Hypertension during pregnancy

THE SAHLGRENSKA ACADEMY

"Factors associated with hypertension during pregnancy in women giving birth in Lusaka, Zambia"

Degree Project in Medicine

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Abstract

Factors associated with hypertension during pregnancy in women giving birth in Lusaka, Zambia

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Background: In 2015, the country of Zambia still had a very high maternal mortality rate, 224 per 100 000 live births. Globally, 14 per cent of all maternal deaths is related to hypertension. In order to prevent hypertension during pregnancy risk patients have to be identified.

Aim: To give enlarged information about the proportion of various hypertensive disorders during pregnancy and their specific risk factors in women who gave birth in Lusaka, Zambia.

Method: A retrospective cross-sectional study was conducted using secondary data from Zambia Electronic Perinatal Record System (ZEPRS) on women who attended antenatal care and delivered in Lusaka between January 1st, 2008 and December 31st, 2012.

Results: 104 936 women were included in the study. 15 per cent of maternal deaths were connected to hypertension. 8 per cent had some kind of hypertension. The proportion of various hypertensive disorders were; Chronic hypertension (1.74 %), gestational hypertension (4.02 %), preeclampsia (2.19 %) and eclampsia (0.06 %). Independent risk factors for any type of hypertension was an increasing BMI over 25 and taking more than one dose of malaria prophylaxis. Multiple pregnancy and nulliparity were significant predictors for developing preeclampsia.

Conclusion: The number of maternal deaths caused by hypertension has decreased and the frequency of hypertension during pregnancy was in accordance with the global average. The incidence of the different kind of hypertensive disorder was lower than expected. Risk factors in Zambian women did not differ from other studies. Early and regular blood pressure, proteinuria measurements and increased monitoring in nulliparous, women having a multiple

pregnancy or a BMI over 25 is crucial due to their amplified risk for the hypertensive complications.

Key words: Chronic hypertension, Gestational hypertension, Preeclampsia, Eclampsia, University Teaching Hospital, Lusaka, Zambia

Abbreviations

ANC Antenatal care

BMI Body mass index

DIC Disseminated Intravascular Coagulation

HELLP-syndrome Hemolysis - Elevated Liver enzymes - Low Platelets syndrome

LMP Last menstrual period

MMR Maternal Mortality Ratio

UTH University Teaching Hospital

WHO World Health Organization

Introduction

Maternal mortality in a global perspective

The maternal mortality ratio (MMR); defined as death during pregnancy and up to 42 days after delivery, has decreased with 45 per cent worldwide between 1990 and 2013, from 380 deaths per 100 000 live births till 210. Yet, approximately 800 women around our globe die every day due to pregnancy or delivery complications (1). Reducing maternal mortality even further is a part of United Nations Sustainable Goals established 2015. By the year of 2030 the global average ought to be at most 70 deaths per 100 000 live births, with no country exceeding 140 deaths per 100 000 live births. Almost all maternal deaths occur in developing regions. In sub-Saharan Africa great progress was made between 1990 and 2013, reducing the numbers with 49 per cent, from a MMR of 990 to 510. Still, this region account for 66 per cent of all deaths globally. In Zambia, mortality dropped from 577 to 224 per 100 000 live births between 1990 and 2015, equivalent with a 61 per cent reduction (2). Nevertheless, to reach the global ambition by 2030, additional reduction is necessary.

Maternal mortality caused by hypertension during pregnancy

The leading direct cause of death worldwide is haemorrhage. Second most common, standing for 14 per cent of all maternal deaths, is related to hypertension (3). Even in countries with low maternal mortality, for instance in the United Kingdom, hypertension was connected to 15 per cent of all maternal deaths (4). This percentage is predicted to be higher in low- to middle-income countries, but the exact impact of hypertension on maternal deaths in these countries remains fairly unknown (5). This particular subject was investigated in an ancient study at UTH in Lusaka, Zambia. During one year 60 maternal deaths occurred, the leading cause was hypertensive disorders, causing 12 out of 60 deaths, equivalent to 20 per cent. Haemorrhage followed by induced abortion and sepsis was other common causes (6).

Hypertension during pregnancy can lead to the pregnancy specific syndromes preeclampsia and eclampsia, which are the reasons why hypertension can lead to maternal death. These two conditions probably account for 50 000 maternal deaths worldwide each year. Eclampsia on its own, accounts for 12 per cent of all deaths. Preeclampsia and eclampsia are associated with substantial maternal complications, both acute and long-term. The major final cause of death is usually intracerebral haemorrhage. The majority of deaths caused by preeclampsia often depend on eclampsia or the HELLP-syndrome. Both these disorders can cause a condition called DIC, which causes blood clotting at first and then heavy bleeding, resulting in a high risk of death. Common complications due to both preeclampsia and eclampsia are abruptio placentae, pulmonary edema and renal failure (7). Though, they are not only affecting the mother, the fetus is also at risk. Hypertension during pregnancy is a major predisposing factor for stillbirth, even without the onset of preeclampsia the risk is about fivefold (8). It is also associated with intrauterine growth restriction and therefore low birth weight (9). Long-term complications after preeclampsia has proven to be cardiovascular disease such as hypertension or renal disease but also ischemic stroke (10, 11).

Proportion of hypertensive disorders during pregnancy

Approximately 5-10 per cent of all pregnancies are complicated because of hypertension according to The National High Blood Pressure Education Program Report (12). These percentage vary a lot because of difficulties in obtaining accurate estimations due to different classification systems (13). Studies in India and China showed a frequency of 7.8 per cent respectively 5.2 per cent (14, 15). A greater percentage was presented in Finland, 17.2 per cent were affected by some sort of hypertension (16). In Zambia, a recent study conducted at Ndola Central Hospital presented that out of 248 patients records, 44 had been diagnosed with some sort of hypertensive disease during pregnancy, this equals 17.7 per cent (17).

Classification of hypertensive disorders during pregnancy

Hypertension is classified as a blood pressure ≥140/90mmHg.

Hypertension during pregnancy is divided into several categories; chronic hypertension, gestational hypertension, preeclampsia-eclampsia and preeclampsia superimposed on chronic hypertension.

Chronic hypertension. Chronic hypertension is classified as high blood pressure established before pregnancy or diagnosed before the 20th week of pregnancy. Hypertension during pregnancy which is not dissolved post partum is also defined as chronic hypertension.

Gestational hypertension. If hypertension is detected for the first time after the 20th week of pregnancy it is considered gestational hypertension.

Preeclampsia-eclampsia. This pregnancy specific syndrome often starts with gestational hypertension and is determined by elevated blood pressure after 20 weeks of pregnancy together with proteinuria. Proteinuria is defined as urinary extraction of ≥0.3g protein for 24 hours. This correlate with 1+ on a dipstick. A 24-hour specimen is however the recommended method. Preeclampsia is usually divided into mild and severe preeclampsia. Severe preeclampsia is classified as a systolic blood pressure of ≥160 mm Hg or a diastolic pressure of ≥110 mmHg, or as proteinuria of ≥5 g per 24 hours. Also, any of the following symptoms indicate severe preeclampsia; cerebral or visual disturbances, epigastric pain, impaired liver function, oliguria <500mL in 24 hours, pulmonary edema or thrombocytopenia. A variant of severe preeclampsia that develops in 20 per cent of women with preeclampsia is HELLP, an acronym for hemolysis, elevated liver enzymes and low platelets count. Eclampsia is classified as the occurrence of seizures in a hypertensive pregnant woman that cannot be related to any other condition.

Preeclampsia superimposed on chronic hypertension implies the development of preeclampsia in a woman with chronic hypertension (18, 19).

Risk factors for hypertensive disorders during pregnancy

Early identification is essential to be able to prevent hypertensive disorders during pregnancy. The National Institute for Health and Care Excellence recommends that high-risk patients are identified before 13 weeks of gestation. Therefore, a great effort has been accomplished to identify demographic and biophysical factors, especially those which predispose for preeclampsia. Women with chronic hypertension, chronic kidney disease, insulin-dependent diabetes and previous preeclampsia is considered to be high-risk patients. Chronic hypertension can increase the risk from about twofold all the way up to sevenfold (20, 21). In similarity, the risk increases from threefold to sevenfold if the woman who had preeclampsia in a previous pregnancy (20, 22). Other risk factors comprise in vitro fertilization, family history of preeclampsia, advanced maternal age (over 40 years), obesity, multiple pregnancy and nulliparity. A two times increase in risk is expected if the mother is over 40 years or has obesity. Both multiple pregnancy and nulliparity increases the risk for preeclampsia about three times (20). Another important risk factor has to do with race. Black women seem to have a tendency of getting preeclampsia at greater extent. A study at King's College Hospital in London investigated the factor considering race. The result revealed that black women had a higher representation in the preeclampsia group and therefore an increased risk (OR; 3.64) (22). In New York a 10-year longitudinal study regarding influence of race was performed among 2.5 million women. During this time 3.3 per cent respectively 8.5 per cent of black women received preeclampsia or severe preeclampsia. The equivalent in white women were 2.0 per cent respectively 5.5 per cent (23). Additional studies on black women in Nigeria and Ethiopia showed that risk factors for preeclampsia are not different from those reported in other studies. For instance, independent risk factors were nulliparity, multiple pregnancy, body weight over 80 kilos, previous history of preeclampsia, diabetes or chronic hypertension, stressful work or home environment together with being unmarried (24, 25). To

my knowledge, only one study has been conducted regarding risk factors in Zambian women. The before mentioned study from Ndola discovered that women become 1.17 times more likely to develop hypertensive disorders during pregnancy with every unit change in BMI. Also, not having any family history of preeclampsia was discovered to decrease the risk for preeclampsia (OR; 0.42) (17).

Routines during antenatal care

ANC is one of the suggested interventions to reduce maternal mortality. According to the new WHO ANC Model a minimum of eight visits are recommended, an increase from the previous suggestion of four visits (26). In 2012, 55 per cent of women in Zambia attended ANC at least four times. This is on the contrary satisfying compared to Ethiopia, where less than 20 per cent attend four or more times (27). However, only 20 per cent of the initial check-ups did occur in the first trimester in Zambia (28). During these visits the health of the mother and fetus are examined. To detect preeclampsia, it is recommended to measure the blood pressure at every visit and if elevated, checking for proteinuria is standard. Follow-up visits every week is suggested if a high blood pressure is detected and the woman is more than eight months pregnant (29). Other common diseases being screened for is HIV, syphilis, tuberculosis and malaria. In regions affected by malaria it is important to intake three doses of prophylaxis during the pregnancy in order to prevent it.

Medical relevance

Hypertension related complications could be prevented if high-risk patients are detected. Being able to connect maternal background factors with higher risk for hypertension during pregnancy is the first step. This provides possibilities to give enlarged information addressed to the high-risk patients. The proportion of hypertensive disorders during pregnancy and associated risk factors have never been investigated in Lusaka, Zambia.

Aim

General objective

To investigate factors associated with hypertension during pregnancy and delivery at the University Teaching Hospital and additional 24 health facilities in Lusaka, Zambia.

Specific objectives

To determine the proportion and maternal risk factors associated with hypertension during pregnancy, and their influence on the outcome for the mother and the newborn.

Material and methods

Study design

A retrospective cross-sectional study was conducted using secondary data from Zambia Electronic Perinatal Record System (ZEPRS) on women who attended antenatal care and delivered in Lusaka between January 1st, 2008 and December 31st, 2012. The data in ZEPRS was collected across 25 health centres, whereof 13 have delivery facilities*. ZEPRS collects detailed medical information about prenatal, intrapartum, and new-born care across the Lusaka public health sector and employs real-time data entry at the point of care. A unique identification number is automatically generated for all neonates on delivery and is linked with the mother's medical record. Data are uploaded on a central server and their quality regularly assessed (30).

*See appendices for detailed information

Data collection

A total of 236 482 women attended ANC care and delivered at UTH or at the other 24 surrounding health centres in Lusaka during the period of January 1st, 2008 to December 31st, 2012. 131 546 women were excluded on the following grounds;

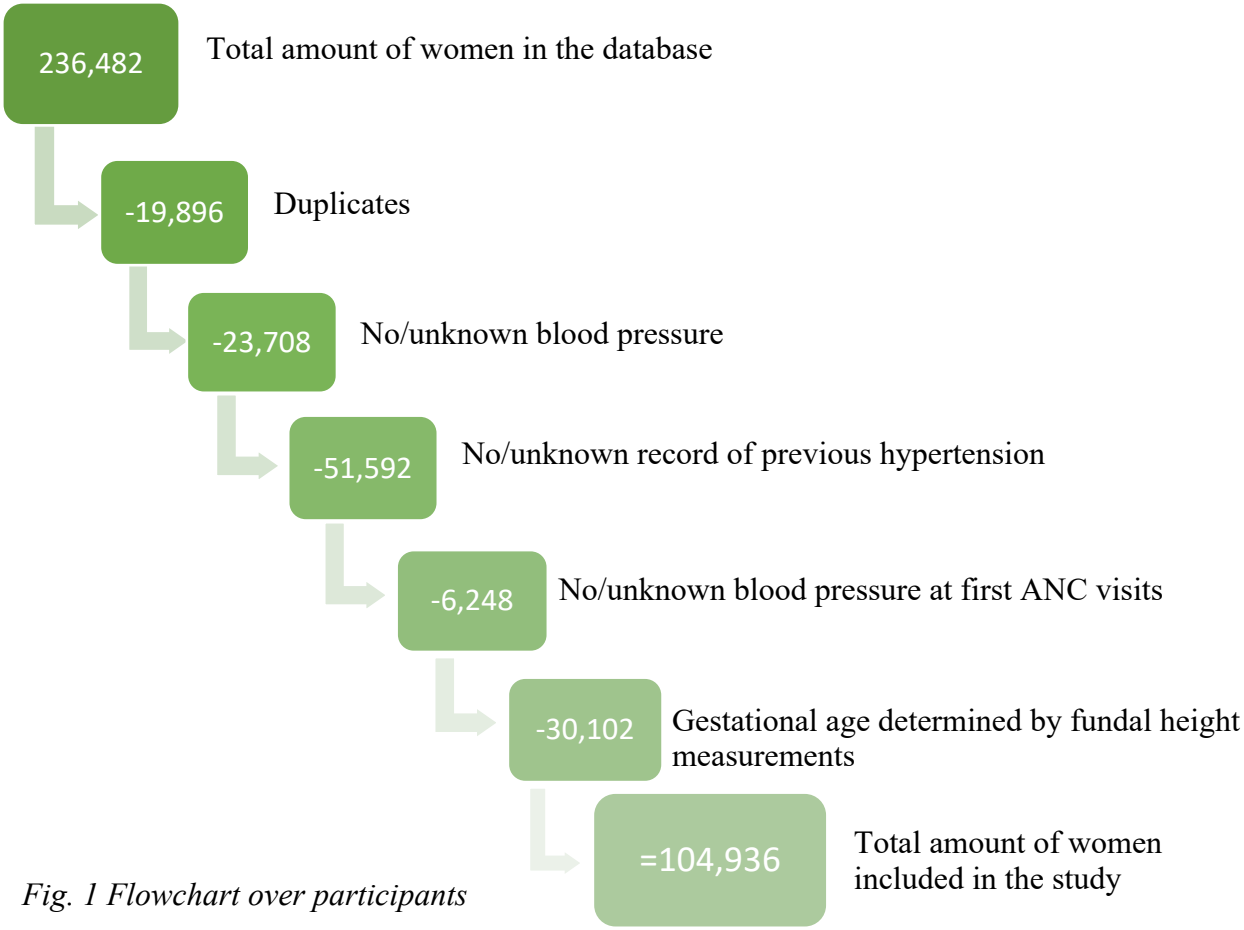

Fig. 1 Flowchart over participants

Since no timeline variables existed in the data, duplicates had to be excluded. Women with no record of any blood pressure being measured was excluded. To create a dependable variable with chronic hypertension, women with no record of previous hypertension diagnose was excluded. Also, exclusions due to observations with no value on gestational age at first ANC visit was made. Gestational age measured with fundal height was excluded because of the fact that it is not a reliable method under 20 weeks of pregnancy. Gestational age under 6 weeks and BMI under 12 and over 40 were excluded, thus only affecting these specific variables and not the total amount of women in the study.

Variables

Maternal factors included age, education, social status, planned pregnancy, number of ANC visits (based on the number of measured blood pressures), trimester at first ANC visit, nulliparity, multiple pregnancies, BMI (interval 12-40), HIV, malaria, number of doses of malaria prophylaxis, syphilis, diabetes, tuberculosis, epilepsy, heart disease and asthma. Variables studied as adverse outcomes were maternal death, caesarean section, any complications, eclampsia, placenta abruption, haemorrhage and neonatal death.

Primary outcome was hypertension divided into chronic hypertension, gestational hypertension, preeclampsia and eclampsia. Chronic hypertension and gestational hypertension did not exist in the data and had to be created. 20-week cut-off variable was created using gestational age at first ANC visit (interval 6-20 weeks). Chronic hypertension was defined as women with hypertension at first ANC visit and/or with a previous hypertension diagnosis. The variables preeclampsia and eclampsia already existed in the data. Gestational hypertension was distinguished by deducting chronic hypertension, preeclampsia and eclampsia from the variable with all registered hypertension. Hypertension was based on one measured blood pressure over 140/90 mmHg.

Statistical methods

The statistical software STATA version 15 was used to analyse the data. Chi-Square test was used to discover any significant difference between nominal variables. To investigate associations and independent risk factors both univariate and multivariate logistic regression was made. A 95 % confidence interval was calculated and a p-value<0.05 was considered statistically significant. Continuous variables were calculated and presented with mean or median if not normally distributed.

Ethics

Ethical permission was given by The University of Zambia School of Medicine Undergraduate Research Ethics Committee (UNZASOMUREC). The permission is attached in the Appendices. All patient data was handled anonymously and in accordance with the Helsinki declaration.

Results

Proportion of various hypertensive disorders in pregnancy

In total, 104 936 women were included in the study. The distribution of hypertension is shown in figure 2. 96 534 (92 %) women had no record of hypertension at any ANC visit or delivery. 8 402 (8 %) women were diagnosed with some sort of hypertension at either ANC visits or during delivery, or both.

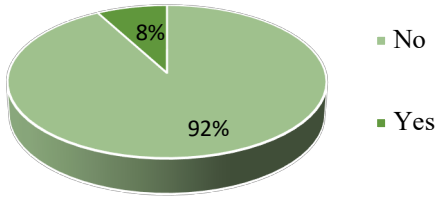

Fig.2 Distribution of hypertension in the study

The incidence of different hypertensive disorder is presented in table 1. Out of 104 936 women, 1 822 women had chronic hypertension (1.74 %) and 4 215 women had gestational hypertension (4.02 %). Gestational hypertension was calculated by elimination of the other hypertensive disorder. The incidence of preeclampsia was 2.19 per cent (2 303/104 936) and the incidence of eclampsia was 0.06 % (62/104 936).

Table 1 illustrates the incidence of the different hypertensive classifications.

Hypertension classification	**n=**	**Percentage in total**
No hypertension	96 534	92.3 %
Chronic hypertension	1 822	1.74 %
Gestational hypertension	4 215	4.02 %
Preeclampsia	2 303	2.19 %
Eclampsia	62	0.06 %

Figure 3 shows the distribution of different hypertension disorders in women with one high blood pressure value in the study. Among 8 402 women, 1 822 (22 %) had chronic hypertension and 4 215 (50 %) women were diagnosed with gestational hypertension, calculated by eliminating the other hypertensive disorders. 2 303 (27 %) and 62 (1 %) women developed preeclampsia respectively eclampsia.

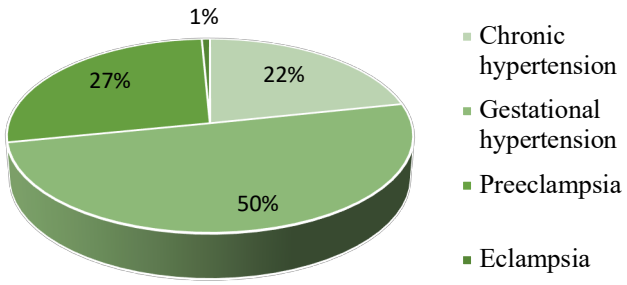

Fig. 3 Distribution of different hypertensive disorders during pregnancy

Table 2 presents how many women in each hypertensive group who developed eclampsia. In total 62 women had eclampsia. 35 (56 %) women were diagnosed at delivery. Remaining 27 cases came from the other three classes of hypertension. 3 (4.8 %) women who had chronic hypertension developed eclampsia. In women with gestational hypertension and preeclampsia there was 7 (11.3 %) respectively 17 (27 %) who developed eclampsia.

Table 2 shows the number of women in each hypertensive group developing eclampsia. 35 women were diagnosed at delivery.

Hypertension classification	**n=**	**Percentage in total**
No previous hypertension	35	56.5 %
Chronic hypertension	3	4.8 %
Gestational hypertension	7	11.3 %
Preeclampsia	17	27 %

Factors associated with hypertension during pregnancy

Table 3. Maternal characteristics. Frequency in women with no hypertension, chronic hypertension, gestational hypertension and preeclampsia. Statistically significant factors were age, education level, social status, if the pregnancy was planned, number of attended ANC visits, which trimester the woman was in at the first ANC visit, nulliparity, multiple pregnancy, BMI, HIV, doses of malaria prophylaxis, diabetes, syphilis, epilepsy, heart disease and asthma. The presence of malaria and tuberculosis had a p-value >0,05. The P-value is calculated with Chi square test.

Maternal factors	NH n= 96 534	CH n= 1 822	GH n= 4 215	Preeclampsia n= 2 303	Eclampsia n= 62	P-value
Age						
<15	285 (0.30 %)	3 (0.16 %)	11 (0.26 %)	12 (0.52 %)	2 (3.23 %)	p= <0.001[c]
15–19	18 143 (18.8 %)	304 (16.7 %)	615 (14.6 %)	441 (19.2 %)	16 (25.8 %)	
20–24	29 603 (30.7 %)	448 (24.6 %)	1 047 (24.8 %)	551 (23.9 %)	9 (14.5 %)	
25–29	25 182 (26.2 %)	438 (24.0 %)	1 058 (25.1 %)	526 (22.8 %)	17 (27.4 %)	
30–34	15 722 (16.3 %)	370 (20.3 %)	838 (19.9 %)	425 (18.5 %)	12 (19.3 %)	
35–39	6 311 (6.54 %)	213 (11.7 %)	512 (12.2 %)	278 (12.1 %)	5 (8.06 %)	
>39	1 275 (1.18 %)	46 (2.52 %)	134 (3.18 %)	70 (3.04 %)	1 (1.61 %)	
Education (n= 93 507)						
Non	2 845 (3.31 %)	50 (3.02 %)	134 (3.52 %)	60 (2.88 %)	1 (1.79 %)	p= <0.001[c]
Primary	33 313 (38.8 %)	488 (29.5 %)	1 268 (33.3 %)	616 (29.5 %)	16 (28.6 %)	
Secondary	45 281 (52.7 %)	920 (55.7 %)	2 045 (53.8 %)	1 196 (57.3 %)	36 (64.3 %)	
Tertiary	4 470 (5.20 %)	195 (11.8 %)	356 (9.40 %)	214 (10,7 %)	3 (5.36 %)	
Social status						
Married	82 873 (85.9 %)	1 508 (82.8 %)	3 591 (85.2 %)	1 948 (84.6 %)	45 (72.6 %)	p= <0.001[c]
Planned pregnancy (n= 91 078)						
Yes	74 094 (88.3 %)	1 373 (86.8 %)	3 103 (86.3 %)	1 723 (87.4 %)	44 (83.0 %)	p= 0.001[c]

NH= No Hypertension, CH= Chronic Hypertension, GH= Gestational Hypertension
c= Chi square test

Number of antenatal visits						
0	3 (0.00 %)	0 (0.00 %)	0 (0.00 %)	0 (0.00 %)	0 (0.00 %)	p= <0.001[c]
1	48 856 (50.6 %)	621 (34.1 %)	1 038 (24.6 %)	918 (39.9 %)	30 (48.4 %)	
2	24 235 (25.1 %)	457 (25.1 %)	1 156 (27.4 %)	660 (28.7 %)	15 (24.2 %)	
3	15 946 (16.5 %)	414 (22.7 %)	1 203 (28.6 %)	418 (18.2 %)	11 (17.7 %)	
≥4	7 494 (7.80 %)	330 (18.1 %)	818 (19.4 %)	307 (13.3 %)	6 (9.70 %)	
Trimester at first antenatal visit						
1st	6 059 (6.28 %)	290 (16.0 %)	245 (5.80 %)	187 (8.10 %)	7 (11.3 %)	p= <0.001[c]
2nd	76 150 (78.9 %)	1 494 (82.0 %)	3 252 (77.2 %)	1 844 (80.1 %)	43 (69.4 %)	
3rd	14 325 (14.8 %)	38 (2.10 %)	718 (17.0 %)	272 (11.8 %)	12 (19.3 %)	
Nulliparity						
Yes	31 120 (32.2 %)	657 (36.1 %)	1 376 (32.7 %)	939 (40.8 %)	28 (45.2 %)	p= <0.001[c]
Multiple pregnancy						
Yes	1 579 (1.64 %)	35 (1.92 %)	102 (2.42 %)	73 (3.17 %)	2 (3.20 %)	p= <0.001 [c]
BMI (n= 70 852)						
<18,5	2 021 (3.10 %)	21 (1.65 %)	54 (1.88 %)	26 (1.64 %)	0 (0.00 %)	p= <0.001[c]
18,5 – 24,9	42 230 (64.9 %)	642 (50.5 %)	1 360 (47.2 %)	838 (52.9 %)	21 (47.7 %)	
25 – 29,9	16 121 (24.8 %)	354 (27.9 %)	912 (31.7 %)	447 (28.3 %)	14 (31.8 %)	
>30	4 704 (7.23 %)	254 (20.0 %)	553 (19.2 %)	271 (17.1 %)	9 (20.5 %)	
HIV (n= 101 556)						
Yes	21 278 (22.8 %)	404 (23.1 %)	963 (23.7 %)	439 (19.9 %)	5 (8.33 %)	p= 0.001[c]
Malaria in current pregnancy (n =101 785)						
Yes	2 188 (2.34 %)	50 (2.90 %)	81 (2.00 %)	64 (2.90 %)	1 (1.64 %)	p= 0.118[c]
Malaria prophylaxis (n= 85 401)						
One dose	44 576 (57.0 %)	644 (43.9 %)	1 446 (38.5 %)	923 (48.2 %)	29 (56.9 %)	p= <0.001[c]
Two doses	21 234 (27.1 %)	464 (31.7 %)	1 250 (33.2 %)	602 (31.5 %)	14 (27.5 %)	
Three doses	12 399 (15.9 %)	359 (24.4 %)	1 064 (28.3 %)	389 (20.4 %)	8 (15.7 %)	

Syphilis (n= 73 368)							
	Yes	2 137 (3.20 %)	30 (2.42 %)	73 (2.42 %)	44 (2.65 %)	0 (0.00 %)	p= 0.039[c]
Diabetes (n= 102 539)							
	Yes	130 (0.14 %)	10 (0.57 %)	8 (0.19 %)	8 (0.36 %)	0 (0.00 %)	p= <0.001[c]
Tuberculosis (n= 102 914)							
	Yes	1 411 (1.49 %)	31 (1.77 %)	48 (1.16 %)	33 (1.46 %)	1 (0.61 %)	p= 0.401[c]
Epilepsy (n= 103 719)							
	Yes	379 (0.40 %)	2 (0.11 %)	9 (0.22%)	13 (0.57 %)	2 (3.28 %)	p= 0.000[c]
Heart disease (n= 100 805)							
	Yes	143 (0.15 %)	6 (0.35 %)	8 (0.20 %)	5 (0.22 %)	1 (1.70 %)	p= 0.009[c]
Asthma (n= 102 922)							
	Yes	1 363 (1.44 %)	45 (2.56 %)	71 (1.72 %)	42 (1.86 %)	1 (1.64 %)	p= 0.001[c]

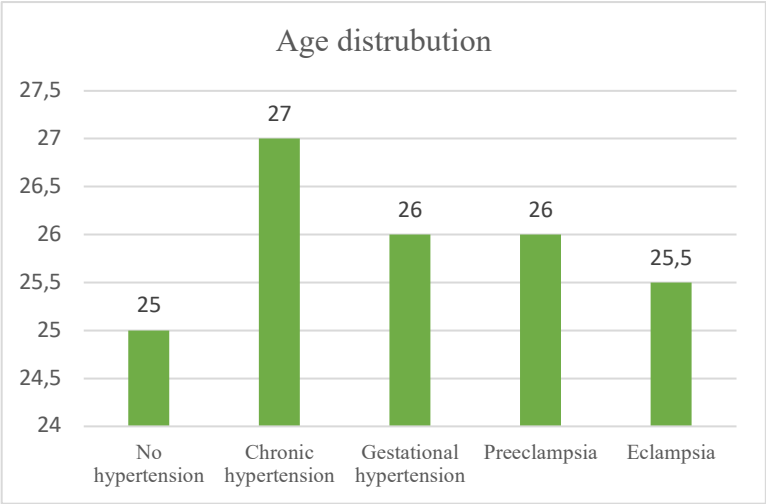

Fig.4 illustrates the median of age in each group

Table 3 describes the frequencies and percentage of women in each group and their characteristics. A significant P-value indicates that there is a statistical difference somewhere in between the groups. The age median in every group is shown in figure 4. In women with no hypertension the median was 25 years, almost equivalent with the median in women with eclampsia (25.5 years). In women with chronic hypertension the median was 27 years and in women with gestational hypertension or preeclampsia 26 years. The median in all women was 25 years (SD ±6). Those with any kind of hypertension had in general a higher level of education, except women with eclampsia. The percentage of married women was around 85 per cent in all groups except for a slight decrease in women with chronic hypertension (82.7 %) and women with eclampsia (72.6 %). The pregnancy was planned in a somewhat greater extent in women with no hypertension, 88.3 per cent, compared to between 83.0 per cent and 87.4 per cent in the other groups. The HIV incidence was around 20 per cent in all groups except for in women with eclampsia who had a frequency of 8 per cent. Similar applies to tuberculosis, diabetes and syphilis, where the incidence in eclamptic women was practically zero. However, epilepsy and heart disease were more common in women with eclampsia. Asthma was more common in women with chronic hypertension.

The groups had an even distribution considering malaria, except for a lower frequency in women with eclampsia, however not resulting in a statistically significant p-value. Concerning the number of antenatal visits and in what trimester women attended antenatal care (ANC) for the first time, a significant difference was discovered. In women with no hypertension, 50 per cent attended ANC once, compared to 24.6 per cent in the gestational hypertension group. Also, only 7.8 per cent attended ANC four or more times in the no hypertension group, compared to 19.4 per cent of women with gestational hypertension. Regarding the trimester factor, 16 per cent of women with chronic hypertension attended ANC in the first trimester and only 2.1 per cent went on their first ANC visit in the third trimester. In the group with gestational hypertension is was quite the opposite, simply 5.8 per cent attended their first ANC visit in the first trimester, whereas 17.1 per cent were already in the third trimester when attending ANC for the first time. There was a marginal difference between the frequency of nulliparous and multiple pregnancies between women with preeclampsia or eclampsia and the rest of the groups. The highest frequency was found among women with eclampsia, 45 per cent were nulliparous and 3.2 per cent were parous. In women with no hypertension, the same variables were 32.2 per cent respectively 1.64 per cent. The most prominent factor was BMI and is presented in figure 5. 7.23 per cent of women with no hypertension had an BMI over 30, compared to 17.1, 19.0, 20.0 and 20.5 per cent in the other four groups. The mean BMI was 24.1 (SD ±3.8). In women with no hypertension the mean was 23.9, while the mean varied from 25.5 till 26.3 in the other groups.

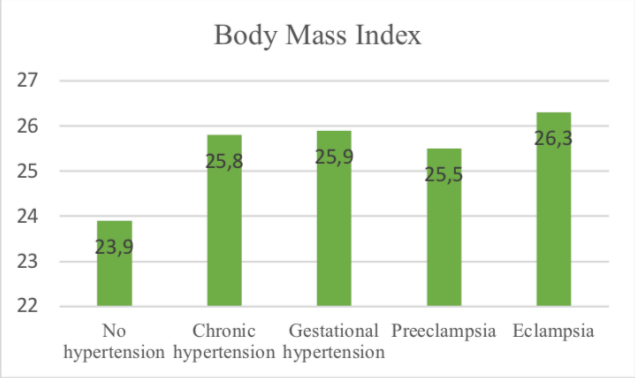

Fig.5 illustrates the mean of Body Mass Index in each group

Table 4. Incidence of specific factors in women with chronic hypertension compared to reference group (=1). Adjusted odds ratio was calculated with multivariate logistic regression.

Maternal factors	Chronic hypertension	
	Adjusted OR (95 % CI)	P-value
Age		
<15	1	
15–19	2.22 (0.31 – 16.0)	0.430
20–24	2.13 (0.29 – 15.4)	0.456
25–29	2.36 (0.32 – 17.2)	0.397
30–34	2.55 (0.35 – 18.6)	0.357
35–39	3.54 (0.48 – 26.1)	0.214
>39	3.07 (0.38 – 24.4)	0.288
Education		
No education	1	
Primary	0.76 (0.49 – 1.18)	0.224
Secondary	1.02 (0.66 – 1.57)	0.928
Tertiary	1.26 (0.76 – 2.08)	0.370
Social status		
Married	0.64 (0.52 – 0.79)	0.000
Not married	1	
Planned pregnancy		
Yes	1.04 (0.84 – 1.29)	0.711
No	1	
Trimester at first antenatal visit		
1st	1	
2nd	0.42 (0.33 – 0.53)	0.000
3rd	0.05 (0.03 – 0.10)	0.000
Nulliparity		
Yes	1.35 (1.10 – 1.66)	0.004
No	1	
Multiple pregnancy		
Yes	0.71 (0.38 – 1.33)	0.285
No	1	
BMI		
<18,5	1	
18,5 – 24,9	2.00 (1.06 – 3.8)	0.031
25 – 29,9	3.31 (1.74 – 6.27)	0.000
>30	6.69 (3.48 – 12.8)	0.000
Malaria prophylaxis		
One dose	1	
Two doses	1.33 (1.12 – 1.58)	0.001
Three doses	1.83 (1.53 – 2.19)	0.000
Diabetes		
Yes	2.02 (0.44 – 9.36)	0.368
No	1	
Epilepsy		
Yes	0.33 (0.05 – 2.42)	0.277
No	1	
Heart disease		
Yes	2.27 (0.69 – 7.44)	0.177
No	1	
Asthma		
Yes	1.47 (0.91 – 2.38)	0.116
No	1	

Table 5. Incidence of specific factors in women with gestational hypertension compared to reference group (=1). Adjusted odds ratio was calculated with multivariate logistic regression.

Maternal factors	Gestational hypertension	
	Adjusted OR (95 % CI)	P-value
Age		
<15	1	
15–19	0.78 (0.28 – 2.17)	0.640
20–24	0.79 (0.29 – 2.19)	0.652
25–29	0.76 (0.27 – 2.09)	0.593
30–34	0.82 (0.29 – 2.27)	0.698
35–39	1.21 (0.44 – 3.40)	0.706
>39	1.59 (0.54 – 4.65)	0.397
Education		
No education	1	
Primary	0.77 (0.57 – 1.04)	0.086
Secondary	0.95 (0.71 – 1.28)	0.741
Tertiary	1.23 (0.86 – 1.76)	0.255
Planned pregnancy		
Yes	0.95 (0.81 – 1.11)	0.540
No	1	
Trimester at first antenatal visit		
1st	1	
2nd	1.03 (0.80 – 1.33)	0.809
3rd	1.20 (0.90 – 1.61)	0.206
Multiple pregnancy		
Yes	1.39 (0.98 – 1.98)	0.063
No	1	
BMI		
<18,5	1	
18,5 – 24,9	1.14 (0.77 – 1.70)	0.515
25 – 29,9	1.91 (1.27 – 2.87)	0.002
>30	3.50 (2.31 – 5.31)	0.000
Malaria in current pregnancy		
Yes	0.83 (0.56 – 1.23)	0.349
No	1	
Malaria prophylaxis		
One dose	1	
Two doses	2.12 (1.86 – 2.41)	0.000
Three doses	3.22 (2.81 – 3.69)	0.000
Syphilis		
Yes	0.96 (0.69 – 1.36)	0.838
No	1	
Tuberculosis		
Yes	0.34 (0.16 – 0.72)	0.005
No	1	
Epilepsy		
Yes	0.32 (0.08 – 1.30)	0.111
No	1	

Table 6. Incidence of specific factors in women with preeclampsia compared to reference group (=1). Adjusted odds ratio was calculated with multivariate logistic regression.

Maternal factors	Preeclampsia	
	Adjusted OR (95 % CI)	P-value
Age		
<15	1	
15–19	0.71 (0.29 – 1.75)	0.454
20–24	0.65 (0.26 – 1.61)	0.352
25–29	0.79 (0.32 – 1.96)	0.607
30–34	0.93 (0.37 – 2.34)	0.882
35–39	1.43 (0.56 – 3.62)	0.448
>39	2.37 (0.90 – 6.28)	0.082
Education		
No education	1	
Primary	0.89 (0.62 – 1.28)	0.535
Secondary	1.10 (0.77 – 1.58)	0.587
Tertiary	1.13 (0.73 – 1.75)	0.579
Social status		
Married	1.19 (0.99 – 1.44)	0.071
Not married	1	
Trimester at first antenatal visit		
1st	1	
2nd	0.96 (0.73 – 1.26)	0.781
3rd	0.87 (0.63 – 1.19)	0.390
Nulliparity		
Yes	2.19 (1.85 – 2.58)	0.000
No	1	
Multiple pregnancy		
Yes	1.59 (1.10 – 2.31)	0.015
No	1	
BMI		
<18,5	1	
18,5 – 24,9	1.69 (1.04 – 2.75)	0.034
25 – 29,9	2.42 (1.48 – 3.97)	0.000
>30	4.25 (2.56 – 7.06)	0.000
HIV		
Yes	0.88 (0.75 – 1.03)	0.112
No	1	
Malaria in current pregnancy		
Yes	1.28 (0.89 – 1.86)	0.187
No	1	
Malaria prophylaxis		
One dose	1	
Two doses	1.30 (1.14 – 1.49)	0.000
Three doses	1.36 (1.16 – 1.60)	0.000
Diabetes		
Yes	1.58 (0.48 – 5.13)	0.450
No	1	

Table 4,5 & 6 shows the adjusted odds ratio and p-values. The factors included in the tables are based on the overall p-value calculated in the univariate logistic regression (see table 8 in appendices), where a p-value ≤ 0.1 qualifies. The results in this multivariate logistic regression shows independent risk factors for chronic hypertension, gestational hypertension and preeclampsia. Eclampsia could not be included in either univariate or multivariate regression due to the small number of women in the group. An increase in BMI was statistically significant in all hypertension classes in every BMI category (18.5 – 24.9), (25 – 29.9) and (>30), except for BMI 18.5 – 24.9 in women with gestational hypertension. All hypertensive patients were more likely to have a BMI over 30, (OR 6.69; CI 3.48 – 12.8) for women with chronic hypertension, (OR 3.50; CI 2.31 – 5.31) in patients with gestational hypertension, and in the preeclampsia group (OR 4.25; CI 2.56 – 7.06). Being nulliparous was associated with an increased risk for both chronic hypertension (OR 1.35; CI 1.10 – 1.66) and preeclampsia (OR 2.19; CI 1.85 – 2.58). Nulliparous women with gestational hypertension were not included in the multivariate logistic regression due to an overall p-value of 0.809 in the univariate logistic regression. Preeclampsia was more common in women with multiple pregnancies (OR 1.59; CI 1.10 – 2.3), however not statistically significant in the two other groups. In women with chronic hypertension both being married and attending the first ANC visit in third trimester was protective. Furthermore, having tuberculosis showed a statistically decreased risk, but only in the gestational hypertension group. All hypertensive women were more likely to have taken more than one doses of malaria prophylaxis during the pregnancy, chronic hypertension (OR 1.83; CI 1.53 – 2.19) gestational hypertension, (OR 3.22; CI 2.81 – 3.69) and in women with preeclampsia (OR 1.36; CI 1.16 – 1.60). Variables that showed statistical association in the univariate logistic regression such as age, education, planned pregnancy, HIV, diabetes, malaria, syphilis, epilepsy and asthma were not significant in the multivariate logistic regression.

Table 7. Comparison of adverse outcomes in women with no hypertension, chronic hypertension, gestational hypertension and preeclampsia. All the outcomes were statistically significant except for haemorrhage. P-values are calculated with Chi square test.

Adverse outcomes	NH	CH	GH	Preeclampsia	Eclampsia	P-value
Maternal mortality						
Yes	116 (0.12 %)	2 (0.12 %)	5 (0.12 %)	10 (0.43 %)	4 (6.45 %)	p=< 0.001[c]
No	96 408 (99.8 %)	1 819 (99.8 %)	4 209 (99.8 %)	2 300 (99.6 %)	58 (93.5 %)	
Caesarean section (n= 103 933)						
Yes	4 037 (4.22 %)	191 (10.5 %)	352 (8.42 %)	395 (17.3 %)	11 (17.7 %)	p= <0.001[c]
No	91 552 (95.8 %)	1 618 (89.4 %)	3 831 (91.6 %)	1 895 (82.7 %)	51 (82.3 %)	
Any complications						
Yes	3 774 (3.88 %)	154 (8.50 %)	291 (6.90 %)	750 (32.6 %)	2 (3.23 %)	p= <0.001[c]
No	92 790 (96.1 %)	1 668 (91.5 %)	3 924 (93.1 %)	1 553 (67.4 %)	60 (96.8 %)	
Placental abruption						
Yes	1 429 (1.48 %)	12 (0.66 %)	49 (1.20 %)	51 (2.20 %)	1 (1.20 %)	p= 0.001[c]
No	95 105 (98.5 %)	1 810 (99.3 %)	4 166 (98.8 %)	2 252 (97.8 %)	61 (98.4 %)	
Haemorrhage						
Yes	1 079 (1.12 %)	30 (1.65 %)	53 (1.26 %)	18 (0.78 %)	2 (3.23 %)	p= 0.040[c]
No	95 455 (98.9 %)	1 792 (98.4 %)	4 162 (98.7 %)	2 285 (99.2 %)	60 (96.8 %)	
Neonatal death						
Yes	2 030 (2.10 %)	82 (4.50 %)	138 (3.27 %)	112 (4.86 %)	9 (14.5 %)	p= <0.001[c]
No	94 504 (97.9 %)	1 740 (95.5 %)	4 077 (96.7 %)	2 191 (95.1 %)	53 (85.5 %)	

NH= No Hypertension, CH= Chronic Hypertension, GH= Gestational Hypertension

Table 7 displays frequencies of adverse outcomes in women with no hypertension compared to women with any kind of hypertension. The incidence of maternal death was 0.12 % in women with chronic hypertension and gestational hypertension, as amongst the normotensive patients. Women with preeclampsia, had a four-fold higher incidence (0.43 %) and women with eclampsia were affected the hardest of maternal death, with an incidence of 6.45 per cent. Each hypertensive group had a greater frequency of caesarean section, with a maximum of 17.7 per cent in the eclampsia group. Women with preeclampsia had ten times more complications than women with no hypertension, respectively four times more than women with chronic or gestational hypertension. Additionally, these women also had a higher frequency of placental abruption, on the other hand the lowest incidence of haemorrhage than any other group. The highest incidence of haemorrhage occurred in the eclampsia group. Furthermore, neonatal death was seven times more common in women with eclampsia than women with no hypertension.

Discussion

Proportion of various hypertensive disorders

Out of 104 936 women, 8 402 were diagnoses with any kind of hypertension, this equals an incidence of 8 per cent. This is within the framework of what previous studies have shown. The frequency of different hypertension disorders during pregnancy were 1.74 per cent for chronic hypertension, 4.02 per cent for gestational hypertension and 2.19 per cent for preeclampsia. The incidence for eclampsia was only 0.06 per cent. These results are however lower than expected compared to former studies. For example, in a study made in Australia on 185 416 women the prevalence of gestational hypertension was 9.7 per cent. The prevalence of preeclampsia was calculated to 3.4 per cent (31). In the country of Sweden, they found a gestational hypertension prevalence of 4.4 per cent in a total of 10 700 women. In the same study the prevalence of preeclampsia were 5.2 per cent (32). Conversely, studies in low-

to middle income countries show a genuinely higher incidence. In Zimbabwe's capital Harare, a study involving 289 women calculated a prevalence of gestational hypertension at 19.4 per cent. The frequency of preeclampsia was lower than in this study, namely 1.7 per cent. The frequency of eclampsia was however higher, specifically 0.3 per cent (33). At the Usmanu Danfodiyo University Teaching Hospital in Sakoto, Nigeria, they recruited 216 women visiting antenatal care for a longitudinal study. 6 weeks after partum the data were compiled. 9.7 per cent (21/216) had got gestational hypertension and 4.6 per cent (10/216) developed preeclampsia (34). The percentage presented in these sub-Saharan studies are perhaps the incidence you should expect in this study as well, especially because of the increased risk for black women showed in previous studies. The low frequencies in this study are probably the consequence of the majority of women only attending one ANC visit during their pregnancy. This is however surprising, considering UNICEF's report on maternity care usage in Zambia, where approximately 55 per cent attended four ANC visit or more in 2012 (27). In contrast, the ANC variable in this study is not reliable since it is based on the number on blood pressure measurements registered in each woman. Nevertheless, the low participation in this study means that diagnoses such as gestational hypertension and preeclampsia may not be discovered and therefore not diagnosed. This is distinctly illustrated in women with no hypertension where 50 per cent attended ANC once and only 7.8 per cent attended four or more times. The chance of missing a diagnosis in these women is extensive. However, the blood pressure was also measured during and after delivery, increasing the chances of finding a high blood pressure. While in those with gestational hypertension, 24.6 per cent attended ANC once and 19.4 per cent attended four or more, resulting in a higher chance of detecting a diagnosis. When a high blood pressure was detected and therefore more ANC visits were necessary, this might explain the statistically significant correlation between multiple ANC visits and hypertension. Of course, multiple visits for other reasons also increases the risk to detect hypertension. Furthermore, 81 548 women had missing or uncertain data regarding

blood pressure, whether it was not measured during ANC or not put in the database is not clear. However, studies show that only 88.9 per cent have their blood pressure measured during ANC visits (35). This contributes to several cases of missing diagnoses. Though, low frequencies were also presented in a study made at Zimba Mission Hospital in Zambia among 1,712 women. 17 women (0.9 per cent) developed gestational hypertension and 25 women (1.4 per cent) were diagnosed with preeclampsia. However, this result can also be a result of a small sample size (14).

Factors associated with hypertension during pregnancy

The main findings were that a BMI over 25 was significantly associated with a higher rate of every kind of hypertension during pregnancy, so were taking more than one tablet of malaria prophylaxis during the pregnancy. Being nulliparous and having a multiple pregnancy was statistically associated with a higher rate of preeclampsia. Nulliparity was also statistically associated with chronic hypertension. On the other hand, being married and attending the first ANC visit in the third trimester was protective against chronic hypertension. Unexpectedly, tuberculosis was associated with a lower risk for gestational hypertension.

The incidence rate of having any kind of hypertension increased with escalating BMI. Even though the average between the groups only differed slightly there was a greater number of women with hypertension who had a BMI over 30. The fact that high BMI is an independent risk factor for hypertension during pregnancy is well known and frequently shown in previous studies. A study conducted in the U.S. on 38 188 women showed that the incidence rate of both mild and severe hypertension disorders of pregnancy rises with increasing BMI. The risk was about 2-fold for a BMI of 25, 3-fold for a BMI of 30 and almost 5-fold greater for a BMI of 35 and over (36). In accordance with these results a study in Finland presented an increased risk with accelerating BMI, however increasing even further with rising age (37). High age in

itself is also a risk factor for hypertension during pregnancy. Maternal age over 40 is correlated with an augment for chronic hypertension, gestational hypertension and preeclampsia (38). However, in this study maternal age was not a statistically significant predictor of hypertension during pregnancy, although the p-value decreased with cumulative age, indicating that in fact the risk of hypertension increases with escalating age.

Being nulliparous was associated with higher incidence of chronic hypertension and preeclampsia. However, this was not statistically significant in women with gestational hypertension when univariate logistic regression was performed (p= 0.809). This might be explained by the fact that the frequency of nulliparity in this group was equivalent with the frequency in the control group. Nonetheless, studies have shown that nulliparous have an increased risk for developing hypertension during pregnancy. A case-control study performed in Norway included 12 800 women to determine certain risk factors. Results indicated that nulliparous have an almost fourfold higher risk of developing preeclampsia (OR 3.6, CI 2.6-5.0) (39). In contrast to the result in my study, others have found that the risk for gestational hypertension is associated with nulliparity (40). However, being nulliparous do not have to implicate a higher risk for hypertension, studies have reported that abortion seems to be protective, however, this probably due to the early phase in which abortions often occur. In a cohort study including 4 314 women at five different health facilities in the U.S. the odds ratio for preeclampsia were decreased (OR 0.86) with one earlier abortion and even further (OR 0.73) with two or more abortions (41). The non-significant association between nulliparity and gestational hypertension in this study might be interrelated with the number of abortions in the control group, perhaps they had more abortions and therefore a decreased risk for hypertension even though there were a great amount of nulliparous in the group. This is unfortunately not examined in this study.

Multiple pregnancy was an independent risk factor for developing preeclampsia, but not associated with higher risk for chronic hypertension and gestational hypertension when controlling for confounders. In women with gestational hypertension the p-value was 0.063 (CI 0.98 – 1.98), indicating perhaps a clinical relevance. The increased risk for preeclampsia when having more than one baby is supported in numerous studies, for instance a study from Washington, presenting a relative risk of 3.5 for receiving preeclampsia (42).

The result of this study implies that being married was associated with a decreased risk for chronic hypertension. Previous studies have pointed out that mental stress affect the development of hypertension disorders during pregnancy (43). In Zambia it is not socially accepted to have a child without being married, why being unmarried might cause a mental distress during the pregnancy, leading to hypertensive disorders. However, this may probably not be reliable due to the fact that women in Zambia are likely to say that they are married because of these cultural reasons. On the other hand, Zambia has one of the highest rate of child marriage in the world, around 31 % of women are married by the age of 18, resulting in a high total amount of marriages in the country (44).

Taking less than three doses of malaria prophylaxis during the pregnancy was associated with a decreased risk for any kind of hypertension. This has a possible connection to the number of ANC visits every woman attended. If a woman attends more ANC visits, she is more likely to take all three doses of the malaria prophylaxis, while at the same time increasing the likelihood of receiving a hypertension diagnosis. If the result in this study was true, malaria would not be a risk factor for developing hypertension during pregnancy which prior studies have opposed to, in fact malaria is associated with a higher frequency of for example preeclampsia (45). Therefore, in oppose to my results, taking less doses of malaria prophylaxis should be associated with increased risk for malaria and consequently

hypertension during pregnancy. Practically the same phenomenon is revealed considering the decreased risk for chronic hypertension when attending ANC in the third trimester. This can probably be explained by the fact that chronic hypertension is diagnosed before 20 weeks of pregnancy, meaning that in the first trimester (≤12 weeks) and the second trimester (13-27 weeks) is where the diagnose is established. A high blood pressure in the third trimester, on the other hand, could be diagnosed as gestational hypertension instead.

In this study tuberculosis seemed to be protective against gestational hypertension. Women with gestational hypertension had in general a lower frequency of tuberculosis compared to the other groups, however not that distinctive. When using a Chi-square test to compare the groups, there was no significant difference between them ($p=0.305$). Therefore, it might result in a statistical difference but should not be considered to be of clinical relevance. Several studies have shown that tuberculosis carry a great responsibility for maternal deaths (46), studies on the connection between tuberculosis and hypertension during pregnancy is not established.

Proven risk factors such as diabetes had no significant association in this study. The data regarding diabetes was particularly inadequate, with only 156 patients diagnoses out of 102 539 (0.15 %). Generally, in Zambia the prevalence is 2.9 %, without the expected hidden statistics (47). Nevertheless, several studies point out the impact of diabetes on hypertension during pregnancy, for example a study made in the U.S. on 471 pre-gestational diabetes women found that the preeclampsia frequency rose significantly with increasing severity of diabetes and a similar study discovered a odds ratio of 1.5 for every category of pregnancy-induced-hypertension (48, 49).

Adverse outcomes

Eclampsia was associated with an elevated frequency of maternal deaths, namely fifteen times more common than in the preeclampsia group. They also had a higher incidence of haemorrhage, which might explain the number of deaths. Preeclampsia was connected to a higher rate of complications compared to the other groups, except for bleeding. Complications such as haemorrhage and placental abruption are commonly due to eclampsia and preeclampsia. The rate of caesarean section is expected to be high because it is often a better treatment than induction of labour in these cases. However, the number of maternal deaths caused by hypertension in this study is remarkably low. During a 5-year period, 137 maternal deaths occurred and about 20 deaths (15 %) were caused by hypertension. In the previous report from UTH there were 215 maternal deaths during a 2-year period, where 42 % were due to direct obstetric causes. The exact number caused by hypertension was however not displayed (46). The decrease in mortality can be explained by several factors according to a study at UTH using the same data. At the time of observation an initiative called Medical Education Partnership took place, which sought to enhance obstetrics training and investments in blood transfusion and ambulance transport were introduced. Also, complicated obstetrics cases were referred to a newly built hospital nearby (50).

Methodical considerations

The data analysed in the present study was obtained from an electronic medical record system (ZEPRS) which allows large numbers of samples otherwise impossible with records on paper. The great number of women included in this study contributes to a credible result. Another consideration is that a large number of observations often lead to significant results even though it might not be of clinical relevance. The database had a lot of missing values leading to potential bias. The reason why data was missing is unknown. Hopefully, the missing data was spread out randomly, suggesting that the longitudinal comparisons were faultless. Some

data was evidently incorrect and so contributes to a great uncertainty, for examples BMIs over 100 and women having an age over 70.

To be able to diagnose hypertension of pregnancy, two values over 140/90 mmHg have to be measured during different times, preferably after five minutes of rest (19). As mentioned before the majority of women attended ANC only once, in order to be able to include as many women as possible, one value over 140/90 mmHg was considered having hypertension in this study. Therefore, many women were given the diagnose hypertension even though it might be related to stress, the white-coat syndrome or health professionals having an incorrect approach on measuring blood pressure.

To classify different hypertensive disorders during pregnancy a 20-week cut-off is necessary, since chronic hypertension is diagnosed before the 20th week of pregnancy and gestational hypertension after the 20th week of pregnancy. The data did not say in what week each blood pressure was measured and therefore a 20-week cut-off variable had to be created. A variable saying what gestational age every woman had at their first ANC visit was used. If the woman attended her first ANC when ≥20 weeks pregnant she was considered as having chronic hypertension. However, several women were measured using fundal height, which is not a reliable method under 20 weeks of pregnancy, thus only women with LMP as a tool to determine gestational age were included. This arrangement imply that a great number of women had to be excluded and information was lost. Though, LMP is also risky as a method if having late ovulation.

Future studies

The variable eclampsia could not be analysed with logistic regression due to small sample size. However, in women with eclampsia it was more common to be nulliparous, having a multiple pregnancy and having a higher BMI than 25. Less women were married and the pregnancy was not planned in a greater extent. Additionally, only 9 per cent attended ANC four or more times and they attended ANC later than any other group. You could expect a different of statistically significant risk factors being present in these women, but a greater number of women are needed to be able to draw any conclusions. Future research in Lusaka can eventually focus on solitary eclamptic women.

To be able to achieve a reliable result, at least three blood pressure should be measured in order to diagnose hypertension. However, this acquire that every woman attends a minimum of three ANC visits, or, ideally follow the recommended amount by WHO, which is eight visits (26). Noting in what pregnancy week every blood pressure was measured in is necessary to be able to identify the different classifications of hypertension. The significance of filling in the database correctly should also be pointed out. Perhaps using fill-in forms where women can answer questions themselves regarding diseases and previous obstetric history etc. could decrease the extent of missing data. Research questions of interest could be to look at the genetic factor in hypertension during pregnancy, especially because of the increased risk for black women to develop these conditions, or the association with stress. I also discovered a research gap when trying to explore the connection between tuberculosis and hypertension during pregnancy.

Conclusions

In this study, the proportion of hypertensive disorders and factors associated with hypertension during pregnancy in women attending ANC and giving birth in Lusaka was investigated.

8 per cent were found to suffer from any hypertensive disorder during pregnancy, which is in accordance with the global average. The proportion of different hypertension classifications were; chronic hypertension (1.74 %), gestational hypertension (4.02 %), preeclampsia (2.19 %) and eclampsia (0.06 %). These outcomes are lower than expected and are probably a result of women not attending ANC visit as recommended and an excessive amount of missing data. Hypertensive disorders were responsible for 15 per cent of all maternal deaths. The total amount of maternal deaths was 137 deaths during a 5-year period. Hence, the maternal mortality caused by hypertension has decreased at the investigated delivery wards in Lusaka.

Nulliparity was an independent risk factor for chronic hypertension and preeclampsia (OR; 1.35 & 2.19). Having a multiple pregnancy was associated with an increased risk for preeclampsia (OR; 1.59) and a BMI over 25 was statistically significant with an increased risk in every hypertensive disorder (OR; 1.91 – 6.69). Being married was associated with a decreased risk for chronic hypertension (OR; 0.64). Therefore, risk factors for hypertensive disorders during pregnancy among Zambian women are not different from those reported in other studies.

In order to prevent hypertension during pregnancy enlarged information has to be given to women expecting their first child and women with multiple pregnancies, but also women with a BMI over 25. Regular blood pressure and proteinuria measurements together with increased monitoring is crucial due to their amplified risk for hypertensive complications.

Populärvetenskaplig sammanfattning

Faktorer associerade med hypertoni under graviditet hos kvinnor i Lusaka, Zambia.

Mellan 1990 och 2013 sjönk den globala mödradödligheten med 45 procent. Ändå dör cirka 800 kvinnor varje dag på grund av komplikationer kopplade till graviditet och förlossning. Ett av de globala målen för hållbar utveckling är att minska mödradödligheten, nämligen till ett globalt genomsnitt på 140 dödsfall på 100 000 levande födslar. Nästan alla dödsfall sker i låg- & medelinkomstländer. I Subsahariska Afrika minskade dödligheten med 49 procent mellan 1990 och 2013, ändå sker cirka 66 procent av dödsfallen här.

2015 var mödradödligheten 224 dödsfall på 100 000 levande födslar i Zambia. En tidigare studie från University Teaching Hospital visade att cirka 20 procent av alla dödsfall berodde på hypertoni. Den totala utbredningen och de olika typerna av hypertoni har dock aldrig blivit undersökta. Inte heller riskfaktorer kopplade till hypertoni under graviditet har analyserats. Denna studien syftar därför till att fastställa just detta.

En retrospektiv tvärsnittsstudie genomfördes genom att använda sekundärdata från databasen ZEPRS (Zambia Electrical Perinatal Record System), vilken innehåller prenatal och intrapartal information gällande 236 482 kvinnor. Data samlades in på UTH och 24 andra kliniker i Lusaka mellan 1 januari, 2008 och 31 december, 2012.

Totalt blev 104 936 kvinnor inkluderade i studien. 8 procent av dessa hade någon form av hypertoni under graviditeten eller förlossningen. De olika hypertonigruppernas frekvenser var; kronisk hypertoni (1.74 %), graviditetshypertoni (4.02 %), preeklampsi (2.19 %) och eklampsi (0.06 %). 15 procent av dödsfallen gick att koppla till hypertensiva sjukdomar. Studien hittade betydande riskfaktorer i form av flerbördsgraviditet, förstföderskor och kvinnor med BMI över 25.

Studiens resultat tyder på att maternell dödlighet kopplad till hypertoni minskat och att frekvensen av hypertoni under graviditet var i enlighet med den genomsnittliga frekvensen globalt. Förekomsterna i de olika hypertonigrupperna var oväntat låga, eventuellt på grund av lågt deltagande på antenatal besöken. Riskfaktorerna funna hos zambiska kvinnor skiljde sig inte från riskfaktorer hittade i andra studier. För att förhindra hypertoni under graviditeten bör fördjupad information ges till kvinnor som väntar sitt första barn, har en flerbördsgraviditet eller ett BMI över 25. Regelbundna blodtrycksmätningar och screening för protein i urinen samt ökad övervakning rekommenderas starkt hos dessa patienter.

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Appendices

Table 8. The incidence of specific factors in women with chronic hypertension, gestational hypertension and preeclampsia compared to the reference group (=1). Unadjusted odds ratio calculated with univariate logistic regression.

Maternal factors	**Chronic hypertension**			**Gestational hypertension**			**Preeclampsia**		
Social factors	0R (95% CI)	P-value	Overall P-value	OR (95% CI)	P-value	Overall P-value	OR (95% CI)	P-value	Overall P-value
Age									
<15	1		0.000	1		0.000	1		0.000
15–19	1.63 (0.52 – 5.13)	0.399		0.90 (0.49 – 1.64)	0.723		0.54 (0.31 – 0.95)	0.032	
20–24	1.49 (0.46 – 4.66)	0.496		0.94 (0.51 – 1.72)	0.841		0.41 (0.23 – 0.72)	0.002	
25–29	1.68 (0.54 – 5.26)	0.373		1.11 (0.60 – 2.02)	0.744		0.45 (0.26 – 0.72)	0.006	
30–34	2.26 (0.72 – 7.08)	0.161		1.39 (0.76 – 2.55)	0.283		0.58 (0.33 – 1.03)	0.062	
35–39	3.10 (0.99 – 9.74)	0.053		2.07 (1.13 – 3.80)	0.019		0.92 (0.52 – 1.62)	0.768	
>39	3.55 (1.09 – 11.5)	0.035		2.94 (1.57 – 5.50)	0.001		1.25 (0.68 – 2.28)	0.476	
Education									
Non	1		0.000	1		0.000	1		0.000
Primary	0.84 (0.63 – 1.13)	0.253		0.81 (0.68 – 0.96)	0.026		0.90 (0.69 – 1.17)	0.418	
Secondary	1.16 (0.87 – 1.54)	0.323		0.95 (0.79 – 1.14)	0.590		1.26 (0.97 – 1.64)	0.082	
Tertiary	2.35 (1.72 – 3.22)	0.000		1.62 (1.32 – 1.98)	0.000		2.15 (1.61 – 2.87)	0.000	

Social status									
Married	0.79 (0.69 – 0.89)	0.000	0.000	0.95 (0.87 – 1.03)	0.268	0.271	0.90 (0.80 – 1.00)	0.072	0.075
Not married	1			1			1		
Planned pregnancy									
Yes	0.87 (0.75 – 1.0)	0.081	0.086	0.83 (0.76 – 0.92)	0.000	0.000	0.90 (0.79 – 1.04)	0.149	0.153
No	1			1			1		
Trimester at first antenatal visit									
1st	1		0.000	1		0.000	1		0.000
2nd	0.41 (0.36 – 0.47)	0.000		1.09 (0.95 – 1.24)	0.207		0.81 (0.70 – 0.94)	0.007	
3rd	0.06 (0.04 – 0.08)	0.000		1.31 (1.13 – 1.52)	0.000		0.64 (0.53 – 0.77)	0.000	
Current pregnancy									
Nulliparity									
Yes	1.18 (1.08 – 1.30)	0.001	0.001	1.02 (0.96 – 1.09)	0.546	0.809	1.44 (1.33 – 1.57)	0.000	0.000
No	1			1			1		
Multiple pregnancy									
Yes	1.13 (0.84 – 1.65)	0.483	0.491	1.45 (1.19 – 1.78)	0.000	0.000	1.91 (1.50 – 2.42)	0.000	0.000
No	1			1			1		

Physical factors									
BMI									
<18,5	1		0.000	1		0.000	1		0.000
18,5 – 24,9	1.45 (0.94 – 2.24)	0.097		1.19 (0.91 – 1.57)	0.208		1.53 (1.04 – 2.27)	0.033	
25 – 29,9	2.03 (1.30 – 3.16)	0.002		2.06 (1.56 – 2.72)	0.000		2.09 (1.41 – 3.12)	0.000	
>30	4.59 (2.93 – 7.18)	0.000		4.05 (3.05 – 5.38)	0.000		3.97 (2.65 – 5.96)	0.000	
HIV									
Yes	1.02 (0.91-1.14)	0.714	0.715	1.06 (0.98 – 1.14)	0.123	0.124	0.83 (0.75 – 0.93)	0.001	0.000
No	1			1			1		
Malaria in current pregnancy									
Yes	1.22 (0.92 – 1.63)	0.156	0.169	0.83 (0.66 – 1.04)	0.104	0.095	1.25 (0.97 – 1.60)	0.081	0.091
No	1			1			1		
Malaria prophylaxis									
One dose	1		0.000	1		0.000	1		0.000
Two doses	1.46 (1.29 – 1.65)	0.000		1.79 (1.66 – 1.93)	0.000		1.33 (1.20 – 1.47)	0.000	
Three doses	1.89	0.000		2.58 (2.38 – 2.80)	0.000		1.43 (1.27 – 1.61)	0.000	
Syphilis									
Yes	0.77 (0.53 – 1.10)	0.152	0.135	0.76 (0.60 – 0.96)	0.026	0.020	0.83 (0.61 – 1.13)	0.250	0.238
No	1			1			1		

Diabetes										
	Yes	3.94 (2.07 – 7.49)	0.000	0.000	1.29 (0.63 – 2.62)	0.488	0.504	2.40 (1.18 – 4.89)	0.016	0.034
	No	1			1			1		
Tuberculosis										
	Yes	1.20 (0.83 – 1.70)	0.351	0.338	0.79 (0.59 – 1.05)	0.101	0.088	0.97 (0.69 – 1.38)	0.900	0.899
	No	1			1			1		
Epilepsy										
	Yes	0.28 (0.07 – 1.13)	0.074	0.026	0.54 (0.28 – 1.04)	0.067	0.043	1.48 (0.85 – 2.57)	0.168	0.193
	No	1			1			1		
Heart disease										
	Yes	2.21 (1.00 – 5.16)	0.057	0.090	1.38 (0.71 – 2.71)	0.345	0.368	1.39 (0.57 – 3.39)	0.468	0.489
	No	1			1			1		
Asthma										
	Yes	1.76 (1.33 – 2.42)	0.000	0.000	1.17 (0.92 – 1.49)	0.201	0.212	1.26 (0.93 – 1.72)	0.140	0.154
	No	1			1			1		

The clinics in Lusaka where data was collected from:

UTH, Bauleni, Chainama, Chainda, Chawama, Chazanga, Chelstone, Childenje, Chipata, Civic Ceter, George, Kabwata, Kalingalinga, Kamwala, Kanyama, Kaunda Square, Lilayi, Makeni, Mandevu, Matero Main, Matero Reference, Mtendere, Ng'ombe, Railway & State Lodge.

Ethical permission

THE UNIVERSITY OF ZAMBIA

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IRB00001131 of IORG0000774

1st October 2018

Prof. Bellington Vwalika

Dept. of Obstetrics and Gynaecology

School of Medicine, University of Zambia

Lusaka

SUBJECT: REQUEST FOR WAIVER TO CONDUCT MEDICAL RESEARCH

Reference is made to the above subject where you requested for waiver for visiting students under your mentorship to conduct research using routinely and de-identified data in the Zambia Electronic Perinatal Record Systems for data collected between 2006 to 2016 at the Women and New Born Hospital concerning the following study topics: 1) *Factors associated with Hypertension during prenatal care or delivery at UTH. 2) influence of number of visits on adverse fetal outcomes. 3) Factors associated with preterm delivery.* The waiver has been granted subject to the following conditions.

1. The waiver only applies to the three topics stated above.
2. The research should be for academic purpose only.

Yours sincerely,

Oliver Mweemba, PhD, MPhil.

Chairperson - UNZASOMUREC

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