitals.

INDUCTION OF LABOUR

Induction of labour may be undertaken in women with pre-eclampsia.

- Cervical ripening and amniotomy are used as for any other induction
- Give oxytocin 2 units in 200 mL Ringer-Lactate or normal saline, starting at 12 mL/hour, increasing to 24, 36 and 48 mL/hour (3, 6, 9, 12 drops/minute from a 15 drops/mL dropper) every 30 minutes until contractions are adequate

Considerations during labour in pre-eclampsia or eclampsia

- Monitor the fetus with CTG wherever possible, as there is a high risk of fetal distress, especially with severe pre-eclampsia
- Measure blood pressure hourly
- Use an indwelling urinary catheter to measure urine output hourly
- Give intravenous fluids (normal saline or Ringer-Lactate) at 80 mL/hour
- For augmentation of labour, give oxytocin from a 200 mL bag of fluid (as for induction)
- Give magnesium sulphate only if there are symptoms of imminent eclampsia
- Use intravenous dihydralazine if the BP ≥160/110 mmHg, as for emergency BP control (box 6.2)
- Perform vacuum extraction if the BP ≥160/110 mmHg in the second stage
- Ergometrine is contraindicated at all times

Caesarean section

Special anaesthetic considerations for caesarean section in pre-eclampsia and eclampsia are discussed in the chapter on anaesthesia and resuscitation.

POSTPARTUM CARE

- Keep the mother in hospital for at least 24 hours after delivery
- Continue oral antihypertensive medications (e.g. methyldopa) and modify or reduce the dosage as necessary
- Diuretics, e.g. hydrochorothiazide 25 mg daily, may be given
- Treat a BP ≥160/110 with dihydralazine 6.25 mg IM or nifedipine 5 mg orally as single doses, and measure the BP hourly until stabilised
- Discharge the mother from hospital if the BP is <160/110 for 24 hours
- Women discharged on medication should attend after 2 weeks for BP measurement and adjustment (or discontinuation) of therapy

CHRONIC AND GESTATIONAL HYPERTENSION

These are the nonproteinuric forms of hypertension in pregnancy, and they have much better prognoses for mothers and babies. There is however a danger that these patients may develop superimposed pre-eclampsia.

ANTENATAL CARE

- Antenatal care should be conducted by an advanced midwife or doctor
- Routine hospital admission is not required
- Take baseline urea and creatinine levels at the first antenatal visit
- Stable chronic hypertensive women may be seen every 2 weeks
- Gestational hypertensive women should be seen every week
- Give antihypertensive drugs if necessary (see box)
- Replace diuretics, angiotensin converting enzyme (ACE) inhibitors and reserpine with methyldopa in chronic hypertensive women
- Admit to hospital if the BP ≥160/110 or proteinuria is 1+ or more
- Induce labour at 38-40 weeks

DELIVERY AND POSTPARTUM CARE

Precautions are the same as for pre-eclampsia, although the risk of perinatal or maternal complications is much lower.

CHRONIC RENAL DISEASE

Pregnant women with renal disease are at risk for further kidney damage. At ≥26 weeks, management is the same as for pre-eclampsia, with close attention given to renal function. At <26 weeks, referral to a level 2 or level 3 hospital is indicated for specialist assessment and a plan for further management.

CHAPTER FOUR

GUIDELINES FOR THE PREVENTION AND TREATMENT OF PREGNANCY-RELATED SEPSIS

4.1. INTRODUCTION

Pregnancy-related sepsis is the fourth commonest cause of all maternal deaths in South Africa, being responsible for 19% of direct, and 12% of all maternal deaths. Pregnancy- related sepsis includes cases of septic abortion and puerperal sepsis. According to the Confidential Enquiries into Maternal Deaths in South Africa, there were 67 maternal deaths attributable to pregnancy-related sepsis in 1998. Of these, 26 occurred as a result of septic abortion. These deaths are still underreported.

The major errors committed by health workers were (i) failure to diagnose septic abortions, (ii) failure to recognise the severity of puerperal sepsis and septic abortions, and (iii) significant delays in management, combined with poor observations. The medical personnel generally failed to recognise the problem of sepsis and take appropriate action, according to standard management protocols. This was due to either very superficial assessment of patients or lack of monitoring thereafter[1].

For these guidelines, individual recommendations have been graded according to the level of evidence on which they are based.

Grade A: randomised controlled trials

Grade B: other robust experimental or observational studies

Grade C: more limited evidence but the advice relies on expert opinion and has the endorsement of respected authorities.

HYPERTENSION IN PREGNANCY

Hypertensive disorders of pregnancy are a leading cause of maternal mortality in South Africa. Early detection and timely intervention is essential to prevent maternal and perinatal complications.

DEFINITION OF HYPERTENSION

A diastolic blood pressure (BP) of 90 mmHg or more, on 2 occasions at least 4 hours apart

DEFINITION OF PROTEINURIA

The presence of 2+ proteinuria or more on reagent strip (dipstick) testing on 2 clean catch urine specimens taken at least 4 hours apart and persisting through pregnancy

or:

Protein excretion ≥300 mg in a 24 hour specimen of urine

CLASSIFICATION AND GRADING

This is shown in table 6.1 and depends on:

- The time of onset of the hypertension, whether before or after 20 weeks of pregnancy
- The presence or absence of proteinuria

Table 6.1. Classification of hypertensive disorders of pregnancy

HYPERTENSION:	Onset before 20 weeks (chronic hypertension)	Onset after 20 weeks (pregnancy-induced hypertension)
With no proteinuria	Essential hypertension	Gestational hypertension
With proteinuria	Chronic renal disease	Pre-eclampsia

DEFINITIONS OF HYPERTENSIVE DISORDERS OF PREGNANCY

Essential hypertension: hypertension without proteinuria diagnosed before 20 weeks of pregnancy, or a history of essential hypertension prior to the pregnancy

Chronic renal disease: hypertension with proteinuria, diagnosed before 20 weeks of pregnancy, or a history of chronic renal disease prior to the pregnancy

Gestational hypertension: hypertension without proteinuria, detected after 20 weeks of pregnancy

Pre-eclampsia (gestational proteinuric hypertension, pre-eclamptic toxaemia): hypertension and proteinuria, both detected after 20 weeks of pregnancy

Unclassified hypertension: hypertension detected in a woman in whom the BP was not measured before 20 weeks of pregnancy. This may be proteinuric or non-proteinuric.

Superimposed pre-eclampsia: pre-eclampsia that develops in a woman with chronic hypertension

MEASUREMENT OF BLOOD PRESSURE IN PREGNANCY

- The right and left lying semi-lateral, and sitting positions are acceptable
- The supine position (lying flat on the back) should not be used after 24 weeks
- The cuff must be at the level of the heart
- The diastolic blood pressure is taken at the point where the sounds disappear (Korotkoff phase 5). In patients where the sounds do not disappear, the point of muffling (Korotkoff phase 4) may be used.

Box 6.1. Measurement of blood pressure in pregnancy

GRADES OF PRE-ECLAMPSIA

Mild pre-eclampsia: a diastolic BP of 90-109 mmHg, with 1+ or 2+ proteinuria

Severe pre-eclampsia: a diastolic BP of 110 mmHg or more measured on 2 occasions at least 4 hours apart, or 120 mmHg or more on one occasion, or persistent 3+ proteinuria irrespective of the level of blood pressure, or organ dysfunction irrespective of the level of blood pressure

Imminent eclampsia: symptoms and signs that develop in a pre-eclamptic woman: severe headache, visual disturbances, epigastric pain, hyperreflexia, dizziness and fainting, vomiting

Eclampsia: generalised tonic-clonic seizures after 20 weeks of pregnancy and before 7 days after delivery, associated with hypertension and proteinuria, in the absence of other causes of convulsions

HELLP syndrome: the presence of haemolysis, elevated liver enzymes and low platelets, almost always in association with hypertension and proteinuria

PATHOPHYSIOLOGY OF PRE-ECLAMPSIA

Pre-eclampsia is a multiorgan disease affecting predominantly the circulatory system, renal system, central nervous system, coagulation, liver etc. as shown in figure 6.1.

A placental immunological or chemical defect causes a prostaglandin imbalance, which affects the endothelium (lining) of blood vessels resulting in spasm of blood vessels, platelet aggregation and leakage of plasma from capillaries

Pre-eclampsia complicates 5-10% of pregnancies in South Africa. There is still no effective method of prevention and the only known cure is termination of pregnancy. Early detection, treatment and follow up may help in reducing death and morbidity from complications of pre-eclampsia.

Maternal deaths are most frequently caused by:

- Eclampsia, cerebral haemorrhage and cerebral oedema
- Pulmonary oedema
- Haemorrhage from abruptio placentae or liver rupture
- Acute renal failure

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REPUBLIC OF NAMIBIA

Ministry of Health and Social Service

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Enquiries: Ms. M. Zauana **Ref.:** 17/3/3/AP **Date:** 28 September 2004

OFFICE OF THE PERMANENT SECRETARY

Dr. Berhe Hailemariam
Private Bag 2789
Swakopmund

Dear **Dr. B. Hailemariam,**

Pre-eclampsia and its outcome in two referral hospitals, Windhoek and Katutura referral Hospitals, Namibia.

1. Reference is made to your application to conduct the above-mentioned study.

2. The proposal has been evaluated and found to have merit. However, some issues in the proposal need to be revisited. Please find attached comments/recommendations for consideration.

3. Kindly be informed that approval has been granted under the following conditions:

3.1. The data collected is only to be used for your Masters degree;
3.2. A quarterly progress report is to be submitted to the Ministry's Research Unit;
3.3. Preliminary findings are to be submitted to the Ministry before the final report;
3.4. Final report to be submitted upon completion of the study;
3.5. Separate permission to be sought from the Ministry for the publication of the findings.

Wishing you success with your project.

Yours sincerely,

DR. K. SHANGULA
PERMANENT SECRETARY

Directorate: Policy, Planning and HRD
Subdivision: Management Information and Research

Forward with Health for all Namibians by the Year 2000 and beyond