Master thesis

Pre-eclampsia in Tanzania and Norway. Differences and similarities in follow-up and treatment, and how this affects maternal and perinatal/neonatal health.

- **A combined literature and case study**

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Place and Date: Tromsø, 1th of June

Preface:

This is a master thesis written on 5th year of medical school at The Arctic University of Norway, Tromsø. The thesis is based on total of 8 cases with pre-eclampsia in Tanzania and Norway. There exists a lot of theory about pre-eclampsia, but not a lot of case-studies that I could find in literature. To conduct this thesis I had to travel to Tanzania, and I received 2800 NOK from the university to be able to do so. I want to thank Jørgen and Karoline Linde who gave me contact with Haydom Lutheran Hospital and a place to live during my stay in Tanzania, to the doctors and midwifes at Haydom Lutheran Hospital who I worked with and patiently answered all my questions, to all the midwifes and nurses at the birth department at the University Hospital of Northern Norway, Tromsø, who called me when they had pre-eclamptic patients, so I was able to closely follow up these patients. I also want to thank my supervisor Jon-Øyvind Odland for great supervising and good advices when writing this thesis.

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1.0 Abstract

Background: This thesis is about pre-eclampsia in Tanzania and Norway, and the differences and similarities in how they follow up pre-eclamptic patients, the management and treatment, and the outcome for the mother and the foetus/neonate. It is a combined literature and case study.

Material and methods: I followed up a total of 6 patients at the University Hospital of Northern Norway in Tromsø and 2 patients at Haydom Lutheran Hospital in Tanzania. At Haydom Lutheran Hospital I collected information about their local guidelines. In Norway I searched for the national guidelines in literature. I also collected information from a birth protocol at the University Hospital of Northern Norway, Tromsø. I searched and read through a lot of articles, and chose the ones that highlighted the title of the thesis.

Results: Comparison between the two countries shows that the incidence of pre-eclampsia is probably higher in developing countries. Most of them who develop pre-eclampsia are primigravidae. Caesarean section is performed in 70% of women with pre-eclampsia or complications due to pre-eclampsia. There exist several medications used for treatment of this disease. The standard of New-born Intensive in these two institutions was very different, and the new-born neonate was in greater risk in Tanzania compared to Norway. Since pre-eclampsia may lead to prematurity, they are in greater risk in Tanzania due to lack of equipment. A big problem in Tanzania is that as many as 50% deliver their baby at home, which is a huge risk factor for both the mother and the foetus.

Conclusion: The guidelines for these two institutions were somewhat the same, but it is more difficult to follow-up patients in Tanzania due to more challenges in great travel distance, expensive costs of care and lower socioeconomic standard. They used somewhat the same medications in Norway and Tanzania. I found some small differences in which drug they preferred to use. Because of lower socioeconomic standard in Tanzania, both the mother and the foetus have a worse outcome compared to Norway, and that can also be due to home deliveries. If the pre-eclamptic woman is able to come to Haydom Lutheran Hospital in Tanzania and gets admitted, she gets adequate health care, and lives can be saved.

2.0 Introduction

2.0.1 What is pre-eclampsia? A definition

Pre-eclampsia is diagnosed if a pregnant woman has hypertension and proteinuria after 20 weeks of pregnancy [1]. Pre-eclampsia is a multiorgan disease by an unknown aetiology [2]. It can be asymptomatic until the disease become more severe, with debut of cerebral symptoms like generalized seizures (eclampsia) or cortical blindness [3]. About 10 % of pre-eclampsia occurs before 34 weeks of gestation, and this is why delivery due to pre-eclampsia is one of the reasons for preterm births. Delivery is the only cure, and decisions regarding when to deliver and mode of delivery should be based on a combination of maternal and foetal factor [2]. In such case pre-eclampsia represents a major health problem and affects both maternal and foetal health. Pre-eclampsia may cause intrauterine growth retardation, preterm birth, perinatal death, antepartum and postpartum haemorrhage, acute hepatic and renal failure and maternal death [4].

Hypertensive disorders, including pre-eclampsia, are important factors of severe morbidity, disability and death among mothers, foetus and infants. Management of pre-eclampsia aims to minimalize any pregnancy related complications, avoiding unnecessary prematurity and maximize maternal and perinatal/neonatal survival. Pre-eclampsia and eclampsia are the major causes of maternal and perinatal morbidity and mortality. Most of the deaths are avoidable, and optimizing health care to both prevent and treat these women are important steps towards achieving the Millennium Development Goals [5].

2.1 Presentation of the two study sites

This study is done at Haydom Lutheran Hospital in Tanzania and at the University Hospital of Northern Norway, Tromsø, where I followed up a total of 8 patients with pre-eclampsia and/or severe complications due to pre-eclampsia.

Haydom Lutheran Hospital became the chosen hospital in Tanzania because I had friends living there and they gave me contact with this hospital. It is a district hospital 300 km from Arusha, and is situated in a rural site in the Mbulu area in northern Tanzania. The hospital have 450 beds and serves approximately 450 000 people in the area. People living there are very poor, the roads are extremely bad and public transport is almost non-existing. Primary

care does not exist, except mother-baby-stations organized by the hospital. At the birth department there are approximately 3 500 births a year. The average parity of each woman is 5,24. 50 % of the mothers deliver at home. Some of them do not go to the hospital because it is expensive to get there and to be admitted [6].

The University Hospital of Northern Norway, Tromsø, became the chosen hospital in Norway because it is my university hospital. This hospital serves the population in the northern part of Norway. It is a big region hospital, but also a local hospital for the county of Troms and parts of Nordland [7]. In the period from 20.08.12 – 20.08.13 there were 1342 deliveries at the birth department (see table 9).

2.2 Objectives

My objectives were to identify risk factors of pre-eclamptic women and to point out the limitations and challenges with these kinds of patients at Haydom Lutheran Hospital in Tanzania and at The University Hospital of Northern Norway in Tromsø. There were four specific points I wanted to look at: The follow-up of pre-eclamptic patients, the management and treatment, the pregnancy outcome for the foetus/neonate and the pregnancy outcome for the mother.

2.2.1 The follow-up of pre-eclamptic patients

Pregnancy care in Norway: The pregnant women either go to a mid-wife or a doctor. The first control is in week 8-12 where they receive information regarding recommended weeks of control, way of living while pregnant, checks weight and BMI, ask for smoking, course with emphasis on becoming parents and information regarding different tests and examination. They measure blood pressure (BP), haemoglobin (Hb), blood typing, rhesus-status, antibodies, immunity of rubella, HIV, syphilis, hepatitis B and C on indication, screening for asymptomatic bacteriuria in women who has had repeated urine tract infections (UTI's), checks for protein- and glucoseuria and do a chlamydia test in women below 25 years old or on indication. The first ultrasound is in week 17-19 of gestation to consider the exact week of gestation, identify multiple pregnancies, location of the placenta and structural anomalies [8].

In week 24, 28, 32, 36, 38, 40 and 41 they do symphysis- fundus measurement, checks BP, weight, protein- and glucoseuria and auscultation of the foetal heart. In week 28 and 36 it is also control of antibodies in Rhesus negative women. Lie of the baby is checked in week 36, 38, 40 and 41. With breach presentation in week 36, the woman should be referred to an ultrasound for consideration of external inversion. In week 41 she is referred to assessment due to overtime [8].

Pregnancy care in Tanzania: There are 27 mother-baby-stations driven by Haydom Lutheran Hospital in Tanzania. 6 of the stations are so far away that the employees have to go there by a small plane. In one year nearly 30 000 mothers and 70 000 children are examined at these stations. The pregnant woman is sent to control in week 16, 20-24, 28-32 and 36 of gestation and the management at this site involves:

- History and information regarding previous pregnancies and births
- Physical examination, including palpation and examination of the foetus
- Health information, education and supervising
- Lab tests: haemoglobin, blood type, syphilis and vaccine against tetanus
- Malaria prophylaxis twice during pregnancy [6].

Developing countries have more challenges regarding poverty, long distance to the hospital and lack of doctors. I wanted to see and compare to Norway how this affects how they are able to follow-up pre-eclamptic patients in Tanzania, and the outcome regarding this.

2.2.2 The management and treatment

There are many ways of treating pre-eclamptic women. Should the mother be at home or admitted to the hospital? This depends on whether her condition is stable or not. In Norway it is recommended that all pregnant women with diastolic pressure > 90 mm Hg and newly discovered proteinuria should be admitted because it is a condition that can develop to become severe quite rapid. If the condition is stable, she can go home with information about severe symptoms and frequent monitoring. Pregnant women with severe pre-eclampsia, eclampsia and mild pre-eclampsia that occur in week 24-35 of gestation should stay at the hospital until they have delivered [9].

With pre-eclampsia before week 27 of gestation, the goal is to prolong the pregnancy which provides the best outcome for the foetus. The risk for the mother and the foetus should be monitored frequently. In Norway the monitoring of the mother consist of considering her general condition (where we emphasize headache, visual disturbances, pain in the abdomen), blood pressure, if she gains weight, urine and the degree of potential oedema. Monitoring of the foetus consists of doing a non-stress test, which is done after week 32 of gestation, to check the baby's well-being. This will be done with an ultrasound to control the activity of the foetus, to check and measure volume of amniotic fluid, foetal growth and maturity of the placenta. Measurement of the blood flow in a. umbilicalis and a. cerebri media are done some places. Increased resistance in a. umbilicalis can be an expression for pathologic conditions in the placenta. The only curative treatment of pre-eclampsia is delivery. They aim to give vaginal birth, but in some situations caesarean section is required [9].

There are a number of different medications that can be used treating pre-eclampsia, where Methyldopa (Aldomet), Labetalol (Trandate), Calcium antagonist and Beta blockers are appropriate medications [9]. It is expected that there are greater challenges treating patients with pre-eclampsia in developing countries, because it is more common with a delay in seeking help, delay to get in time to the hospital, and delay in health care [10]. I wanted to see if these expectations were correct and if they had the same management and used somewhat the same drugs in Tanzania as in Norway. I wanted to learn if the challenges developmental countries have could make this more difficult.

2.2.3 The pregnancy outcome for the foetus/neonate

Perinatal mortality is death of a foetus or death during first week of life, which also is early neonatal death, with birth weight of 500 grams or more [11]. The progress on United Nation's Millennium Developmental goal 4 (MDG4) to reduce the mortality of children under five years old has been slower than anticipated. The main reason for that is due to high neonatal mortality in developing countries. Worldwide there are about 4 million neonatal deaths each year, and three quarter of these occur in the first week of life, having a huge risk at the first day of life [12]. I wanted to look at if pre-eclampsia could be one of the reasons why there still are a large number of neonatal deaths in developing countries such as

Tanzania. Pre-eclampsia is also the reason for approximately 20 % of all preterm births [13]. With that acknowledge, I wanted to see if prematurity caused by pre-eclampsia could be a reason for neonatal death.

2.2.4 The pregnancy outcome for the mother

Definition of maternal death from The World Health Organization and ICD-10 is the death of a woman while she is pregnant or within 42 days after delivery. The eight millennium development goal is to reduce maternal mortality rate by 75 % from 1990 to 2015. The MMR (maternal mortality rate) in developing countries is quite high with 450 maternal deaths per 100 000 live births. In developed countries in comparison it is 9 per 100 000 live births [2]. I wanted to look at why there are such a high number of maternal deaths in developing countries such as Tanzania compared to Norway which is a developed country with fewer maternal deaths. I wanted to learn if pre-eclampsia could be a reason for that.

2.3 Theory

2.3.1 Epidemiology

WHO estimate the incidence of pre-eclampsia to be seven times higher in developing countries compared to industrial countries. In Tanzania the incidence varies from 1.8% to 7.1% [10]. In my own research, searching through the birth protocol from 20.08.12-20.08.13 at the University Hospital of Northern Norway, Tromsø, I found the incidence to be 2.8 % (see table 9). 65 – 75 % of pre-eclamptic women are primigravidae [9].

2.3.2 Pathophysiology

The aetiology of pre-eclampsia is not fully understood, but it is known that the pathophysiology of this disease involves maternal and foetal/placental factors. It is necessary to have placental tissue to develop pre-eclampsia [2]. Disturbed interactions between foetal trophoblasts and maternal cells can cause defective trophoblast invasion, and this is considered to be important in the pathophysiology [13]. The cytotrophoblast cells infiltrate the spiral arteries in the decidual portion, but fail to go through the myometrial segment [2]. Reduced placental perfusion and spiral artery remodelling are also considered to create oxidative stress and a release of inflammatory factors into the maternal circulation [13]. Spiral arteries fail to develop into large vascular channels, and a shallow placentation

leads to dysfunctional placenta. This combined with atherosis may be one of the causes for reduced placental perfusion, and poor placental perfusion is proposed to be the cause of pre-eclampsia. Reduced placental perfusion results into different production of agents in the placenta, and this leads to activated and injured endothelial cells. Trophoblast products cause this disease through endothelial dysfunction and cell damage through deported microvilli. Endothelial dysfunction increases sensitivity to normal endogenous pressors. The results of that are increased vascular permeability and activation of the coagulation cascade. There are two main factors that we know of that could be causes of pre-eclampsia: poor placental perfusion and endothelial dysfunction [2].

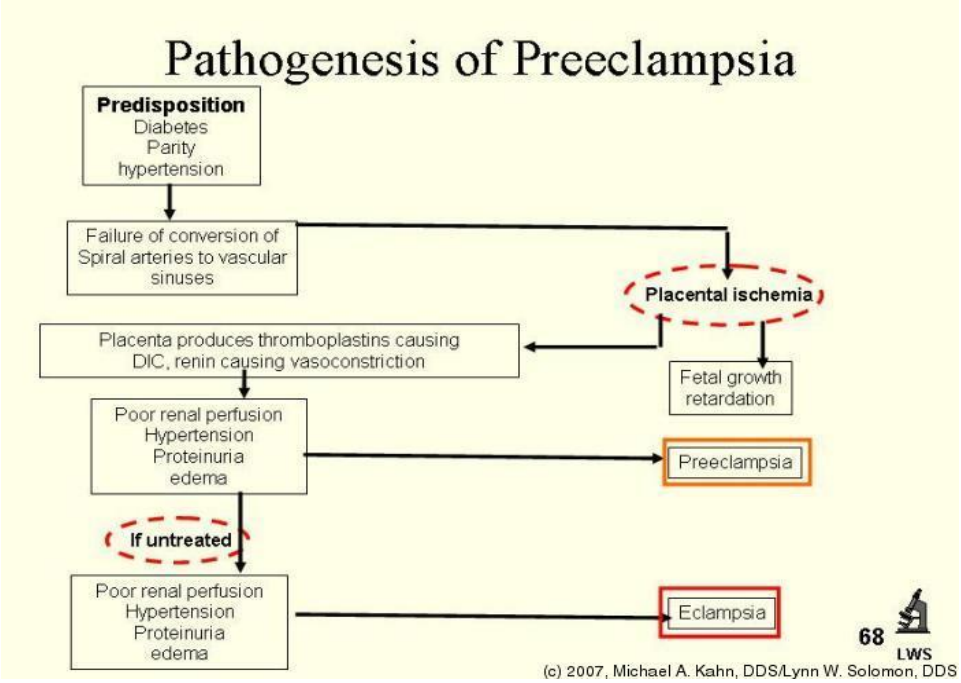

Figure 1: Pathogenesis of pre-eclampsia [14].

2.3.3 Predisposing factors:

- Pre-eclampsia in a previous pregnancy
- First pregnancy (null parity, primigravidae)
- 10 years since a previous pregnancy
- Age 40 or more (older maternal age)
- BMI > 35 (obesity)
- Multiple pregnancy

- Family history of pre-eclampsia
- Underlying medical conditions that were present before the pregnancy, such as hypertension, renal disease, diabetes and anti-phospholipid antibodies [15].

2.3.4 Diagnostics

To obtain correct diagnose of the pregnant woman with a high blood pressure, one have to distinguish between several groups:

- Chronic hypertension
- Pregnancy induced hypertension
- Mild pre-eclampsia
- Severe pre-eclampsia [9].

Chronic hypertension: Hypertension that is proven before week 20 of gestation [9].

Pregnancy induced hypertension: If a former normotensive woman got a systolic blood pressure > 140 mm Hg and/or diastolic blood pressure > 90 mm Hg, and she does not have proteinuria, it is called pregnancy induced hypertension [9].

Mild pre-eclampsia: Mild pre-eclampsia is classified as a syndrome with hypertension (>140/>90 mm Hg), proteinuria (>0, 3 g/24 h) and possible edema [9].

Severe pre-eclampsia: Severe pre-eclampsia occurs if the systolic blood pressure is > 160 mm Hg and/or the diastolic blood pressure is > 110 mm Hg, or if the loss of protein is > 3 g per day or more. Further, if the loss of protein is above 3 g/day, it is also severe pre-eclampsia, even though the blood pressure only satisfies the requirement of mild pre-eclampsia [9].

2.3.5 Complications

Eclampsia: Both mild and severe pre-eclampsia occurs after 20 weeks of gestation, and can lead to severe complications such as eclampsia if not treated [10]. Symptoms can be headache, visual disturbances and restlessness [16]. The occurrence is convulsions superimposed on pre-eclampsia, during pregnancy, delivery or in the first 10 days after delivery, that cannot be attributed to any other cases [2]. As with pre-eclampsia the entire aetiology of eclampsia is not understood either. 5- 8 % of women with pre-eclampsia present with eclampsia in developing countries [5]. Eclampsia is associated with 10 % of

maternal deaths and 2-3 % of those who are affected get permanent neurological sequel [16], [17].

Abruptio placentae: About 1 % of all pregnancies is complicated by abruptio placentae, and can be a complication to severe pre-eclampsia. Abruptio placentae can occur dramatically with pain, bleeding and affected general condition, but symptoms are not always present. It can be life threatening both for the mother and the foetus if the abruption is total [16].

HELLP-syndrome: In the term HELLP the H stands for haemolysis, E and L for elevated lever enzymes (abnormal liver function tests), L and P for low platelets (thrombocytopenia). This condition is rare, but occurs more frequently than eclampsia. Symptoms of HELLP are epigastric pain or pain below right costae, and sometimes nausea and vomiting are present [16]. This condition is associated with endothelial damage and is an important predictor for organ dysfunction and mortality [5].

2.3.6 Medications

Mechanism of action of the different medications used in Tanzania and Norway:

Methyldopa (Aldomet): Methyldopa is taken into neurones by an active transport and is converted to alpha methyl noradrenaline which is a potential alpha-2-reseptorstimulator. Thereby the blood pressure decreases by inhibition of sympathetic nerve system primarily by CNS-effects, but also by an effect on the peripheral sympathetic nerve endings [18].

Labetalol (Trandate): Labetalol is an adrenergic alpha-1-betareceptorantagonist which lowers the blood pressure by several mechanisms. Alpha-1-receptor blockade is more prominent in Labetalol than other adrenergic alpha-1-betareceptorantagonist medications. It reduces peripheral resistance. Beta-receptor blockade lowers the heart rate and prevents tachycardia [18].

Nifedipine (Adalat): Nifedipine is a calcium-antagonist which inhibits influx of calcium ions through slow calcium channels primarily in smooth muscle cells in vessel wall, but also in myocardial cells. The effects are vasodilatation and reduced myocardial contraction and heart rate. In normal dose of Nifedipine the conduction velocity in the AV node will not be affected, as it will in other calcium-antagonists. It might give initial tachycardia, but to reduce that one can give prolonged-release tablets which gives slow absorption [18].

Hydralazine: Hydralazine causes selective dilatation in the arteriole without affecting known receptors. It seems likely to be converted to NO and thereby increase cGMP in smooth muscle and perhaps open potassium channels. Hydralazine should never be used alone, and in patients with pre-eclampsia it is often used together with Methyldopa (Aldomet) [18].

Magnesium sulphate: Magnesium sulphate is given if an eclamptic woman gets generalized tonic-clonic seizures inside hospital [18]. It can be used for prevention and treatment of eclampsia [5], [17], [19].

Calcium gluconate: That can be administrated if there is suspected magnesium toxicity after administration of magnesium sulphate. It will reverse the effects of the toxicity [19].

Diazepam: Diazepam is a part of the group benzodiazepines. It has an effect on specific receptors and alters the inhibitory effect of GABA in the central nervous system [18].

Misoprostol (Cytotec): Misoprostol is a prostaglandin which will make the uterus contract, and is used in induction of labour and if post-partum haemorrhage occurs [18].

Pethidine: Pethidine is an opioid agonist. When using Pethidine as pain killers before and during labour, it is observed impaired search and sucking behaviour, delayed lactation, reduced level of alertness and respiratory depression in new-born babies [18]. Pethidine passes easily across the placenta by passive diffusion, and the metabolite Norpethidine has a half-life of 60 hours in the new-born baby [20].

Dihydralazine (Nepresol): The mechanism of action is almost the same as for Hydralazine. It causes dilatation of arterioles, reduces peripheral resistance and increases cardiac output. It also increases renal blood flow. It is partially converted to Hydralazine [18].

Captopril: Captopril is an ACE- inhibitor which decreases conversion of angiotensin I to angiotensin II and the breakdown of bradykinin. The effects are mainly caused by reduction of angiotensin II which leads to increase of renin that further increase angiotensin I. Reduction of angiotensin II decreases sympathetic activity which leads to a dilatation of arteries and veins. The peripheral vascular resistance decreases. It is also a release of aldosterone from the adrenal glands. That causes increased excretion of sodium and water and decreased excretion of potassium and magnesium. Renal perfusion increases [18].

Betamethasone: It is a glucocorticoid that is given to the mother if expected threatening preterm birth > 23 weeks and < 34 weeks of gestation, to increase the lung maturation of the foetus. It is ideal that it is given 24 hours before delivery, but should be given even though the birth is expected earlier [18].

Surfactant: Curosorf is a naturally surfactant from pork. There are also other unregistrated lung surfactant as Bovint Beraktant (Survanta) and synthetic surfactant (Exosurf). It is used in premature children < 34 weeks of gestation for lung maturation [18].

Aminophylline: The substance in aminophylline is theophylline ethylen diamin [21]. Aminophylline can be used to reduce apnea and stimulate breathing in preterm infants [22].

2.3.7 Guidelines

At Haydom Lutheran Hospital there were guidelines on management of pre-eclampsia and eclampsia. Short version is below:

Management of mild pre-eclampsia:

- Full assessment which includes the following: daily measurement of blood pressure (BP) x 2, urine to quantify protein and check of reflexes. They take cross-match and check urea, creatinine, bilirubin, AST and ALT. If BP > 150/>100 mmHg, they give maintenance anti-hypertensive medication. If BP is >160/>110 mmHg they give emergency anti-hypertensive medication.
- Ultrasound to assess foetal growth and amniotic fluid.
- If proteinuria is stable at 1+, BP well controlled and <160/<110 mmHg, normal blood tests and no symptoms, the patient can be managed as an outpatient with follow-up of BP, urine and foetal condition two times per week. If protein rises to 2+ or rise in BP, the patient is readmit to the hospital.
- Induction of labour above week 37 of gestation [23].

Management of severe pre-eclampsia:

- Admission. If diastolic BP > 110 mmHg, emergency anti-hypertensive medication is given.
- Consider starting infusion of magnesium sulphate if birth is planned within 24 hours.

- Give Betamethasone (6 mg intra muscular (i.m) every 12 hours for 48 hours – total 24 mg)) if 26-36 weeks of gestation.
- Check Haemoglobin (Hb), cross-match, liver function tests, urea, creatinine, clotting status.
- Every hour – check BP, pulse rate (PR), respiratory rate (RR), urine output, reflexes, auscultation of lungs (for pulmonary oedema).
- Limit maintenance fluid to 80 ml/hour. If severe oedema/shortness of breath/unwell, then catheterize, measure urine output hourly, and start strict fluid balance chart.
- Discuss delivery. Control BP, then deliver baby within 24 hours if:
- > 34 weeks completed weeks of gestation
- Severe refractory hypertension (BP > 160/>110 mmHg despite treatment)
- Rapidly worsening symptoms/signs
- Worsening blood tests
- If no immediate delivery, arrange ultrasound to assess growth and amniotic fluid every 2 weeks [23].

Management of eclampsia:

- Call for help, protect from injuries, standard check ABCD (Airways, Breathing, Circulation, Disability).
- Give Magnesium Sulphate.
- If diastolic BP > 110 mmHg, emergency anti-hypertensive medication is given.
- Catheterize measure urine output hourly, start strict fluid balance chart.
- Check Hb, Glasgow Coma Scale (GCS), blood slide, liver function tests, clotting status.
- Every hour – check BP, PR, RR, urine output, reflexes, and auscultation of lungs.
- Monitor for signs of magnesium toxicity (low respiratory rate, loss of reflexes, and urine < 30 ml per hour). Give calcium gluconate 10 ml 10 % if signs of toxicity.
- Deliver baby within 12 hours (when patient is stable) [23].

Post –natal for all these patients: The patient can be discharged if BP is controlled <150/<100-80 mmHg, and arrangement of weekly follow-up of hypertension should be scheduled. Review 6-8 weeks after birth [23].

Guidelines of medical treatment at Haydom Lutheran Hospital, Tanzania:

Methyldopa (Aldomet), Nifedipine (Adalat) and Hydralazine are the standard drugs which are used for moderate hypertension (BP > 150/>100 mmHg and <160/<110 mmHg). For Methyldopa it is normal to start with 250 mg per os (p.o), with maximum daily dose of 1 g. For Nifedipine one can start with 10 mg p.o, with maximum daily dose of 30 mg. For Hydralazine starting dose is 25 mg p.o, and you can titrate with the same dose times four. Methyldopa should be changed to a more effective alternative within 2 days after delivery [23].

Hydralazine intra venous (i.v) and intra muscular (i.m), and Nifedipine sublingual (under the tongue) are the standard drugs which are used for severe hypertension (BP >160/>110 mmHg). Hydralazine is given 5 mg i.v (over 3-4 minutes) and repeated every 30 minutes if diastolic BP > 110 mmHg (maximum total of 20 mg). Hydralazine can also be given 12, 5 mg i.m, and be repeated every 2 hours if diastolic BP > 100 mmHg. If the diastolic pressure does not decrease after 30 minutes, Nifedipine is given. If Hydralazine is not available or BP is not responding, Nifedipine 5 mg sublingual is given and repeated after 10 minutes if diastolic BP > 110 mmHg, then 10 mg every 4 hours [23].

There were national guidelines for management of pre-eclampsia and eclampsia in Norway and a short version is below:

Management of both mild and severe pre-eclampsia:

- Measure blood pressure (BP). How often depends on the clinical assessment of the pregnant woman.
- With proteinuria: check urine dip-stick, quantify 24 hour urine, and total protein/creatinine ratio.
- Blood samples: Hb, platelets, AST, ALT, LD, uric acid and creatinine. With severe pre-eclampsia and HELLP-syndrome also measure albumin, INR, cephotest, fibrinogen, D-dimer, anti-thrombin and haptoglobin.
- CTG, ultrasound and Doppler (a. umbilicalis/a. cerebri media).
- Corticosteroid is given to the mother (in 23/24-34 week of gestation) for lung maturation of the foetus, which increases survival for the foetus.

- Cervical assessment and clinical options for birth induction.
- The condition is closely monitored daily, and it can be appropriate to start treatment for high BP, treatment with i.v fluid and seizure prophylaxis. Since development of pulmonary oedema can occur even after small amounts of fluid i.v, this has to be monitored [24].

Findings and symptoms in mothers that indicate urgent delivery includes uncontrolled BP with severe headache and visual disturbances, rapidly increasing and significant proteinuria and/or rise in creatinine, eclampsia, thrombocytopenia with rapid decline, severe liver affection and pulmonary oedema [24].

Findings and symptoms in foetus that indicate urgent delivery includes pathologic CTG, small amount of amniotic fluid, severe intrauterine growth retardation, pathologic Doppler and a missing or reduced flow in the diastole in measurement of the a.umbilicalis [24].

Post natal: If the woman still has hypertension when she is discharged, she needs to be followed up. If she had severe pre-eclampsia, eclampsia or HELLP-syndrome, a further assessment should be considered (hypertension, renal function, thrombophilia, anti-phospholipid syndrome) [24].

Management of eclampsia:

- Call for help. Airway control and prevent any injury.
- Treatment: Diazepam, 10-20 mg, given i.v or rectally will often stop seizures, but sometimes a higher dose is necessary. Seizures can also be primarily treated with magnesium sulphate. If the first eclamptic fit is stopped by using diazepam, prophylactic treatment with magnesium sulphate should be started to prevent a new fit.
- If magnesium sulphate is given, toxicity may occur, so the patient has to be monitored the first 2 hours after treatment. If patellar reflex ceases, respiratory rate is lower than 10/min and/or urine output is below 25 ml/hour, the infusion of magnesium sulphate should be stopped. Antidote can be considered, which is Calcium Gluconate.

- The patient has to be stabilized before delivery. Often caesarean section is indicated if vaginal delivery cannot be expected shortly.
- The patient is sent to Intensive Care Unit (ICU) after an eclamptic fit to be treated and monitored [25].

National guidelines of medical treatment in Norway:

With blood pressure > 160/110 mmHg it is indication for medical treatment. The most common drugs used to treat pre-eclampsia in Norway are Labetalol (Trandate) and Nifedipine (Adalat). One can start with Labetalol (Trandate) 200 mg p.o as a starting dose. It should have an effect after 30 minutes. It can be repeated after a few hours. If oral therapy cannot be tolerated due to for example nausea, vomiting or rapidly rise in blood pressure, it can be given i.v and that should have an effect after 5-10 minutes. It is usual to start with 20 mg, and if that does not have any effect, one can increase to 40-50 mg i.v. Maximum dose is 220 mg. Nifedipine is given orally 10 mg x 2, and maximum per day is 40 mg x 2. Nifedipine and/or Labetalol are often given in combination with Methyldopa (Aldomet). Dihydralazine was previously the leading i.v drug, but is withdrawn from the market in Norway. Seizure prophylaxis should be considered in rapid onset of severe pre-eclampsia, and it is Magnesium Sulphate that should be given [24].

2.4 Limitation of the thesis

There exists a lot of literature about pre-eclampsia, but I limited the thesis with choosing four specific points I wanted to look at; how they follow-up pre-eclamptic women, the management and treatment, and the outcome for the mother and the foetus/neonate. The subject was chosen due to great interest in gynaecology/obstetrics and Africa, and I wanted to compare the health facilities in Tanzania with Norway. I chose case-study because I wanted to learn more about the process with these patients at hand, and literature study to learn more about the subject.

3.0 Methods

3.1 The work process

I followed up 6 patients at the University Hospital of Northern Norway, Tromsø, in February-May 2013 before my travel to Tanzania in July 2013. With this experience and more acknowledge about the subject, I travelled to Haydom Lutheran Hospital in Tanzania and worked at a birth department. There were only 2 relevant patients at Haydom the one week I worked there, and that is the reason why I have more cases from Norway than in Tanzania. In Tanzania I also met some challenges especially regarding the language. I had learned some Swahili before I went to Tanzania, and could communicate on an easy level. I had some colleagues to translate into English, and I also read the patients' journal which was in English. It was a handwritten journal, which sometimes could be hard to understand. I collected approval and signature from the women in my 8 cases, and assured them that they would be anonymous. I went through the local guidelines of pre-eclampsia at Haydom Lutheran Hospital and in Norway I had to find the national guidelines in literature. At Haydom Lutheran Hospital in Tanzania I asked the staff questions about how they follow up pre-eclamptic patients, the management, and what they thought were the challenges about this group of patients thinking about the outcome for the mother and foetus/neonate. I also spent some time at the New-born Intensive at Haydom Lutheran Hospital, where I followed up a preterm infant born in 34 weeks of gestation by an eclamptic mother.

At the University Hospital of Northern Norway, Tromsø, I searched through the birth protocol from 20.08.12- 20.08.13 to look at the incidence of pre-eclampsia, percent of primigravidae, percent of preterm deliveries and the choice of delivery. In Tanzania I did not have the opportunity to do so due to lack of research approval. The process of getting the approval was very complicated and I found out that it was not necessary to get it for this small thesis. That is why I had to find the incidence of pre-eclampsia in Tanzania in literature. Literature also describes the rate of primigravidae, preterm births and the rate of caesarean section in this group of patients.

Regarding literature I mostly searched in Pubmed, Cochrane and The Norwegian Medical Association. My search criteria were "pre-eclampsia", "pre-eclampsia in Tanzania", "pre-eclampsia in Norway", "perinatal mortality", "neonatal mortality", "maternal mortality",

“management pre-eclampsia”, “medications pre-eclampsia” and “prematurity pre-eclampsia. I searched and read through a lot of articles, and chose the ones that highlighted my title. During fall 2013 I read through the chosen articles about the subject pre-eclampsia and I also started writing the thesis in this period. The work with writing the thesis continued from January to May 2014.

3.2 The methods validity and reliability

I followed up a total of 8 patients in Norway and Tanzania with interviews and registration of medical information. It is not enough patients to draw any conclusions, but the cases highlights different aspects of the disease described in literature. Since I have been in these two different institutions working, gaining experience, seeing similarities and differences, I have made my own reflections regarding the subject at hand, and I tried to find the same results in literature. The few cases in this study cannot be used for any statistic assessment.

3.3 Available literature and quality of literature

In my study of the birth protocol at the University Hospital of Northern Norway, Tromsø, I found an incidence of pre-eclampsia to be 2, 8 %. This is not a very reliable source since it was not stated in the birth control that my case number 3 had pre-eclampsia even though it was present. That is why I cannot say that the incidence really was 2, 8 %. In discussion with mid-wives at the University Hospital of Northern Norway, Tromsø, it reflects that the incidence might be a bit higher. The rate of primigravidae, preterm birth and the rate of caesarean section are more reliable, and can be considered as a true fact since it is more likely that this is written down in the birth protocol.

The literature I found is mostly evidence based literature which is reliable. I tried to find literature where I could draw lines to my cases, and literature which could answer my title.

4.0 Results

Results of my study are based on cases from Haydom Lutheran Hospital in Tanzania and the University Hospital of Northern Norway in Tromsø.

They took a lot more blood samples of the women in Norway than in Tanzania, and they measured more frequently, but they did not measure glucose in Norway as they do in

Tanzania. To compare with Tanzania I write down the same blood samples that were taken in Tanzania, and comment on other blood samples outside the reference area taken in Norway.

Reference areas for the different blood samples in women are: AST: 15-35 U/L, ALT: 10-45 U/L, Creatinine: 45-90 micromole/L, Urea: 155-350 micromole/L (in women age 18-49), Total bilirubin: 5-25 micromole/L, Hb: 11,7-15,3 g/dL (in women age > 12 years), Glucose: 4,0-6,0 mmol/L [26].

4.1 Case presentation

Case 1: The University Hospital of Northern Norway, Tromsø:

Para 0, gravida 1 (primigravidae). Week of gestation: 35+2. A woman who developed HELLP-syndrome. The baby was delivered by emergency caesarean section. It was a girl with a birth weight of 1670 grams.

History: For two days she had difficulties breathing, pain in the epigastric area and shoulder blades, and she went to the doctor. Her blood pressure was measured to be 200/105 mmHg. Platelets were 84 x 10^9/L and she had 3+ protein in the urine. She started developing a severe headache. She was in a bad condition and she was transported to the University Hospital of Northern Norway, Tromsø, and had an emergency caesarean section with spinal anaesthesia.

The day after the delivery the platelets were 35 x 10^9/L, and two days after the platelets were 55 x 10^9/L. She got a platelet concentrate transfusion. Her blood pressure was still high. It was taken a serial measurement of the blood pressure which was: 141-163/102-109 mmHg and she received Labetalol (Trandate) i.v. The day after the platelets increased to 79 x 10^9/L and the blood pressure had decreased to 147/79 mmHg.

The neonate was premature and was transferred to New-born Intensive. Since she was above week 34 of gestation, mother did not get any Betamethasone (steroids) and the neonate did not receive Surfactant. The baby was doing fine.

Blood sample	Highest level	Lowest level
AST	113 ↑	46 ↑
ALT	118 ↑	46 ↑
Creatinine	91 ↑	86
Urea	446 ↑	401 ↑
Total bilirubin	17	6
Haemoglobin (Hb)	14,7 (on admission)	9, 8 ↓(post-caesarean section)

Table 1: Lab results of the woman in case 1 with HELLP-syndrome at the University Hospital of Northern Norway, Tromsø.

This woman also had decreased platelets, calcium, albumin, total protein and haptoglobin. She had increased fibrinogen and anti-thrombin III.

Case 2: The University Hospital of Northern Norway, Tromsø:

Para 1, gravida 2. Week of gestation: 37+3. A woman who developed severe pre-eclampsia. She had an induction of labour and a vaginal delivery. It was a boy with a birth weight of 2590 grams.

History: She went to the doctor for a pregnancy control in week 37 of gestation, and was sent to the University Hospital of Northern Norway, Tromsø. Before the control she had been feeling sick and her hands were swollen. At the time of the control she had high blood pressure (diastolic blood pressure > 118 mmHg), and she had developed oedema in her legs. After admission she also developed a headache. She collected urine, and they measured her blood pressure every fifth minute which was 148-157/87-102 mmHg. They also took blood samples. On the second day after admission they started with induction. Her blood pressure at that time was 161/94 mmHg and she had 4 + protein in the urine. The induction took some time, and the baby was delivered two days after. Her blood pressure after delivery was 126/82 mmHg, and the mother was doing fine.

The first day after delivery they measured the blood glucose of the infant which was 1, 9 mmol/L. They supplemented him with some extra milk, and the blood glucose increased to 3, 1 mmol/L. Other than that the baby was healthy.

Blood sample	Highest level	Lowest level
ALT	14	7 ↓
Urea	557 ↑	474 ↑
Hb	14,9 (on admission)	13,7 (post-delivery)

Table 2: Lab results of the woman in case 2 with severe pre-eclampsia at the University Hospital of Northern Norway, Tromsø.

AST, total bilirubin, glucose and creatinine was not measured.

Case 3: The University Hospital of Northern Norway, Tromsø:

Para 1, gravida 2. Week of gestation: 34 + 2. A woman who developed mild pre-eclampsia. She tried vaginal delivery, but ended up with an emergency caesarean section due to birth asphyxia. It was a boy with a birth weight of 1571 grams.

History: She went for a check to the doctor in week 30 of gestation. Her blood pressure at that time was 138/95 mmHg. Another control in week 32 of gestation she had developed 1+ protein in the urine and her blood pressure was 166/95 mmHg. She also had oedema in her legs. She was transferred to the University Hospital of Northern Norway, Tromsø, to do an ultrasound. The ultrasound showed growth retardation of the foetus. She now had 2+ protein in the urine, a rising blood pressure, and she was admitted. The management were daily serial measurement of the blood pressure, CTG, collection of urine and blood samples were taken. They took an ultrasound every third day to watch the foetus' weight. Even though she was admitted she was allowed to leave the hospital every now and then. They waited with an induction of labour until the foetus was above week 34 of gestation. When she was 34 weeks, they took a stress test (a drip of 10 IE Syntocinon) to start some contractions and see how the foetus responded to that. Then they tried an induction of labour. She was given two 0, 2 mg Misoprostol (Cytotec), and after the second one she started to get powerful contractions. They put on a CTG and saw decelerations to 80 beats per minute (bpm) at every contraction, and they had to do an emergency caesarean section with spinal and general anaesthesia. The mother was recovering well after the caesarean section, but her blood pressure was still a bit high the first couple of days (145-160/95-100 mmHg), and then it decreased (135-140/80-90 mmHg).

The blood glucose of the infant was low, and he was given glucose i.v. He also got a probe. He was transferred to New-born Intensive and put in an incubator. He was given Surfactant 100 mg/kg/dose, and he was breathing on his own.

Blood sample	Highest level	Lowest level
ALT	25	16
Creatinine	93 ↑	
Urea	483 ↑	382 ↑
Hb	13,6	12

Table 3: Lab results of the woman in case 3 with mild pre-eclampsia at the University Hospital of Northern Norway, Tromsø.

AST, total bilirubin and glucose was not measured.

Case 4: The University Hospital of Northern Norway, Tromsø:

Para 0, gravida 1 (primigravidae). Week of gestation > 38. A woman who developed severe pre-eclampsia. They tried induction of labour, but ended up with an emergency caesarean section. It was a boy with a birth weight of 2840 grams

History: At first she had a normal blood pressure, but 3+ protein in the urine. Platelets were 128 x 10^9/L. Then she developed a headache and pain over the right side of the lower abdomen. Blood pressure at that time was 153/86 mmHg. She started to collect urine. The day after the blood pressure was 155/95 mmHg, and she had also developed oedema in her legs. The blood pressure was increasing, to 180/110 mmHg. They gave her 10 mg Nifedipine (Adalat) p.o, and the blood pressure stabilized. She now experienced severe headache and some radiation to her eyes. The blood pressure increased again, now to 173/103 mmHg. She again received 10 mg Nifedipine (Adalat) p.o, and the pressure was normalized. At that time they had tried induction of labour where she received five 0, 2 mg Misoprostol (Cytotec). Nothing happened, and they had to perform an emergency caesarean section.

Two days after delivery she was feeling sick, some seconds she lost her consciousness, slurred speech, flashing lights and headache. She was advised to lie flat in the bed, and she took 100 mg Labetalol (Trandate) p.o. Her blood pressure again was normalized. Two days after that episode she had a new episode with dizziness, flashing lights, headache and pain in the abdomen. Blood pressure at that time was 177/104 mmHg and she received 10 mg

Nifedipine (Adalat) p.o, with effect. After a few days she got a fever, and CRP and leukocytes were increased. Her blood pressure was 157/92 mmHg. The doctors thought about endometritis, and she got treatment for that. She also got antibiotics i.v in case of a urine tract infection.

The infant was doing fine after the caesarean section.

Blood sample	Highest level	Lowest level
ALT	11	
Urea	215	195
Hb	13,4	11,6

Table 4: Lab results of the woman in case 4 with severe pre-eclampsia at the University Hospital of Northern Norway, Tromsø.

AST, total bilirubin, creatinine and glucose was not measured. She had increased CRP and leucocytosis.

Case 5: The University Hospital of Northern Norway, Tromsø:

Para 0, gravida 1 (primigravidae). Week of gestation: 34+3. A woman who developed severe pre-eclampsia and eclampsia after delivery. The baby was delivered by an emergency caesarean section due to severe pre-eclampsia and that the baby had a breech presentation. It was a girl with a birth weight of 1982 grams.

She went to a control in week 32+2 of gestation where they discovered an increased blood pressure, 140/90 mmHg and 1+ protein in the urine. They estimated the foetus' weight and found growth retardation. In week 33 of gestation she went to another control. Now the blood pressure was 150/100 mmHg, and still 1+ protein in the urine. In week 34 she developed a constant severe headache, flashing lights and now she had 3+ protein in the urine. Blood pressure was 190/110 mmHg. She was given 100 mg Labetalol (Trandate) p.o with small effect. Platelets were 143 x 10^9/L. She was very swollen in her face and hands as well, and they performed a caesarean section. After that she was feeling weird, she could see, but not interpret visual stimuli. Then she developed generalized tonic-clonic seizures. They were severe and she was intubated and given Diazepam 7, 5 mg i.v. They took a CT-scan afterwards which showed some changes in the occipital area.

The infant was transferred to New-born Intensive. She got a probe, but otherwise she was doing fine.

Blood sample	Highest level	Lowest level
AST	129 ↑	90 ↑
ALT	128 ↑	31
Creatinine	63	
Urea	467 ↑	305
Hb	9,1 ↓	8,5 ↓

Table 5: Lab results of the woman in case 5 with severe pre-eclampsia and eclampsia postpartum at the University Hospital of Northern Norway, Tromsø.

Total bilirubin was not measured. She also had leucocytosis, decreased haematocrit and platelets which were normalized and increased magnesium. Since she had eclampsia it was also taken a blood gas.

Case 6: The University Hospital of Northern Norway, Tromsø:

Para 0, gravida 1 (primigravidae). Week of gestation: 35+5. A woman who developed severe pre-eclampsia, eclampsia before delivery and HELLP- syndrome. The baby was delivered by an emergency caesarean section because the mother has had seizures. It was a girl with a birth weight of 1670 grams.

History: In week 33+6 she went to a control, and there they found out that the foetus had not gained weight the last two weeks. She had symptoms like flashing lights, pain in her neck, blunt, black spots in front of her eyes, headache, nausea and vomiting, and she was admitted. Blood pressure on admission was 190/119 mmHg. They gave her Hydralazine i.v and Nifedipine 5 mg sublingual. She still had a severe headache, flashing lights, nausea and vomiting, and then she was given Labetalol (Trandate) 100 mg x 3 p.o since the blood pressure did not decrease. AST og ALT were increased, and platelets were 100 x 10^9/L. She got a Nepresol infusion (Dihydralazine) and Nifedipine (Adalat) 20 mg p.o. They also did an ultrasound which showed little amniotic fluid.

She developed eclampsia before delivery, and had generalized clonic-tonic seizures. They stopped the seizures with Diazepam 7, 5 mg i.v. Initial status after the seizures was: no contact, partly airway obstruction and froth around the mouth. She had centred and normal pupils. They gave her a bolus dose of Magnesium Sulphate. She also received an infusion of

Labetalol (Trandate) because of systolic blood pressure 150-160 mmHg. Respiratory rate was 10, and she was blunt. She also had low diuresis and she was swollen. They ordered a CT-scan which showed some oedema changes along water shade zones in the brain. It could be an acute hypertensive encephalopathy or maybe embolic infarctions. They also ordered a MRI, which showed most likely PRES-changes in the brain. After she had been to the MRI without oxygen, she developed problems focusing with her eyes; she could not look to the sides, only straight forward. The pupil on the left side was a little bigger, but both pupils reacted to light. Another thing that happened when they removed the oxygen was that the SaO2 decreased from 97% to 88%.

After delivery AST and ALT decreased, and platelets were somewhat the same. Her blood pressure was still high, and she received antihypertensive medication. She still had problems with focusing and she had noticed a few changes in her personality. She did not remember anything from the seizures, and was feeling bad.

The infant was ill after the delivery. She was cyanotic and blunt. They had to stimulate the baby, ventilate with mask and bag and start with heart compressions. The colour improved and the baby whined. Heart rate after 2 min > 150 beats per min. Movement of the baby after 4 min. She was transferred to New-born Intensive.

Blood sample	Highest level	Lowest level
AST	87 ↑	44 ↑
ALT	140 ↑	72 ↑
Creatinine	75	68
Urea	691 ↑	309
Total bilirubin	3 ↓	2 ↓
Hb	9,4 ↓	8,7 ↓

Table 6: Lab results of the woman in case 6 with severe pre-eclampsia, eclampsia before delivery and HELLP-syndrome at the University Hospital of Northern Norway, Tromsø.

She also had leucocytosis, decreased haematocrit, platelets which were normalized, albumin and total protein, and increased LD. It was also taken a blood gas due to eclampsia.

Case 7: Haydom Lutheran Hospital, Tanzania

Para 3, gravida 4. Week of gestation: 33+3. A woman who developed eclampsia on her way to the hospital. Her condition before that is uncertain. They tried induction of labour, but

ended up with an emergency caesarean section. It was a girl with a birth weight of 1500 grams.

History: I saw this woman two days post caesarean section. She was transferred to the hospital by an ambulance. She had headache, dizziness, oedema in her face, vomiting, and six seizures on her way to the hospital. Blood pressure on admission was 180/120 mmHg and 2+ protein in the urine. They gave her Magnesium Sulphate i.v and Nifedipine 10 mg sublingual. The blood pressure only decreased to 163/110 mmHg. Then she was given Captopril 12, 5 mg p.o, and the blood pressure decreased to 167/81 mmHg. After a while the blood pressure increased again, 136-145/101-110 mmHg. She got Nifedipine 5 mg sublingual, and the blood pressure dropped again. She was given Betamethasone 12 mg i.m (steroids) because of gestation < 34. 0, 2 mg Misoprostol (Cytotec) for induction of labour was given times seven, but with no effect. They gave her Pethidine 50 mg x 2 i.m due to pain. It ended up with an emergency caesarean section in spinal anaesthesia because of induction failed. She received antibiotics afterwards, to prevent infection.

Her blood pressure after delivery was 100-160/70-104 mmHg. Nifedipine 20 mg sublingual was given. She still had 2+ protein in the urine. The mother was not feeling good even though the blood pressure was decreasing. Her reaction was slow, and she did not seem well.

The infant was transferred to New-born Intensive and there she received Aminophylline due to apnoea, and she also received glucose and lactogen

Blood sample	Level
Glucose	6,2 ↑
AST	68 ↑
ALT	46 ↑
Creatinine	110 ↑
Urea	637 ↑
Total bilirubin	8
Hb	12,8

Table 7: Lab results of the woman in case 7 with eclampsia before delivery at Haydom Lutheran Hospital in Tanzania.

Case 8: Haydom Lutheran Hospital, Tanzania

Para 1, still born 1, gravida 3. 32 weeks of gestation on admission. A woman with known pregnancy induced hypertension, and who suddenly developed proteinuria. Pre-eclampsia? Pregnancy induced hypertension and a UTI?

History: She developed pre-eclampsia in her first pregnancy, which is a risk factor for getting pre-eclampsia in next pregnancy [15]. Foetus in her first pregnancy unfortunately died, and she was really scared of getting pre-eclampsia again. Her symptoms this time were headache, palpitations in her chest, epigastric pain and vomiting. In week 29 of gestation her doctor measured a high blood pressure. He gave her Labetalol (Trandate) p.o which she took daily. She continued measuring blood pressure every day since she lived near the hospital, and that her blood pressure changed all the time.

On admission to the hospital she had developed proteinuria and small oedema in her legs. They did a serial measurement of her blood pressure. One measurement was 170/110 mmHg, and then she received Nifedipine 10 mg sublingual. The blood pressure decreased to 160/100 mmHg, and then 100/80 mmHg. Five days after, the doctor put her on Antibiotics in case she had a urine tract infection. Urine dip-stick showed: Nitrite negative. Protein and leukocytes positive. She was also put on Methyldopa (Aldomet) 125 mg p.o, and the plan was to give Nifedipine 5 mg sublingual if blood pressure > 150/>100 mmHg.

Unfortunately I do not have more information about this woman, since I had to leave Haydom Lutheran Hospital before she delivered. This case shows the aspect of differential diagnosis. Did she develop pre-eclampsia? Or did she have a pregnancy induced hypertension and developed an UTI?

Blood sample	Highest level	Lowest level
AST	37 ↑	21
ALT	55 ↑	25
Creatinine	90	78
Urea	450 ↑	370 ↑

Table 8: Lab results of the woman in case 8 with pregnancy induced hypertension and an UTI or pre-eclampsia at Haydom Lutheran Hospital in Tanzania.

Age	Para/gravida	Gender	Gest. age	Weight	Delivery	Causes
32	P1/G2	Girl	37+3	2810	C/S	Pre-eclampsia
19	P0/G1	Boy	>38	2240	Vaginal	Pre-eclampsia
26	P1/G2	Boy	>38	4475	Vaginal	Pre-eclampsia
18	P0/G1	Boy	>38	3380	Vaginal	Pre-eclampsia
39	P2/G3	Boy	27+6	764	C/S	Pre-eclampsia
29	P1/G2	Boy	>38	3640	Vaginal	Pre-eclampsia
32	P0/G1	Girl	35+2	1670	C/S	HELLP syndrome
29	P1/G2	Boy	37+3	2590	Vaginal	Pre-eclampsia
27	P1/G2	Boy	34+2	1571	C/S	Pre-eclampsia
20	P0/G1	Girl	>38	2031	C/S	Eclampsia
31	P1/G2	Girl	<38	4335	C/S	Pre-eclampsia
25	P0/G1	Boy	>38	3740	Vaginal	Pre-eclampsia
25	P0/G1	Boy	>38	2840	C/S	Pre-eclampsia
31	P2/G3	Girl	>38	2845	Vaginal	Pre-eclampsia
44	P2/G3	Boy	>38	3910	C/S	Pre-eclampsia
26	P0/G1	Girl	34+3	1982	C/S	Eclampsia post C/S
27	P0/G1	Girl	35+5	1670	C/S	Eclampsia
37	P0/G1	Twins	31+5	1247/1810	C/S	Severe pre-eclampsia
38	P4/G5	Girl	27+4	686	C/S	Severe pre-eclampsia
23	P0/G1	Boy	>38	3800	C/S	Pre-eclampsia
24	P0/G1	Girl	30+4	1085	C/S	Severe pre-eclampsia
23	P0/G1	Girl	>38	3240	C/S	Pre-eclampsia
20	P0/G1	Girl	>38	3420	C/S	Severe pre-eclampsia
20	P0/G1	Boy	>38	3460	Vaginal	Pre-eclampsia
32	P0/G1	Girl	>38	4200	C/S	Severe pre-eclampsia
37	P1/G2	Girl	>38	4110	Vaginal	Pre-eclampsia
27	P0/G1	Girl	36	1892	C/S	Pre-eclampsia
31	P0/G1	Boy	>38	4235	C/S	Pre-eclampsia
34	P0/G1	Boy	30+1	1160	C/S	Severe pre-eclampsia
31	P0/G1	Boy	>38	2915	C/S	Eclampsia
20	P0/G1	Boy	33+5	1895	C/S	Severe pre-eclampsia
37	P1/G2	Boy	35+4	2070	Vaginal	HELLP syndrome
19	P0/G1	Boy	29+2	1209	C/S	Eclampsia
36	P1/G2	Boy	>38	4700	C/S	Pre-eclampsia
26	P0/G1	Boy	>38	3920	Vaginal	Pre-eclampsia
29	P0/G1	Boy	33+3	3110	C/S	Severe pre-eclampsia
28	P0/G1	Twins	29	1081/745	C/S	Pre-eclampsia
28	P1/S1/G3	Girl	30	1225	C/S	Severe pre-eclampsia

Table 9: Birth protocol from the University Hospital of Northern Norway, Tromsø, in the period 20.08-12 – 20.08.13.

There were 38 cases of pre-eclampsia (eclampsia and HELLP-syndrome are included since pre-eclampsia usually is present at first) among 1342 deliveries, so the incidence of pre-eclampsia was: 38/1342 = 2, 8 %.

5.0 Discussion

5.0.1 How they follow-up women with pre-eclampsia in Tanzania and Norway

There are guidelines on how to follow-up pre-eclamptic women in both Norway and Tanzania, but as mentioned earlier Tanzania has greater challenges due to long travel distance, that it is expensive to both get there and to stay at the hospital [6], [10]. The challenges may also be a result of inadequate information on when to seek help and maybe where to seek help and this is worsened by poverty and the costs of health care. Lack of access to quality care is a big obstacle to reduce maternal mortality in low-income countries. This is due to the location and the distance to the hospital and lack of transport. The last fact is that it is a delay in health service provision. Lack of trained personnel and lack of equipment and supplies are the main reason for that [10]. In a case-control study done in rural northern Tanzania, at Haydom Lutheran hospital, they discovered that some women in their study did not dare to go to the hospital or other health facility care without their husband's permission. If their husband is not at home at the time of the delivery, it can lead to a severe outcome for both the mother and the foetus/neonate [27].

The follow-up regimes in Tanzania differ from the Norwegian follow-up protocol simply due to poor funding of the health care system, lack of diagnostic tools, great travel distances, expensive journeys and expensive treatment, relative to the socio-economical state of the country [6], [10]. They have greater challenges regarding sending home a pre-eclamptic woman or not. Since it is expensive to stay at the hospital, some women choose to leave the hospital even though it is necessary that they stay there. Sometimes it is not possible to follow up the woman if she lives far from a hospital or a mother-baby-station. Complications both for the mother and the foetus/neonate may occur, and she might give birth at home, and in that case Tanzania has more challenges compared to Norway.

5.0.2 Treatment in Tanzania and Norway

It was regarding the treatment I found the biggest similarity in these two countries, to my surprise since there are socioeconomic differences. They use somewhat the same medications and have somewhat the same standards and guidelines on when they are being given. The only differences I found in this case was that in an eclamptic fit in Norway, the

women are more likely to receive Diazepam to stop the seizures, and in Tanzania they give Magnesium Sulphate. Two of my cases from the University Hospital of Northern Norway, Tromsø, developed eclampsia, and the seizures were controlled by giving Diazepam. In Tanzania is seems like they use more Magnesium Sulphate, which also is according to guidelines from WHO [5]. In Norway they also used Magnesium Sulphate to prevent another seizure. When the mother had an eclamptic fit, it was taken a blood gas in Norway, but this was not done in Tanzania due to lack of equipment.

In Norway the most common drug was Labetalol (Trandate), and in Tanzania this drug was not in their guidelines, but can clearly be used for pregnancy induced hypertension since my patient in case 8 from Haydom received Labetalol (Trandate). Nifedipine was often used in both of these countries, the only difference was that in Tanzania it was more normal to give it sublingual, and in Norway it is more common to give orally. Despite that, a woman in one of my cases from Norway received Nifedipine sublingual due to malignant hypertension.

My experience is that Pethidine is frequently used in developing countries, after working in both Tanzania and South-Africa. It is almost never used in Norway anymore due to the fact that it gives more sedation than an effect on the pain, and is correlated to a number of adverse effects on both the mother and the foetus. The metabolite Norpethidine formed by Pethidine might give the new-born baby severe respiration depression and the drug has now been dissuaded as birth analgesia in Norway [20]. In Tanzania they did not use epidural anaesthesia, and I think that can be a reason for the frequently use of Pethidine. Regional anaesthesia like epidural and spinal or a combination of these two gives great pain relief and lowers incidence of side effects [20].

Dihydralazine (Nepresol) is supposed to be withdrawn from the market according to the national guidelines in Norway, but was still used in my case number 6. I did not see this medicine in Tanzania. Captopril should not be used in pregnant women due to risk of renal dysplasia in the foetus, growth retardation and foetal death [18]. This drug was given to my case number 7 at Haydom Lutheran Hospital in Tanzania. She had malignant hypertension, but it is uncertain why they chose to give her this drug rather than other drugs which are better for the foetus.

After working at Haydom Lutheran Hospital in Tanzania, I discovered that every woman that needed caesarean section received antibiotics afterwards, to prevent infection. After working at the birth department at the University Hospital in Northern Norway in Tromsø for 3 years, I have not seen this being given as a prophylaxis.

5.0.3 The pregnancy outcome for the mother in Tanzania and Norway

About 50 000 maternal deaths occur each year due to eclampsia, which is a severe complication of pre-eclampsia, and the majority is in developing countries because of low standard of health care and limited resources [28]. Maternal death in Europe is a rare event and the maternal mortality ratio (MMR) is a lot higher in developing countries [2]. Pre-eclampsia and eclampsia globally accounts for 10-15% of all maternal deaths [29].

Maternal mortality in Tanzania is 117, 2 per 100 000 births and abortions [6]. Tanzania has in that case one of the highest maternal mortality rate in sub-Saharan Africa. An increased risk of maternal deaths was found in women with higher age. In a case-control study in rural northern Tanzania they found the mortality to be higher in the age group 35-49 years compared to 15-24 years. The main catchment area of this study was done at Haydom Lutheran Hospital, Tanzania. Several other studies have revealed risk factors for maternal deaths in Tanzania and elsewhere, and the risk factors discovered were parity, age, education of mothers, obstetric factors, lack of health facilities and trained personnel and socio-economic factors [27]. Seen that the parity in Tanzania is higher in Norway, that there are more trained personnel and better equipment in Norway and better information for the pregnant woman about when to seek health care, I mean that the women in Norway will have a better outcome compared to Tanzania.

50 % of all births in Tanzania occur at home [6]. Regarding that Tanzania has even more challenges than Norway, and there are higher complications both for the mother and the foetus/neonate in Tanzania due to home deliveries. A pre-eclamptic woman needs treatment and health care, because it is a potential lethal disease which can be complicated by for an example eclampsia. These women need to be in the hospital to get a better outcome [30]. Eclampsia could be prevented with early booking for antenatal care services, early identification of pre-eclampsia and institution of appropriate therapy. In a study poor utilization of antenatal care services has been identified as a contributing factor to a high

incidence of eclampsia. Eclampsia is also a potentially lethal disease which can be treated, but it is better to try and prevent this from occurring [29].

The rates and adverse outcomes of women with pre-eclampsia are higher in developing countries due to greater challenges in health care [6], [10] Pre-eclampsia alone is the reason for 12- 18 % of maternal mortality, and the highest maternal mortality rate due to this disease is reported in developing countries. In a study in a tertiary care centre in a developing country, they concluded that close and frequent observation of maternal status showed reduced risk for the mother [30]. It is essential that these women are followed up closely, receive the right treatment and deliver when it is appropriate for both the mother and the foetus. It is important that the pre-eclamptic women are present at the hospital when they develop eclampsia so it can be treated. The outcome can be severe for the mother if she gets seizures at home. The neonate might be premature and/or has low birth weight for an example and needs treatment. The woman in case number 7 from Haydom Lutheran Hospital in Tanzania got seizures at home, but got to the hospital quite rapid and received adequate and good health care, and even though the infant was preterm, she survived and was doing fine.

Seen from table 9, nulliparous women (primigravidae) at the University Hospital of Northern Norway, Tromsø, was: 24/38 = 63 %, which correlates well to other findings in literature, where it is written that 65-75 % of pre-eclamptic women are primigravidae [9]. As mentioned previously null parity is a predisposing factor for developing pre-eclampsia [15]. In a case-control study done in rural northern Tanzania, they observed that primigravidae and women with parities of higher order were at increased risk of maternal death [27]. Since pre-eclampsia most frequently occurs in primigravidae, and that higher maternal age also is one of the risk factors for developing pre-eclampsia, some maternal deaths may be indirectly caused by pre-eclampsia.

In case 5 and 6 from the University Hospital of Northern Norway, Tromsø, the women developed trouble with vision after they both had generalized tonic-clonic seizures. Visual changes are reported in 20 % of women with pre-eclampsia and in 50 % of women that develops eclampsia [3].

5.0.4 The pregnancy outcome for the foetus/neonate in Tanzania and Norway

When it comes to the outcome for the foetus/neonate, I found huge differences in Tanzania compared to Norway. Perinatal mortality reflects maternal health. It also reflects antenatal, intra-partum and new- born care, and that is why perinatal mortality is an important health indicator. According to a registry based study done at a tertiary care hospital in Northern Tanzania in 2000-2010, pre-eclampsia and eclampsia are the leading causes for perinatal mortality among the maternal conditions. Perinatal mortality was ranging from 27-124 deaths/1000 births, depending on the geographical area [11].

Neonatal mortality has decreased since 1990, but still many countries have no measureable progress in that matter. 99 % of the neonatal deaths occur in developing countries. Over the half of the deaths occurs because of childbirths at home without a mid- wife or a doctor present. Infections, birth asphyxia and preterm birth are the causes of approximately 90 % of all neonatal deaths [31]. Since pre-eclampsia can lead to preterm birth, it also means that pre-eclampsia can lead to a severe outcome for the foetus/neonate, especially in developing countries like Tanzania. In about 20 % of the cases with early onset pre-eclampsia, the neonate has a low birth weight [32]. Since New-born Intensive in Tanzania is not well equipped, the preterm babies and babies with low birth weight were in greater risk there compared to Norway.

Seen from table 9, the percent of pre-eclamptic patients delivering full-term was: 20/38 = 52, 5 %, which makes 47, 5 % deliver preterm. Preterm birth is a major cause of mortality among new-borns and is estimated to be a reason for about 28 % of neonatal mortality worldwide each year. There is a huge difference in survival rates between preterm babies born in developing countries compared to those who are born in developed countries. In Africa there is a strong association between preterm birth and perinatal mortality. A registry-based cohort study done in northern Tanzania showed that among other conditions, pre-eclampsia was a reason for delivering preterm. This association has also been reported by others [33]. This seems to be the case in Norway as well, according to my data from the birth protocol. I have previously mentioned several risk factors for developing pre-eclampsia, and history of a previous pregnancy complicated by pre-eclampsia is one of them [15]. In the same registry-based cohort study they found that pre-eclampsia in a previous pregnancy

increased the risk of preterm birth threefold. They also mentioned that recurrent pre-eclampsia increase the likelihood of delivering preterm, and that is also due to complications related to pre-eclampsia and the doctor's tendency for early intervention such as caesarean section [33]. Since there is limited access to neonatal care in Tanzania, there is an increased risk for the babies there compared to Norway, where there is high standards and well equipped New-born Intensive.

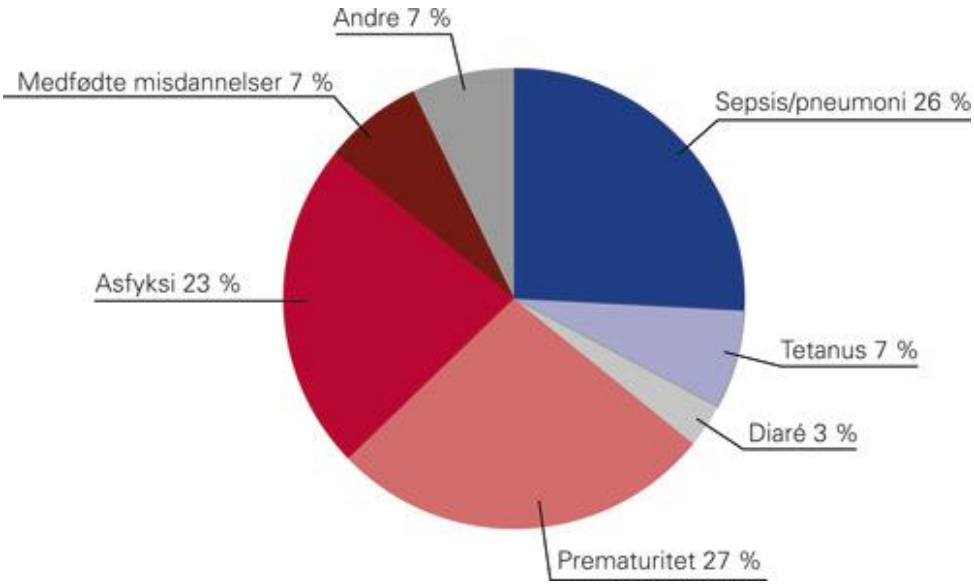

Figure 2: Causes of neonatal death globally in the period 2000-2003 [31].

Prematurity is the leading cause of neonatal death [31]. It is a huge problem and something I think medical doctors should think of dealing with pre-eclamptic patients, since pre-eclampsia may lead to prematurity.

The 8 cases show that infants of pre-eclamptic women often are premature and/or have low birth weight. If the baby is preterm, the mother gets Betamethasone (steroids) before delivery, and this is done both in Tanzania and Norway. If indicated and age of gestation is < 34, the neonate in Norway receives Surfactant after being born. This is an expensive drug, and is not given to the preterm infants in Tanzania. Instead they are given Aminophylline if they have apnoea. It might be important for the neonates to get a CPAP for improved respiration and gas exchange, but they are not equipped with this in Tanzania. They do have a respirator, but without the possibility to take a blood gas. Preterm infants and infants with

low birth weight often have low blood glucose, which is always measured at New-born Intensive in Norway. In Tanzania they do not measure that, but all preterm gets glucose and lactogen to prevent low blood glucose (Linde pers com)

Looking at table 9, the rate of caesarean section in pre-eclamptic women was: 27/38 = 71 %. The global rate of caesarean section in pre-eclamptic women is also estimated to be around high, and around 70 % of these deliver preterm [1]. The high rate of caesarean section among these women is very disturbing. Those two factors preterm and high rate of caesarean section can be factors for a poor outcome for the neonates, especially in Tanzania. Caesarean section has for example shown a high risk of neonatal transfer to New-born Intensive [12]. Caesarean sections are of course performed to reduce the risk of maternal and foetal complications, and are often necessary. Pre-eclampsia and eclampsia are known indications for caesarean section. In a study from Medicines sans Frontiers in sub-Saharan Africa, they found out that one in seven caesarean sections resulted in early neonatal death. They said it could be a reflection of inadequate labour management and a late transfer to the hospital [34]. Dr. Linde who I spoke to at Haydom Lutheran Hospital mentioned the same problem. Pregnant women in Tanzania often arrive late to the hospital, and that is one of the reasons that they are late in doing caesarean section, which can result in a poor outcome for both the mother and the foetus, superimposed on that caesarean section itself can be a risk-factor [12]. Pre-eclampsia/eclampsia and caesarean section have an association with early neonatal mortality and maternal mortality [34]. Women with pre-eclampsia have a lower tolerance for blood loss and a greater risk of haemorrhage; therefor vaginal delivery is the best for the mother, but sometimes the maternal condition is severe and it will be important to terminate the pregnancy immediately. Nevertheless the foetus could be in great stress and needs to be delivered to save the life of the foetus as well. Then the obstetricians have to think of the best mode of delivery and the best time for delivery for this particular mother and foetus [1].

6.0 Conclusion:

Pre-eclampsia is not a rare disease in pregnant women, and occur most frequently in primigravidae, and this seems to be the same in Tanzania as for Norway, but the incidence of pre-eclampsia is probably slightly higher in Tanzania. Several complications both for the mother and the infant can occur due to pre-eclampsia, and that is why it is important and necessary to follow-up and treat these women on an adequate level. The problem in Tanzania is caused by long way to the hospital, expenses connected with transport and to stay at the hospital. Therefore many women choose to give birth at home, as many as 50 %. It is difficult to follow-up these patients who do not go to the hospital or cannot afford to stay there and they have to be sent home. If the pre-eclamptic woman gets admitted and stay in the hospital, she gets adequate healthcare and is followed up frequently. In Norway we do not have these kinds of challenges as Tanzania, and therefore it is a lot easier to follow-up a pre-eclamptic woman in Norway.

The management of this disease is quite similar in Norway and Tanzania; they take relevant blood samples, collect urine, and use somewhat the same drugs both to treat and prevent pre-eclampsia and eclampsia. Both institutions use anti-hypertensive medication, but there are some differences in which medicine they prefer to use.

Pre-eclampsia can lead to prematurity because it is necessary to end the pregnancy due to either maternal or foetal factor. The neonates also have risk of low birth weight due to intrauterine growth retardation caused by pre-eclampsia. The New-born Intensive at Haydom Lutheran hospital in Tanzania was not well equipped, so preterm infants and infants with low birth weight were at risk there. The outcome of the infant is better in Norway since we have more equipment to help the neonates.

There is high maternal mortality in Tanzania, and one of the reasons can be because of pre-eclampsia and complications that can occur like for an example eclampsia and/or HELLP-syndrome. If the woman develops these kinds of severe diseases, she has to be admitted to the hospital, get medical treatment and be monitored frequently to have a certain control of the situation. In Norway this usually is not a problem since it is free to stay at the hospital and they get good health care.

A large percentage of pre-eclamptic mothers end up having a caesarean section, which is a risk factor in itself, both for the mother and the foetus. The mother is in risk of great blood loss and infection, and the baby can be delivered preterm, which is a risk factor as mentioned. In Tanzania they give all women with caesarean section antibiotics prophylactic to prevent infection, and this is not done in Norway.

To reduce the large number of both maternal and perinatal/neonatal deaths in developing countries such as Tanzania, I mean one should focus on how to follow up and treat women with pre-eclampsia. I think it is possible to greatly reduce the morbidity and mortality connected with pre-eclampsia and the following complications. In rural areas with limited resources, this is one of the easiest things to look at and to do something with. In Norway I found the standard of health care very satisfying, and there are very few maternal and perinatal/neonatal deaths in Norway. It is important to have good guidelines, which I think both of these countries did have. Both of these institutions give good health care in my opinion. The main difference is the socioeconomic standard, which gives Tanzania a lot more challenges dealing with pre-eclamptic patients. I think that if it is possible to get the pregnant women in Tanzania to the hospital in time, I mean that more lives can be saved.

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