Management of women with hypertensive disorders in pregnancy in the immediate postpartum period: A retrospective review of practices in a busy tertiary hospital in Gauteng, South Africa

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DECLARATION

I, Rangwato Pearl Mashoene declare this research is my original work that was done unaided. Itis submitted for the Degree of Master of Medicine at the University of the Witwatersrand, Johannesburg.

Signed on 8 March 2022 in Johannesburg, South Africa

DEDICATION

This work is dedicated to all those who made their contribution in imparting knowledge and continuation of education and better healthcare for maternity healthcare.

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My sincere gratitude goes to the Chris Hani Baragwanath postnatal wards staff for their support during my data collection period, to my supervisors for their dedicated time and support in my work throughout the research.

ABSTRACT

Background

Hypertensive disorders in pregnancy (HDP) are a leading cause of maternal morbidity and mortality globally, accounting for14,8% of the total maternal deaths in South Africa. The burden of HDP continues beyond pregnancy with a third of women continuing to have persistent hypertension beyond pregnancy.

Objective

To describe the management and outcomes of women with hypertension in pregnancy during the immediate postpartum period.

Methods

This was a prospective study conducted at the postnatal ward of Chris Hani Baragwanath Hospital over 12 months on women with hypertensive disorders of pregnancy, who still required blood pressure treatment postdelivery. Post ethics approval, data were collected frompatients and their files managed using REDCap® electronic data capture tools hosted by the University of the Witwatersrand.

Results

A total of 200 participants were included,163 (81,5%) had an abnormal blood pressure of more than the target BP of ≥150/100mmHg within 24 hours of delivery and 37 (18,5%) within 48 hours at an average 3-day duration of stay for BP control. The choices of drugs for blood pressure control were not in line with the stepwise national guidelines on postpartum hypertension management, the commonest of which were Nifedipine, Enalapril, and Methyldopa. Sixty-seven participants (33,5%) still had uncontrolled blood pressure, higher than target BP at the time of discharge but less than severe hypertension of 160/110 mmHg. All discharged participants including those on 3 agents for BP were given a routine postnatal follow-up at a local clinic.

Conclusion

The high number of patients that required treatment within 24 hours of delivery has highlighted the need for continued vigilance and enhanced postnatal care by clinicians

beyond delivery. This includes strict adherence to institutional and national guidelines and protocols on the management of hypertension postdelivery and proper follow-up channels at discharge.

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LIST OF ABBREVIATIONS

AKI	Acute Kidney Injury
ACEI	Angiotensin-Converting Enzyme Inhibitors
BP	Blood Pressure
BMI	Body Mass Index
CHBAH	Chris Hani Baragwanath Academic Hospital
CEO	Chief Executive Officer
CCB	Calcium Channel Blocker
DM	Diabetes Mellitus
HDP	Hypertensive Disorders In Pregnancy
HELLP	Haemolysis Elevated Liver Enzymes Low Platelet Count
HPT	Hypertension
IQR	Interquartile Range
ISSHP	International Society For The Study Of Hypertension In Pregnancy
MOU	Midwife Obstetric Unit
NCCEMD	National Committee On Confidential Inquiries Into Maternal Deaths
PE	Pulmonary Embolism
PIH	Pregnancy Induced Hypertension
SD	Standard Deviation
WHO	World Health Organization
Rx	Treatment

INTRODUCTION

Hypertensive disorders in pregnancy (HDP) are a leading cause of maternal mortality and morbidity worldwide, complicating 3-10% of the pregnancies resulting in 30% of maternal near-miss events. [1] In South Africa HDP have accounted for 14,8% of maternal deaths and have remained consistent for the last decade. [2] The latest triennial (2014-2017) report from the national committee on confidential inquiries into maternal deaths (NCCEMD) identified inappropriate management of women diagnosed with hypertension in pregnancy in all levels of care. [2] The burden of HDP related complications continues beyond the pregnancy, a third of women with HDP have persistent hypertension postdelivery with up to 12% of patients recording diastolic blood pressure greater than 100mmHg. [3]

Postpartum hypertension occurs due to a persistent rise in blood pressure postdelivery in women with HDP or elevated blood pressure appearing for the first time in the immediate postpartum period secondary to other causes. [4] The rise in blood pressure has been attributed to physiological changes postdelivery, a shift in fluid from extravascular to intravascular space resulting in a proportion of women needing treatment. [4-5]

The exact timing of resolution of HDP postdelivery remains variable within the 6 weeks postpartum period with a reported peak in blood pressure on days 3 to 6. [5] This persistence of elevated blood pressure in the postpartum period results in a high proportion of patients needing treatment and considerable risk of complications such as intracranial haemorrhage, eclampsia, and death. [3-5] In South Africa mortality rates remain significantly high, the triennial report (2014-2017) from the national committee on confidential inquiries into maternal deaths reported that 65,5 % of maternal deaths from women with HDPs occurred inthe postpartum period. [2] An American multicentre retrospective study reported that 78 out 151 (51.6%) of women diagnosed with hypertension in the postpartum period required anti- hypertensive medication on discharge. [6]

There is little evidence to guide the management of hypertension postdelivery, consequently, most of the treatment guidelines are based on common usage and experts' opinions. [3-5,7] A Cochrane review of nine trials found no reliable evidence to guide the management of women

with hypertension in the postpartum period.[7] Therefore the management of hypertension in the postpartum period remains a major challenge in all levels of care in South Africa and around the world.[2] This study aimed to investigate the management of women with hypertension in pregnancy during the immediate postpartum period to enhance knowledge and to improve our clinical practice.

METHODS

Study design & setting

This was a prospective study conducted over twelve months (August 2018 to August 2019) involving participants admitted at Chris Hani Baragwanath Academic hospital (CHBAH) with hypertensive disorders in pregnancy requiring postpartum BP control. The study was conducted at the Department of Obstetrics and Gynaecology maternity unit which performs on average 17 000 deliveries annually. The hospital is in Soweto, Johannesburg, in Gauteng province and it is one of the 10 central hospitals in South Africa. Chris Hani Baragwanath Hospital is a teaching hospital for the University of Witwatersrand and a referral centre to two midwife obstetrics units (MOUs), two regional and a district hospital. CHBAH does not have a postnatal clinic, women who deliver at CHBAH including those with HDP are referred to MOUs for postpartum follow-up with an exception for a special group of women who had a maternal near-miss event or a stillbirth, these women are seen at the antenatal clinic.

Study participants

The study included women who had delivered at CHBAH who was diagnosed with hypertensive disorders in pregnancy (Gestational Hypertension, Pre-eclampsia, HELLP (Haemolysis, elevated liver enzymes, low platelet count) syndrome, imminent eclampsia, and Eclampsia) as defined according to the guidelines of the International Society for the study of Hypertension in Pregnancy (ISSHP) who still required treatment postdelivery. [7]
Hypertension was defined as an elevated blood pressure ≥140/90 mmHg or higher measured twice at least four hours apart between delivery and at time of discharge with target optimal BP on treatment <150/100mmHg for discharge.

Sample size and data collection

The sample was estimated at 185 participants based on an assumption of a 6% prevalence of hypertension, a 10% loss, and a ± 3.6% margin of error. Participants who fitted the study criteria were identified in maternity admissions, labour ward, high care area, and postnatal

wards, approached by the researcher on the day of presentation and informed consent obtained to be included in the study and subsequently followed up from immediately post-delivery in postnatal wards and obstetrics high care area until at the time of discharge by the attending doctor. Data were collected and managed using REDCap® electronic data capture tools hosted at the University of the Witwatersrand, this involved asking patients' details, going through their inpatient records daily to check their blood pressure, treatment chart, and discharge notes by attending Doctor.

Data analysis

Descriptive statistics using the Strata14 statistical package (StataCorp, College Station, Texas) were used to analyze and describe the data. Continuous variables are described with the use of means, standard deviations, or medians (interquartile ranges) and frequencies for categorical variables.

Ethical considerations

Permission to conduct the study was obtained from the head of the Department of Obstetrics and Gynaecology as well as the CEO of CHBAH. Wits Human Research Ethics Committee granted ethics clearance (Certificate number: M180433).

RESULTS

The study recruited two hundred participants that were followed up in the postnatal wards up until discharge. The mean age was 30 years (SD ±7, 2, R 15-46 years). Ninety-six percent of women were booked and had attended antenatal care, with 61%, 25% and 14% having booked in 2nd, 1st, and 3rd trimesters respectively. The mean gestation at booking was 19, 9 weeks (SD± 6, 8). (Table 1)

Of the 200 participants, 152 (76%) had a normal blood pressure reading at booking however they went on to develop hypertensive disorders later in pregnancy. Fifty-eight (29%) had abnormal readings at booking and were classified accordingly as per definitions of HDP. The percentages of patients that needed hypertensive treatment according to the types of HDP amongst the participants in the study was 44(22%) (see Fig 1) with essential or chronic hypertension, 2(1, 0%), secondary hypertension, 94(47, 0%) Gestational hypertension, 51(25, 5%) Preeclampsia and 9(4, 5%) with superimposed preeclampsia.

One hundred and twelve participants out of the 200 (56%) had associated risk factors at the time of pregnancy booking (Fig.2). The common risk factor amongst the participants was obesity and 79 (39,5%) had a body mass index (BMI) >30. Other associated risk factors amongst the participants were history of previous HDP in 28(14%),3(2,7%) multiple gestations, 5(2,5%) diabetes mellitus, 5(2,5%) autoimmune disorders, 8(4%) Thyroid disease and 1(0,5%) assisted reproduction.

Characteristics	**Total** **N= 200**
Mean Age (SD)	30,2(7,1)
Race • Black • White • Coloured	 194(97,0%) 3(1,5%) 3(1,5%)
Parity • 0 • 1-4 • 5-7	 63 (31,5%) 132 (66%) 5 (2,5%)
Booked Unbooked	192 (96,0%) 8 (4,0%)
Gestational age at booking Mean (standard deviation)	19,9(6,8)
Distribution of GA at booking • First trimester • Second trimester • Third trimester	 50(25,0%) 122 (61,0%) 28 (14,0%)
Types of HDP • Chronic Hypertension (Essential) • Chronic Hypertension (Secondary) • Gestational Hypertension • Preeclampsia De novo • Superimposed preeclampsia	 42(21,8%) 2 (1,0%) 91 (47,2%) 49 (25,4%) 16(8,0%)

Table 1 Socio-demographic and obstetric characteristics amongst the 200 participants with HDP enrolled in our study.

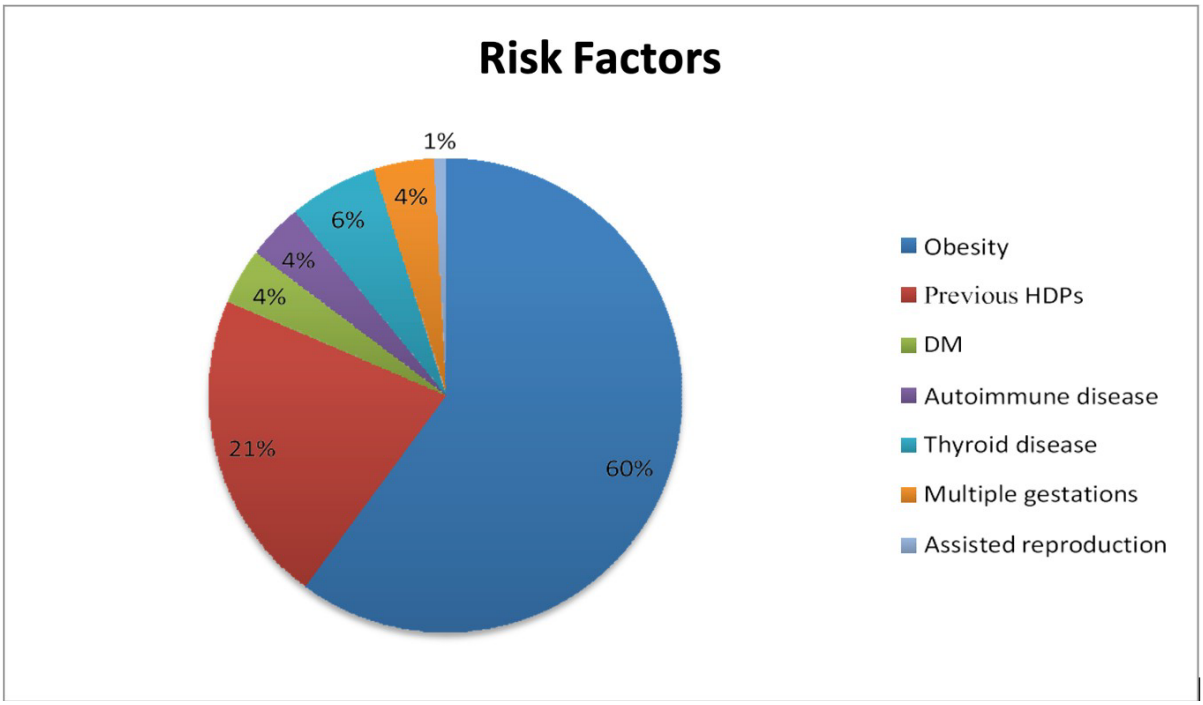

Figure 1. Risk factors amongst the study population at the time of Antenatal booking: Previous HDPs (Hypertensive disorders of pregnancy), DM (Diabetes Mellitus).

The average gestational age at diagnosis of hypertensive disorder in pregnancy in this study was35 weeks (IQR 30-37) with the youngest participant aged 15 and the oldest 46 years of age. A total of 94/200 (47%) developed hypertensive-related complications. In the antenatal period, 188(94,5%) of the 200 participants required less than three hypertensive agents for blood pressure control and 11(5, 5%) required three or more antihypertensive agents.
The average gestational age of delivery was at 37 weeks (R 25-38) of which 144 (72%) was through a caesarean section and 56 (28,0%) through normal vaginal delivery. One hundred and sixty-six (83%) participants warranted immediate delivery due to eclampsia 5 (5,7%), HELLP syndrome 12(13,8%), Imminent eclampsia 42(48,3%), acute Kidney injury 15(17,2%), uncontrolled BPs on 3 agents 6(6,9%), persistent thrombocytopaenia 1(1,1%) and associated fetal complications 51(25,5%). These complications were also found to be associated with longer hospital admission amongst the participants post-delivery.

At 24 hours post-delivery, 163 (81,5%) and 37(18,5%) at 48 hours out of the 200 participants had abnormal blood pressure. The average duration of stay for BP control post-delivery was 3 days (Range 2-6), with a maximum duration of up to 6 days. Participants who had gestational hypertension 91(47,2%) and those that delivered through a normal vaginal delivery

56(28,0%) were quick to recover and subsequently discharged earlier. At 48 hours of initiating treatment, 84 (42,0%) participants had controlled blood pressure on different types of antihypertensive agents reaching the target BP (<150/100mmHg) required for discharge. The median systolic BP on day 3 was 152mmhg (145-161) and diastolic BP 97(90-104) mmHg. At the time of discharge, 132(66, 0%) had controlled target blood pressure on treatment (Table 1) with median systolic BP 139(132- 146) mmHg, median diastolic BP 89(82-94) mmHg, and sixty-seven participants (33,5%) had elevated blood pressure, higher than target BP 150/100mmHg but less than 160/110mmHg.

Postpartum HPT	**BP at 24hrs**	**BP at 48hrs**	**BP at discharge**
≥150/100 mmHg	163 (81,5%)	37 (18,5%)	67 (33,5%)
≤ 150/110 mmHg	37 (18,5%)	84 (42%)	132 (66%)

Table 2. Blood Pressure on treatment in the postpartum period (Target BP <150/100mmHg)

To reach target BP for discharge (≤ 150/100 mmHg), 54(27%) of the 200 participants on treatment for BP control required an additional second anti-hypertensive agent. Twenty-six (48,1%) of the 54 women who required a second agent started it within 24-48 hours of delivery without reaching the maximum dose of the first agent prescribed. Eighteen (33,3%) were within 48-72 hours of and 10 of the 54 participants (18,5%) were within 72-96 hours (Fig. 3) of being on the first agent. Twenty- two participants (11%) required the addition of a third antihypertensive agent to reach target BP for discharge, with 8(4, 0%) of the 22 participants within 24-48hrs, 4 (2,0%) at 48 -72hrs, 9 (4,5%) at 72-96hrs and 1(1%) at more than 96hrs.

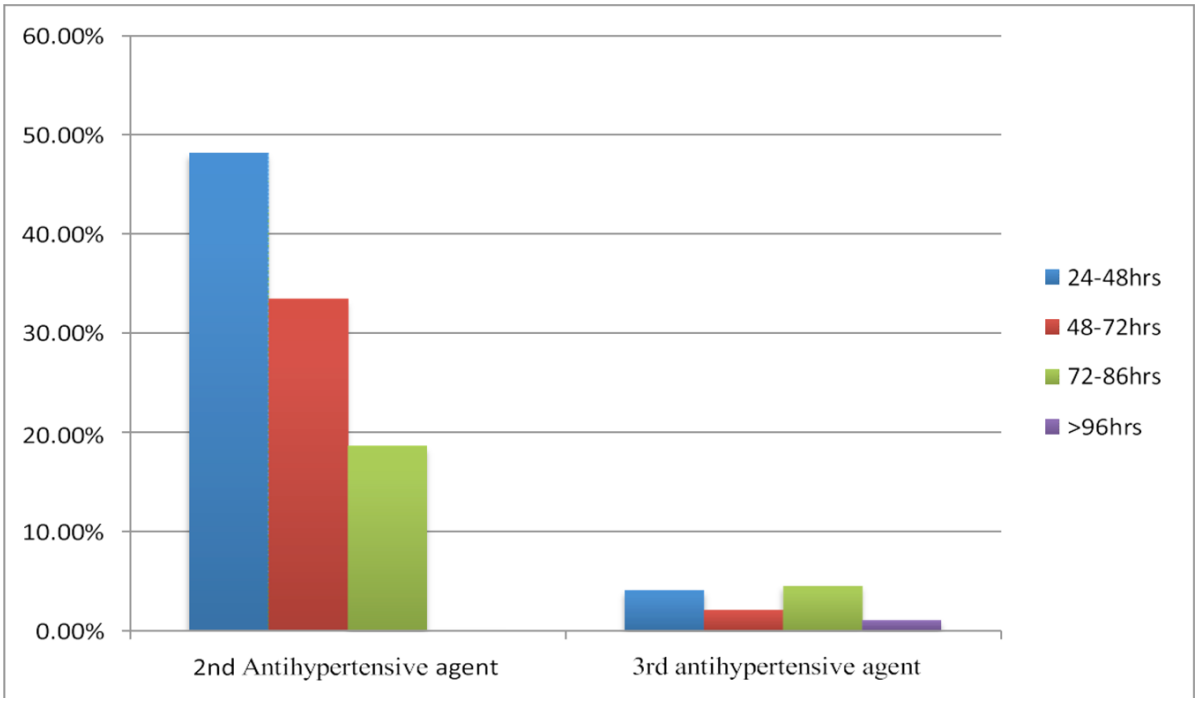

Figure 2. Addition of 2nd and 3rd antihypertensive agent for blood pressure control postdelivery

Hypertensive Agent	**Nifedipine XL**	**Enalapril**	**Hydrochlorothiazide**	**Cardura**	**Atenolol**	**Methyldopa**
1st Agent (N=200)	181 (90,5%)	6 (3%)	0	0	0	13(6,5%)
2nd Agent (N=54)	13(24%)	34(62,9%)	2 (1%)	3(5,5%)	2(3,7%)	0
3rd Agent (N=22)	0	9(40,9%)	2(1%)	10 (45%)	1(4,5%)	0

Table 3: Antihypertensive drugs prescribed post-delivery for BP control

The drugs prescribed for blood pressure control postdelivery were, Calcium Channel Blocker (Nifedipine XL) in 194 (97,0%), Angiotensin-Converting-Enzyme Inhibitors (Enalapril) in 49(24,5%), Alpha 2 agonist (Methyldopa)in 13(6,5%), Beta-blocker (Atenolol) in 3(1,5%), Diuretics (Hydrochlorothiazide) 4 (2,0%), Alpha-blocker (Cardura)10 (5%) of the study participants (Table 2.).Nifedipine XL was the commonest drug prescribed as the first agent in 181 (90,5%) participants, with Enalapril as the second agent in 28 (14%) and Cardura as a third agent in 6(3,0%) of the population.

Eleven Participants out of 200 (5,5%) had postpartum complications requiring maternity high care admission (Fig.6). Preeclampsia was the commonest HDP in this group,7(63,6%) out of the 11 participants with complications, was because of the uncontrolled blood pressure on three oral agents. All the participants that had complications were delivered preterm through a caesarean section. The other complications in this group of the 11 participants with complications included acute kidney injury in 2(1%),2(1%) developed pulmonary embolism, both of which had a medical background history of chronic hypertension and superimposed pre-eclampsia. Furthermore 3 (1,5%) of the participants developed puerperal sepsis, with all three delivered through an emergency caesarean section with 2 of the 3 requiring relook laparotomy. There was one maternal death due to sepsis and no intensive care unit admissions.

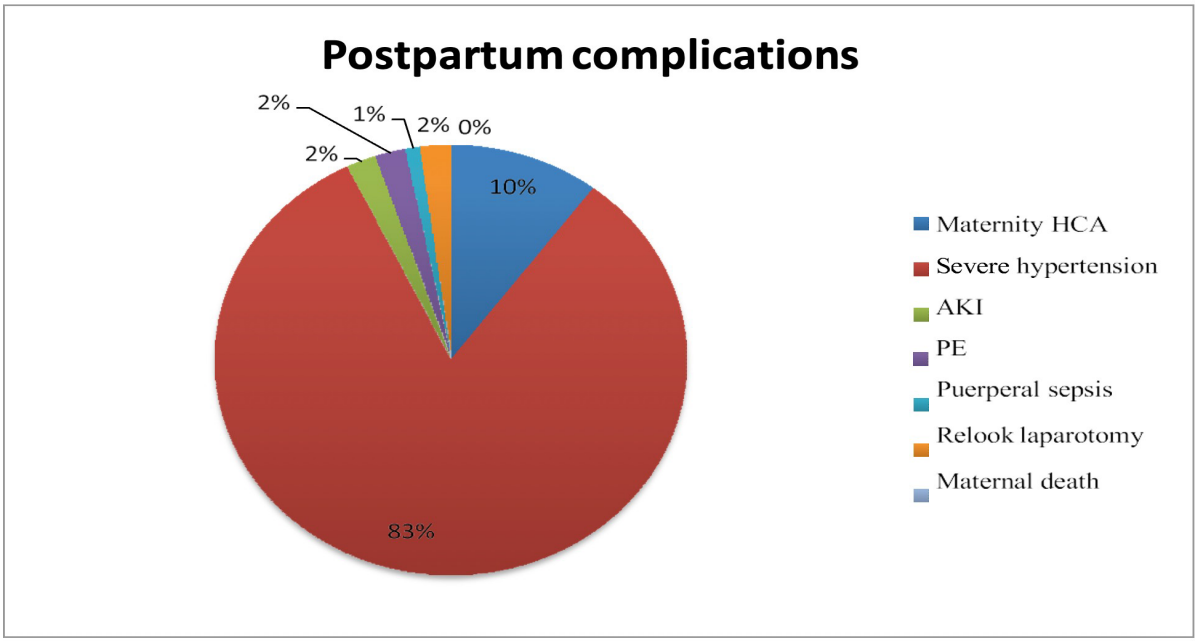

Figure 3. Postpartum complications: HCA (high care admission), AKI (Acute kidney injury), PE (Pulmonary embolism)

One hundred and ninety-nine (99,5%) of the participants were subsequently discharged on treatment with a median systolic BP of 139 mmHg and median diastolic BP of 89 mmHg. All discharged participants were given a routine postnatal follow-up. Those who delivered via caesarean section were seen on day 10 and day 14 for normal vaginal delivery. All patients in absence of an associated stillbirth or near-miss event were discharged with instructions to be reviewed at community health care centres (CHCs).

DISCUSSION

Our study showed that hypertension may persistent postdelivery with associated challenges in its management. The main finding in our study was the use of various antihypertensive agents for blood pressure control postdelivery, up to 6 antihypertensive classes of drugs were prescribed, the commonest of which were Nifedipine, Enalapril and Methyldopa, this is contrary to national stepwise postpartum antihypertensive drugs recommendations [8]. A similar study in KwaZulu- Natal on hypertensive treatment postdelivery in pre-eclamptic patients found as many as 9-22 agents were prescribed for blood pressure control [9]. Furthermore, the order of the drugs prescribed in our study was inconsistent giving the impression that it was left to the preferred choice of the clinician looking after the patient, rather than following the clinical guidelines.

However, there are several factors to be considered on prescribing antihypertensives like breastfeeding, renal function, and some other contraindications, arguably these could have been the reasons for drugs selections among the clinicians. Even so, The National Institute of Health and Clinical Excellence (NICE) reported no known adverse effects to infants of mothers breastfeeding whilst on Nifedipine, Enalapril, Atenolol and Labetalol [10]. Contrary torecommendations by most authorities, our study found that Methyldopa was prescribed as thefirst agent in some participants without tapering off within 48 hours due to its associated maternal risk of depression and postural hypertension [9-10, 11-13]. These findings build on existing evidence on the difficulty in antihypertensive choices postdelivery further supported by arbitrary recommendations in the literature. A Cochrane systematic review on prevention and treatment of postpartum hypertension reported limited data to recommend one antihypertensive agent over another. [11]

Our study also found that there was a large number of participants requiring a second agent within 48 hours without reaching the maximum dose of the first agent to optimize BP contradictory to literature recommendations on the increase of the drug to the maximum agent before the addition of another drug, furthermore the addition of these agents did not lower the BP in all participants. [4] These results and practice by clinicians might explain the large number of participants discharged on polytherapy for blood pressure control. Consensus on therapy for blood pressure treatment postdelivery from expert opinions and clinical

guidelines recommend consideration of treatment if BP >150/100 mmHg with a reported peak on days 3 and 6 [4-5,10-13].

Despite the reported potentially life-threatening complications secondary to HDP postdelivery, complications rate remained low in our study with one maternal death not related to hypertension. It is also important to note that normalization of blood pressure postdelivery and associated complications have been reported to be dependent on several factors, severity of the disease process, maternal associated co-morbidities, and quality of management [3-7]. This was consistent with the findings in our study, by the large number of patients in the complications group with a background HDP of pre-eclampsia.

Our analysis showed that a significant proportion of the participants still had above optimal BP at the time of discharge, this is worrisome as there is enough evidence to support prolonged monitoring postpartum given the growing evidence of risk of cardiovascular and cerebrovascular disease. [4,7,10] This is supported by the national guidelines with reported target BP for discharge of ≤ 150/100 mmHg and further encourages follow-up at a high-risk clinic [8]. We further found that participants with uncomplicated hypertensive disorders of pregnancy and those that delivered through natural birth had quick recovery which was no surprise as studies have shown that the resolution pattern of hypertensive disorders after delivery depends on the severity of the disease. [4,10].

Strengths and weaknesses of our study

The exclusion of women with hypertensive disorders of pregnancy who did not require treatment postdelivery weakness review of maternal complications postdelivery in women with hypertensive disorders in pregnancy. The other weakness is limitations on blood pressuremeasuring, the mean highest blood pressure daily might not be a confident reflection as the number of BP measurements might vary amongst the participants based on the time of admission into the postnatal ward, Day 0 postdelivery is counted from 00:00 up to 23:59 after delivery, and daily blood pressure measurements are taken from any time of delivery with those admitted earlier having more measurements than those admitted later in the day.

Contribution to the body of knowledge

Despite the wide availability of antihypertensive agents, clinicians still struggle in choosing the type and sequence of drugs for blood pressure control. This study was able to highlight the need for continuous education of clinicians on the management of women with hypertensive disorders of pregnancy postdelivery.

The meaning of the study

We were also able to show the shortcoming in the management of hypertension in the first few days after delivery resulting in the high percentage of patients that get discharged from the hospital with persisting high blood pressure. This highlights a need for further education of health care workers by promoting adherence to institution guidelines in postnatal care of women with hypertensive disorders of pregnancy.

Recommendations for future research

Given the growing evidence that shows that hypertensive disorders of pregnancy are associated with persistence of high blood pressure warranting further treatment postdelivery and the associated complications thereof, future studies are needed to follow these women beyond discharge for surveillance and intervention to reduce hypertensive disease long term outcomes.

CONCLUSION

There is substantiated evidence that shows that hypertension can persist beyond pregnancy continuing to pose a risk to maternal wellbeing. Whilst complication rates remained low during the immediate postpartum period in our study, BP remained above optimal target at the time of discharge in a significant number of patients. Efforts to screen, treat and prevent immediate and long-term complications should be strengthened beyond pregnancy and into the post-partum period.

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APPENDIX 1: Approved research protocol

1.1 Introduction

Hypertensive disorders in pregnancy (HDP) are the leading causes of maternal and perinatal mortality (1). Worldwide 10% of women have hypertension during pregnancy with pre- eclampsia complicating 2-8% of those pregnancies (2). Overall, 10-15% of direct maternal deaths are associated with pre-eclampsia and eclampsia (2). In sub-Saharan Africa, the major direct causes of maternal mortality are haemorrhage, pre-eclampsia/eclampsia, obstructed labour and sepsis (3). In South Africa complications of hypertension in pregnancy have remained consistent over the past four years with HDP remaining the second leading cause of death in pregnant women (4). Hypertensive disorders of pregnancy are associated with persistence of elevated blood pressure in the postpartum period, with a reported high proportion of patients needing treatment. This results in lengthy hospital stay and exposing some women to a considerable risk of complications such as stroke, eclampsia and death (5). Part of the strategies of reducing the contribution of HDP on maternal mortality include ensuring that appropriate treatment is initiated post-delivery, discharging them when BP is well controlled and making sure that there are proper follow up plans upon discharge. In a busy hospital such might pose a challenge especially when there is high turnover of staff and patients.

1.2 Literature Review

1.2.1 Definitions

Gestational hypertension is defined as de novo development of hypertension after 20 weeks of gestation (6,7,8). Pre-eclampsia is further defined by coexistence of one or more of the following new onset conditions: Proteinuria, other maternal organ dysfunction and utero placental dysfunction as evidenced by fetal growth restriction (6).

The revised International Society for the Study of Hypertension in Pregnancy (ISSHP) 2013, classifies HDP into four categories:

1. Chronic hypertension
2. . Gestational hypertension or pregnancy induced hypertension (PIH)
3. Pre-eclampsia - de novo or pre-eclampsia superimposed on chronic hypertension
4. White coat hypertension

De novo hypertension is hypertension that develops in the immediate postpartum period and is usually defined as hypertension appearing post-delivery through six weeks postpartum (5). Postpartum hypertension may persist in women who had HDP as classified above or seen for the first time post-delivery up to six weeks postpartum (5).

1.2.2 Pathogenesis

Pathogenesis of pre-eclampsia involves several factors and different stages, but the focus is mainly on the placenta, characterized by abnormal invasion of maternal uterine vessels resulting in failure of trophoblast remodeling of spiral arterioles and maternal-fetal immunological intolerance (6,7,8).

1.2.3 Treatment of Hypertension

Treatment of gestational hypertension includes the control of blood pressure (BP) with anti-hypertensive medication and surveillance for pre-eclampsia and its associated maternal-fetal complications (6). Pre-eclampsia management is based on maternal-fetal severity of disease and delivery remains the mainstay of treatment (6,7,8,9). Different classes of antihypertensive drugs are recommended to control blood pressure in the antenatal period. Acute control of severely elevated blood pressure includes the use of short acting nifedipine, intravenous labetalol or hydralazine and maintenance treatment is with methyldopa, nifedipine, oxprenolol and hydralazine with the aim of maintaining systolic blood pressure above 110 mmHg and diastolic pressure above 80 mmHg (6).

Treatment post-delivery varies according to different guidelines and protocols, with recommendation of treatment if systolic blood pressure is persistently above 150 mm Hg with/or diastolic more than 100 mm Hg (10). There is limited data comparing which of the antihypertensive drugs are best to use post-delivery, the most recent Cochrane review (2005) demonstrated that of the available trials most have a small sample size and are of poor quality (11).

However, there are published recommendations based on expert opinion. National Institute for Health Care and Excellence (NICE) clinical guideline on hypertension in pregnancy recommends that women who have had gestational hypertension/pre-eclampsia to be discontinued on methyldopa within two days after delivery as it is associated with postnatal depression and recommends angiotensin two receptor blockers, angiotensin converting enzyme inhibitors other than enalapril and captopril and amlodipine for those with persistently elevated blood pressures. NICE also looked at safety of the drugs in breastfeeding mothers in which they advised for women to be extensively counselled about insufficient evidence to guide on safe use. Furthermore, at discharge the blood pressure needs to be checked at least once between day three and five and to subsequently have a medical review at the six to eight weeks visit (12). American Congress of Obstetricians and Gynecologist (ACOG) recommends the use of the same drugs with advice for outpatient surveillance at least seven to ten days after delivery (13). The Society of Obstetric Medicine of Australia and New Zealand (SOMANZ) also recommends follow up after six weeks to ensure resolution of pregnancy-related changes and ascertain the need for ongoing care but conversely further states that a reduction in medication may be required within one or two weeks of post-delivery if the women's antihypertensive therapy was augmented in relation to pregnancy (14). World Health organization (WHO) recommends continuation of antihypertensive treatment in women who were on treatment antenatally (15). This is further supported by a statement from the Cochrane review in which they reviewed trials that compared antihypertensive treatment in the postnatal period, routine use versus treatment in women with severe high blood pressure in which they concluded that there was insufficient data to establish benefits versus harm (10).
The use of anti-hypertensives in a stepwise manner is recommended but the order in which to prescribe the drugs is inconsistent. The national guidelines for maternity care in South Africa are more specific on the order of which drugs to use and recommends follow up after three days of discharge at nearest clinic and again six weeks postpartum at high-risk postnatal specialist clinic. The choice of drugs is also influenced by whether the mother is breastfeeding or not and associated medical co-morbidities, for instance asthma and heart failure are contraindications to beta-adrenergic blockade and should first be excluded (16).

In the Cochrane review of prevention and treatment of hypertension in postpartum, authors concluded that there was no reliable data to guide the management of women who are hypertensive postpartum or at increased risk of being so (11).

1.2.4 Complications of hypertensive disorders of pregnancy

Hypertensive disorders of pregnancy increase the risk of maternal-fetal complications, which may occur immediately and later in life following delivery. These complications include maternal target organ damage during pregnancy and subsequent risk of cardiovascular, renal disease and atherosclerosis at a later stage. Fetal complications occur as a result of placental insufficiency and prematurity (6,7,8).

1.2.5 Postpartum resolution of hypertension

Hypertension usually resolves in women who had hypertensive disorders of pregnancy post-delivery but there is conflicting data about when it resolves, several studies, mainly retrospective show variations in resolutions of blood pressure but with most reporting resolution within days of delivery in most women (17). One of those studies is by Sibai, in which he reported that within days following delivery in a pre-eclamptic pregnancy, blood pressure returns to normal, on average withinsix days (18).

There is also conflicting data regarding the time it takes for resolution of proteinuria in the post-partum period in women with pre-eclampsia. The differences reported among various studies are due to different population studied, severity of disease process, duration of follow up, management and criteria used for hypertension or proteinuria. A prospective cohort study involving 54 women with severe pre-eclampsia and eclampsia that was conducted in sub- Saharan Africa described postpartum trends in BP levels, renal function and proteinuria. During follow-up a significant improvement was observed in BP, renal function and proteinuria (all p<0,002). Thirteen (24,1%) patients with renal failure at delivery recovered completely within six weeks. Twenty-six (48,1%), 17 (31,5%) and one (1,8%) patient had persisting proteinuria at six weeks, three months and six months post-delivery, respectively. Corresponding figures for persisting hypertension were 23 (42,6%), 15 (27,8%) and 8914,8%) (19). The postpartum period remains a high-risk period as there is still a risk for persistent of the disease and likely complications highlighting need for vigilance from immediately post-delivery.

1.2.6 Complications of persistent hypertension

It is now evident that hypertension can persists for days and even more post-delivery for some women, further proving that delivery does not necessarily eliminate the risk of persistence of disease and associated complications thereof. Use of other medications in the postnatal period when prescribed in large doses or frequently can also contribute to persistent hypertension and de novo hypertension. Some of those drugs include ibuprofen, ergonovine and decongestants (10).

These studies highlight need for continuous care and a clear management plan which includes strict adherence to treatment guidelines and follow up procedures for women who had HDP in the postpartum period to prevent immediate and long-term complications and to avoid lengthy hospital stay.

1.3 Aim

The aim of this study is to investigate the management of women with hypertension in pregnancy during the immediate postpartum period, to enhance the knowledge and improve our clinical practice.

1.4 Objectives

1. To describe the choices of antihypertensive drugs prescribed to pregnant women at CHBAH and assess whether the choices are in line with national protocol.

2. To investigate blood pressure levels of patients at the time of discharge.

3. To investigate the frequency and nature of hypertension related complications in the immediate postpartum period among the study cohort.

4. To investigate the presence and nature of follow up plans given to the patients at CHBAH.

1.5 Study design

This is a retrospective cross-sectional study of post-delivery women admitted at CHBAH with hypertensive disorders of pregnancy from day zero post-delivery until the day of hospital discharge.

1.6 Methods

This will be a retrospective cross-sectional study, involving all women admitted at CHBAH with hypertensive disorders of pregnancy over a two month period. The following data will be collected from patients record for analysis as per data collection tool (Appendix A):

1. Basic demographic data

2. Complications such as Events such as eclampsia, stroke and pulmonary oedema 3. Type ofantihypertensive medication prescribed in the postnatal period

4. Level of Blood pressure on the date of discharge

3. Information on follow-up plan

1.7 Setting

The study will be conducted at CHBAH hospital, which is the third largest hospital in the world. The Obstetrics and Gynaecology Department has 20 000 deliveries a year. The hospital is in the Soweto area of Johannesburg and is one of the multiple Gauteng provincial hospitals. It is one ofthe teaching hospitals for the University of Witwatersrand and a referral Centre to two MOUs, two regional and one district hospital. CHBAH does not have a routine post-natal clinic. It has a high-risk postnatal clinic for women who had a near- miss event or a stillbirth. Women with hypertension, including eclamptic are required to attend post-natal clinics at the local clinic. A discharge summary for hypertensive women is filled out, and if the hypertension does not resolve, the women are sent to physicians or medical officers at the clinics, since women are seldom seen by obstetricians post operatively.

1.8 Study population

The study will include all women admitted and delivered at CHBAH with hypertensive disorders of pregnancy (Gestational Hypertension, Pre-eclampsia, HELLP syndrome, Imminent eclampsia and Eclampsia) and followed up from day zero post-delivery until discharge.

1.9 Inclusion criteria

All patient admitted with hypertension and delivery and delivered at CHBAH during the study period.

1.10 Sample size

Assuming a 6% prevalence of hypertension, a 10% loss and a ± 3.6% margin of error, it is envisaged that this study will enroll at least 185 participants.

1.11 Data analysis

Descriptive statistics will be used to describe continuous measures while frequencies will be used for categorical measures. A linear mixed model will determine the rate of decline in hypertension from time of birth to hospital discharge. Additionally, time to decline of hypertension by severity and age groups will be assessed by the Kaplan-Meier logrank test.

1.12 Limitations

Most of patients delivering at CHBAH are referred to the local clinic and hence the study will be limited to the immediate postpartum period. However, a similar study design was used in India at Coimbatore Medical College Hospital for a period of three months involving around 100 inpatients of HDP (20).

1.13 Strengths

There are a few studies describing the persistence of hypertension in the postpartum period in the South African setting. Though guidelines are clear, adherence has not been evaluated and neither whether this may contribute to the high maternal mortality. The findings of this study have the potential to shed some insight on the management of hypertensive patients in the immediate postpartum, which might require protocol review of further evaluation.

1.14 Funding

All costs will be borne by the researcher.

1.15 Timeline

Task	Nov-Dec 2017	Jan-Feb 2018	March-April 2018	May-July 2018	August-Sept 2018	Oct- Nov 2018	Dec 2018
Protocol Review Committee assessment	X						
Corrections after postgraduate protocol review committee		x					
Ethics application			X				
Institutional permission				X			
Data collection					x		
Data analysis and write up						x	
Submission for examination							x

1.16 Ethics

Ethics approval will be sought from the Wits HREC. Permission will be sought from the CEO of the Hospital by registering the project online on the National Health Research Database as well as from the Head of Obstetrics and Gynecology at CHBAH.

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APPENDIX 2: Data collection sheet

Record ID	_____
Age	_____
Race	◯ African ◯ White ◯ Asian ◯ Coloured ◯ Other
Marital Status	◯ Single ◯ In a relationship ◯ Married ◯ Divorced
Employment	◯ Unemployed ◯ Employed
Parity	_____
Gravidity	_____
Booked	◯ Yes ◯ No
Rh	◯ Positive ◯ Negative ◯ Unknown
RPR	◯ Positive ◯ Negative ◯ Unknown
RVD Status	◯ Positive ◯ Negative ◯ Unknown
CD4 Count	_____
Viral load	_____
Gestational age at booking	_____
Pregnancy Trimester	◯ Trimester 1 ◯ Trimester 2 ◯ Trimester 3

BP at booking

	Normal	Abnormal
Blood pressure at booking	◯	◯

Maternal Risk Factors

- ☐ Previous preeclampsia
- ☐ Multiple gestation
- ☐ Pregestational DM
- ☐ BMI > 30
- ☐ APLS
- ☐ Assisted reproduction
- ☐ Other

Other Maternal Characteristics

Aspirin

- ◯ Yes
- ◯ No

Type of HDP

- ◯ Chronic hypertension Essential
- ◯ Chronic hypertension- Secondary
- ◯ Gestational hypertension
- ◯ Preeclampsia De novo
- ◯ Preeclampsia Superimposed

Gestation at diagnosis

Hypertensive Complications

- ◯ Yes
- ◯ No

Maternal Complications

- ☐
- ☐ Eclampsia HELLP
- ☐ ~~Syndrome Imminent~~
- ☐ eclampsiaAKI
- ☐ Pulmonary oedema
- ☐ Persistent thrombocytopenia
- ☐ Uncontrolled BP'S on 3 agents
- ☐ Abruptio
- ☐ Pulmonary oedema
- ☐ Preeclampsia de novo
- ☐ Superimposed preeclampsia

Fetal Complications

- ☐ IUGR
- ☐ Abnormal Doppler's
- ☐ Non-reassuring CTG
- ☐ IUFD
- ☐ MSB
- ☐ FSB

Number of antihypertensive during pregnancy

- ◯ < 3
- ◯ >/=3

Labetalol required

- ◯ Yes
- ◯ No

Type of antenatal antihypertensive drug	☐ Methyldopa ☐ CCB ☐ ACEI ☐ B-Blocker ☐ Diuretics ☐ Alpha blocker ☐ Other
Magnesium Sulfate	◯ Yes ◯ No
Gestational age at delivery	_____
Mode of delivery	◯ NVD ◯ Caesarean Section ◯ Assisted delivery
Highest BP in D0	_____
Target BP D0	◯ Normal ◯ Abnormal
BP at initiation of treatment post delivery	_____
Target BP at initiation of treatment	Normal ◯ Abnormal ◯
Highest BP D1	_____
Highest BP D1	◯ Normal ◯ Abnormal
Highest BP D2	_____
Highest BP D2	◯ Normal ◯ Abnormal
Highest BP D3	_____
Highest BP D3	◯ Normal ◯ Abnormal
Highest BP D4	_____
Highest D4	◯ Normal ◯ Abnormal
Highest BP D5	_____

Highest BP D5	◯ Normal ◯ Abnormal
Highest BP D6	_____
Highest BP D6	◯ Normal ◯ Abnormal
BP on discharge	_____
BP at discharge	◯ Normal ◯ Abnormal
Time to Change to Second Class of drug	◯ ~~Post delivery~~ 24 hours ◯ 24-48 hours ◯ 48-72 hours ◯ 72-86 hours ◯ >86 hours
Time to Change to third Class of drug	☐ ~~Post delivery~~ 24hourS ☐ 24-48 hours ☐ 48-72 hours ☐ 72-86 hours ☐ > 86 hours
Time to normalization of BP	◯ Delivefy-48hourS ◯ 48 hours- 5 days ◯ 5-10 days ◯ >10 days
Feeding	◯ Breast-feeding ◯ Formula feeding ◯ both
Type of analgesia	☐ Paracetamol ☐ Opioids ☐ ~~NSaidS~~ ☐ Other
Length of hospital Stay	_____
Number of antihypertensive dugs post delivery	_____
Contraception	◯ Oral ◯ Injectable ◯ Implant ◯ IUCD ◯ Sterilizatio ◯ Condoms ◯ None ◯ Other
Same as pre pregnancy drugs in CHT	◯ Yes ◯ No

Follow up duration period on discharge

- ◯ < 2 weeks
- ◯ > 2 weeks
- ◯ none

Type antihypertensive

- ☐ Methyldopa
- ☐ CCB
- ☐ ACE-inhibitor
- ☐ B-blocker
- ☐ Diuretics
- ☐ Alpha blocker]
- ☐ others

Ofdef in which pfescfibed

	1	2	3	4	5	6
Methyldopa	◯	◯	◯	◯	◯	◯
CCB	◯	◯	◯	◯	◯	◯
ACE-inhibitors	◯	◯	◯	◯	◯	◯
B-blocker	◯	◯	◯	◯	◯	◯
Diuretics	◯	◯	◯	◯	◯	◯
alpha blocker	◯	◯	◯	◯	◯	◯
other	◯	◯	◯	◯	◯	◯

Postpartum Complications

- ◯ Yes
- ◯ No

High Care admission

- ☐ Uncontrolled BP'S
- ☐ Eclampsia
- ☐ PRES
- ☐ AKI
- ☐ HELLP
- ☐ Pulmonary embolus
- ☐ pulmonary oedema
- ☐ CMO
- ☐ CVA
- ☐ Sepsis
- ☐ Relook laparatomy

ICU admission

- ☐ Ventilation
- ☐ DialySiS
- ☐ Severe metabolic acidosis
- ☐ Pulmonary oedema

Length of ICU Stay _____

Maternal death

- ◯ Yes
- ◯ No

Other Complications _____

APPENDIX 3: Ethics Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Rangwato Mashoene et al

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M180433

NAME: (Principal Investigator)	Dr Rangwato Mashoene et al
DEPARTMENT:	Obstetrics and Gynaecology Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Management of women with hypertensive disorders in pregnancy in the immediate postpartum period: A review of practices in a busy tertiary hospital in Gauteng, South Africa
DATE CONSIDERED:	04/05/2018
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Salome Maswime
APPROVED BY:	Prof C Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	02/08/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 301, Third floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed April and will therefore be due in the month of April each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX 4: Author guidelines from South African Medical Journal

Guideline word limit: 4 000 words

The article should contain the following sections: introduction, methods, results, discussion, and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question and must include references to other relevant published studies that lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically.

Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or posthoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

Select figures and tables for your paper carefully and sparingly. Use only those figures that provided added value to the paper, over and above what is written in the text.

Do not replicate data in tables and text.

Structured abstract

this should be 250-400 words, with the following recommended headings:

background: why the study is being done and how it relates to other published work.

objectives: what the study intends to find out

methods: must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.

results: first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.

conclusion: must be supported by the data, include recommendations for further study/actions.

Main article

All articles are to include the following main sections:

Introduction/Background, Methods, Results, Discussion, Conclusions.

The following are additional heading or section options that may appear within these:
Objectives (within Introduction/Background): a clear statement of the main aim of the study and the major hypothesis tested or research question posed

- Design (within Methods): including factors such as prospective, randomisation, blinding, placebo control, case control, crossover, criterionstandards for diagnostic tests, etc.
- Setting (within Methods): level of care, e.g., primary, secondary, number of participating centres.
- Participants (instead of patients or subjects; within Methods): numbers entering and completing the study, sex, age and any other biological, behavioural, social or cultural factors (e.g., smoking status, socioeconomic group, educational attainment, co-existing disease indicators, etc.) that may have an impact on the study results. Clearly define how participants were enrolled and describe selection and exclusion criteria.
- Interventions (within Methods): what, how, when and for how long. Typically for randomised controlled trials, crossover trials, and before andafter studies.
- Main outcome measures (within Methods): those as planned in the protocol, and those ultimately measured. Explain differences, if any.

Results

- Start with description of the population and sample. Include key characteristics of comparison groups.
- Main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the numberneed to treat/harm. Whenever possible, state absolute rather than relative risks.

- Do not replicate data in tables and in text.
- If presenting mean and standard deviations, specify this clearly. Our house style is to present this as follows:
- E.g.: The mean (SD) birth weight was 2 500 (1 210) g. Do not use the ± symbol for mean (SD).
  - Leave interpretation to the Discussion section. The Results section should just report the findings as per the Methods section.
  -

Discussion

Please ensure that the discussion is concise and follows this overall structure – sub-headings are not needed:

- Statement of principal findings
- Strengths and weaknesses of the study
- Contribution to the body of knowledge
- Strengths and weaknesses in relation to other studies
- The meaning of the study – e.g., what this study means to clinicians and policymakers
- Unanswered questions and recommendations for future research
-

Conclusions

This may be the only section readers look at, therefore write it carefully. Include primary conclusions and their implications, suggesting areas for further research if appropriate. Do notgo beyond the data in the article.

Illustrations/photos/scans

- If illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained fromthe copyright holder.
- Figures must be numbered in Arabic numerals and referred to in the text e.g., '(Fig. 1)'.
- Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).
- All images must be of high enough resolution/quality for print.
- All illustrations (graphs, diagrams, charts, etc.) must be in PDF or jpeg form.

- Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g. 0; 1.0; 2.0; 3.0; 4.0 etc.
- Scans/photos showing a specific feature e.g. *Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumor. (H&E stain).* –include an arrow to show the tumor.
- Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

- Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.
- Large tables will generally not be accepted for publication in their entirety. Please consider shortening and using the text to highlight specific important sections, or offer a large table as an addendum to the publication, but available in full on request from the author
- Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.
- Number each table in Arabic numerals (Table 1, Table 2, etc.) and refer to consecutively in the text.
- Tables must be cell-based (i.e., not constructed with text boxes or tabs) andeditable.
- Ensure each table has a concise title and column headings and include units where necessary.

Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc

References

NB: *Only complete, correctly formatted reference lists in Vancouver style will be accepted. Reference lists must be generated manually and not with the use of reference manager software. Endnotes must* ***not*** *be used.*

- Authors must verify references from original sources.
- Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by theWorld Health Organization,[2] and others. [3,4-6]
- All references should be listed at the end of the article in numerical order

of appearance in the Vancouver style (not alphabetical order).

- Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.
- Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.
- Volume and issue numbers should be given.
- First and last page, in full, should be given e.g.: 1215-1217 **not** 1215-17.
- Wherever possible, references must be accompanied by a digital object identifier (DOI) link). Authors are encouraged to use the DOI lookup service offered by CrossRef:
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    - Look for the correct, matching article in the list of results.
    - Click Actions > Cite
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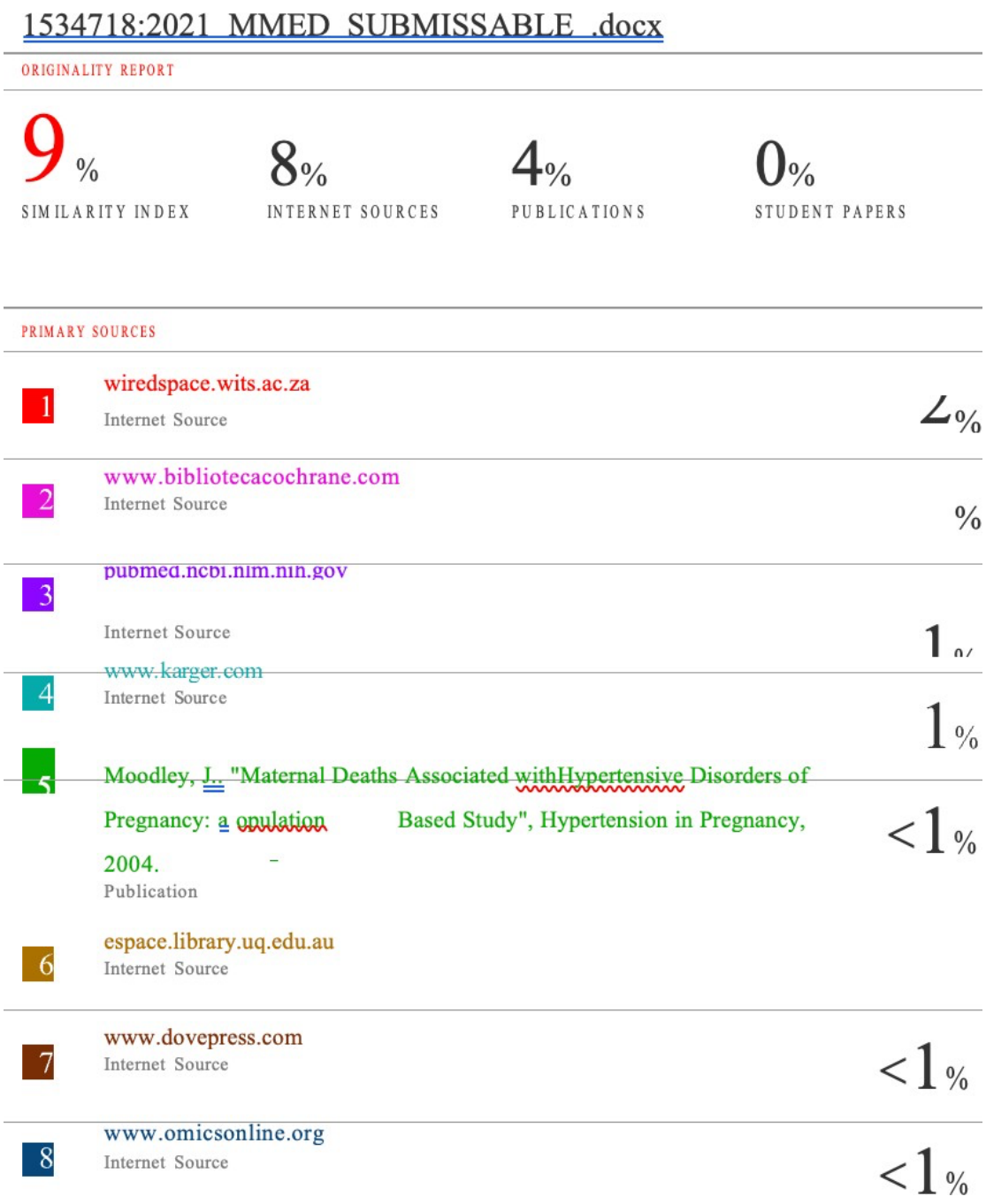
APPENDIX 5: Turnitin plagiarism report



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17	www.cambridge.org Internet Source	<1%
18	www.thieme-connect.com Internet Source	<1%
19	"E-Poster Viewing", European Stroke Journal, 2019 Publication	<1%
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APPENDIX 6: PLAGIARISM CERTIFICATE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I RANGWATO PEARL MASHOENE (Student number: 1534718) am a student registered for the degree of MMED, OBSTETRICS AND GYNAECOLOGY in the academic year 2020

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: Mash Date: 27/11/20.

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