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Feto-maternal outcomes of patients with placenta praevia and accuracy of diagnosis of placenta accreta syndrome at Chris Hani Baragwanath Academic Hospital

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2021
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FETO-MATERNAL OUTCOMES OF PATIENTS WITH PLACENTA PRAEVIA AND ACCURACY OF DIAGNOSIS OF PLACENTA ACCRETA SYNDROME AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

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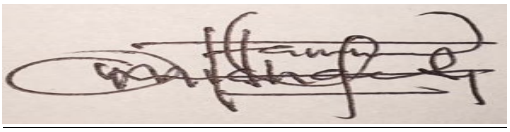
This research reported is submitted to the University of the Witwatersrand Health Sciences Faculty in partial fulfillment of Master of Medicine In Obstetrics and Gynaecology In February 2021

Declaration

I, Michael Nii Armah Hammond declare that this work is original and contains no section copied in whole or in part from any source, I declare that this work has not been submitted to any other University for a post graduate degree.



Signed 01/2/2021 in Johannesburg

Dedication

In loving memory of my mother Irene Naa Kwaley Quartey. Also dedicate this MMed to my wife and daughter, Frances Afia Boadiwa and Naa Kwaley Nkunim Hammond

Presentations/Publications

20/12/2019: Oral presentation during journal club at Charlotte Maxeke Johannesburg Academic Hospital

09/06/2020: Poster presentation at South African Society of Obstetrics and Gynaecology conference at Drakensberg

15/10/2020: Oral presentation at Faculty of Health Sciences Biennial Research Day, University of the Witwatersrand

7/12/2020: Oral presentation during journal club at Chris Hani Baragwanath Academic Hospital

14/12/2020: Poster presentation at FIGO 2020 Regional Kigali Conference

December 2020: Abstract published in the International Journal of Gynecology Obstetrics

Abstract

Background. The incidence of placenta praevia (PP) is 0.3-0.5% of pregnancies and it is a major risk factor for placenta accreta syndrome (PAS). PP and PAS cause immense fetomaternal morbidity and mortality and as a result, place a huge burden on health care resources. Hence accurate diagnosis prenatally of PP and associated PAS, is essential as this allows adequate preparation for potential complications

Objective. To ascertain the accuracy of prenatal diagnosis of PP and PAS, and the feto-maternal outcomes of these conditions in women diagnosed at Chris Hani Baragwanath Academic Hospital (CHBAH)

Methods. This was a retrospective, descriptive study that reviewed 55 women diagnosed with PP at CHBAH from 1st of January to the 31st of December 2018. Maternal demography, clinical presentation, surgical findings, ultrasound and Magnetic Resonance Imaging (MRI) findings were assessed to determine feto-maternal outcomes.

Results. Complete data was obtained for 28 women. The incidence of PP was 0.3%. Seventeen patients (58.6%) required intensive care admissions, 7 (24.1%) patients required blood transfusion, and 4 (12.12%) had hysterectomies. The average gestational age of delivery was 33.84±3.4. Ten (30.12%) babies required neonatal intensive care admissions. Ultrasound had a positive predictive value of 50% while MRI correctly identified PAS in 33.3% of patients

Conclusion. PP and PAS increase the likelihood of maternal and neonatal morbidities. Ultrasound is a useful tool in evaluating placenta implantation and can assist in anticipating adverse feto-maternal outcomes in PP and PAS .MRI has limited clinical value in this setting currently, and should not be done routinely

Acknowledgements

I would like to thank the Department of Obstetrics and Gynaecology at Chris Hani Baragwanath for allowing me access to their patient data as well as my supervisors, Dr. Jayshree Jeebodh and Dr. Chysanthi Georgiou for their immense contribution and support throughout this project

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Abbreviations

CHBAH	Chris Hani Baragwanath Academic Hospital
CS	Caesarean Section
MDT	Multi Disciplinary Team
MRI	Magnetic Resonance Imaging
NICU	Neonatal Intensive Care Unit
PAS	Placenta Accreta Syndrome
PP	Placenta Preavia

Journal Article

Feto-maternal outcomes of patients with placenta previa and accuracy of diagnosis of placenta accreta syndrome at Chris Hani Baragwanath Academic Hospital

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Introduction

Placenta previa (PP) is defined as placenta that implants in the lower uterine segment and covers the internal cervical os partially or wholly. It occurs in about 0.3-1.9% of pregnancies and is an important contributor to maternal morbidity and mortality, prematurity and perinatal mortality due to the possibility of maternal bleeding. [1] Placenta accreta syndrome (PAS), which may occur in association with PP, is defined as invasion of the chorionic villi into myometrial tissue. [2] It is subclassified histopathologically into accreta, increta, and percreta types depending on the depth of penetration into the myometrium. Placenta accreta involves superficial myometrial attachment, placenta increta penetrates the myometrium and placenta percreta penetrates through the myometrium and other pelvic organs, usually the bladder. [2]

Fetomaternal morbidity and mortality from PP and PAS place a significant burden on health care resources. Hence, accurate diagnosis prenatally is essential as this allows both patients and obstetricians to adequately prepare for potential complications. Maternal and fetal morbidity may thus be reduced by prenatal detection. Nevertheless, even series from specialist hospitals show that up to a third of cases of PAS are undiagnosed during pregnancy. [3] This highlights the difficulty in diagnosing these conditions and the poor sensitivity of the present diagnostic techniques. Ultrasound is still the primary modality in the assessment of placental implantation but there has been increased interest in magnetic resonance imaging (MRI) in recent years. [4]

The literature has shown conflicting reports with regards to feto-maternal outcomes of PP. This study aims to ascertain the accuracy of prenatal diagnosis of PP and PAS and the feto-maternal outcomes of these conditions in women diagnosed at Chris Hani Baragwanath Academic Hospital (CHBAH) in Johannesburg. The hospital introduced a new protocol for the management of PP and PAS in 2018. This protocol emphasizes the use of a Multi Disciplinary Team (MDT) in the management of PP and PAS.

Methods

The study was performed at CHBAH, which houses the largest maternity unit in South Africa. The unit serves as a referral center for several community health centers and district hospitals, including centers outside the Gauteng province. A subspecialist

fetal medicine unit offers detailed ultrasound pregnancy scans. The Human Research Ethics Committee of the University of the Witwatersrand approved the study

This was a retrospective descriptive study. Data was collected from 1st June 2019 to 31st July 2019. The inclusion criterion was the diagnosis of PP prenatally at the CHBAH fetal medicine unit from 1st January to 31st December 2018. Data for included patients were obtained from fetal medicine unit records, maternal case records, operating theatre registers, Intensive Care Unit registers, radiology reports, neonatal records and histopathology reports. Each patient was assigned a data collection sheet, which included fields for demographic details and risk factors, clinical presentation, ultrasound and MRI findings, surgical findings, maternal and fetal outcomes, and histopathology reports. A maternal-fetal medicine subspecialist at the fetal medicine unit at CHBAH performed all ultrasound scans. Maternal outcomes that were accessed included intensive care or high care unit admission, acute kidney injury, coagulopathy, sepsis, postoperative ventilation, visceral injury at surgery, relook laparotomy, hysterectomy, blood transfusions and length of hospital stay. Fetal outcomes included 1-minute and 5- minute Apgar scores, newborns small for gestational age, intrauterine fetal death and neonatal intensive care unit (NICU) admission.

The data were entered in a Microsoft Excel spreadsheet and imported into a Stata 14.0 software (StataCorp, College Station, Texas, USA) for statistical analysis. Categorical variables were summarized by frequency and percentage tabulation and also illustrated with bar charts. Continuous variables were summarized using mean ± standard deviation and median and range. Where applicable, Fisher exact test and Student's t-test were used to analyze relationships. A 5% significance level was used

Results

Fifty-five cases of PP were identified. During the period of study, there were 18,728 births at CHBAH, (Prof Yasmin Adam, personal communication) giving a hospital incidence of 0.3% of PP. Complete data were obtained for 28 patients but the remaining patients (n=27) were not excluded from analysis, with data presented wherever available. The mean age of women with PP was 31.65years±6.0years, mean gravidity was 3.0± 1.3 and mean parity was 1.7± 1.3. Eighteen (32.7%) women were

35 years old or more. Fifteen (27.3%) women had previous caesarean sections (CS). Fifteen (27.3%) patients had previous miscarriages. The median body mass index was 32.5Kg/m2. Table 1 and table 2 below show maternal demography and maternal risk factors respectively

Table 1. Showing maternal demography

Variables	**Numbers**	**Percentage (%)**
Age (years)		
<18	1	1.8%
19-34	36	65.5%
>35	18	32.7%
Parity		
0	9	16.4%
1	17	30.9%
2	15	27.3%
3	7	12.7%
4	5	9.1%
5	2	3.6%
Gravidity		
1	7	12.7%
2	11	20.0%
3	17	30.9%
4	13	23.6%
5	4	7.3%
6	3	5.5%
BMI		
<18.5	0	0.0%
18.5-30	9	45.0%
>30	12	55.0%

Table 2. Showing maternal risk factors

Risk factors	Numbers	Percentage (%)
Previous CS		
0	40	72.7%
X1	7	12.7%
X2	7	12.7%
X>2	1	1.8%
Uterine fibroids		
Yes	1	1.8%
No	54	98.4%
Previous PP		
Yes	2	3.6%
No	53	96.4%
Previous miscarriage		
Yes	15	27.2%
No	45	81.8%
Smoking		
Yes	3	5.5%
No	52	95.5%

Whereas 22 (64.7%) of patients presented with vaginal bleeding, 12 (35.3%) were incidental findings on ultrasound. The mean hemoglobin level at presentation was 11.95±2.03g/dl, with 3 (10.7%) patients requiring blood transfusion to optimize their hemoglobin levels prior to surgery. The mean gestational age at presentation was 30.85weeks ±4.4weeks. During the antenatal period, 13 (50%) of the patients had one episode of bleeding, 6 (23%) patients had more than one episode of bleeding while 7 (27%) patients never bled.

All our patients had CS.A greater percentage of our patients (53.85%) had scheduled delivery rather than emergency delivery (46.15%). The indication for emergency CS included antepartum hemorrhage 6(50%), fetal distress 4(33.33%), onset of labour 1(8.3%), intrauterine fetal death 1(8.3%).

Seventeen patients (58.6%) required intensive care or high care unit admissions, 7 (24.1%) patients required blood transfusion either during or after surgery. Five patients (17.2%) developed sepsis post-delivery, 4 patients (12.12%) had hysterectomies. There was no maternal death reported in the study. The mean birth weight was 2244g ±730g. The average gestational age at delivery was 33.84±3.4 (Figure1). Ten (30.12%) babies required admission to NICU. There was no neonatal death reported in the first 24 hours

Overall 13 patients (23.6%) were suspected to have PAS on prenatal ultrasound scanning. Final result (based on histopathology) was obtained for 4 patients only. Three (75%) of these patients had PAS confirmed on histology. Two other patients who were suspected to have PAS on prenatal ultrasound had their placentas separated surgically with no clinical evidence of adherence, hence ultrasound had a positive predictive value of 50%. One patient was confirmed to have PAS on histopathology but had no evidence of PAS on prenatal ultrasound. Six patients underwent MRI and had final report. MRI correctly identified PAS in 2 of 6 patients (33.3%). Table 2 below compares ultrasound findings, surgical findings, histopathology findings and MRI findings.

The incidence of adverse feto-maternal outcomes was increased in women with suspected PAS on prenatal ultrasound compared with patients showing no prenatal ultrasound evidence of PAS. There was an increased incidence of the following outcomes with statically significant p-values, mean blood loss, hysterectomy, visceral injury at surgery, ventilator support postoperative, 1 minute and 5-minute Apgar scores. This is shown in table 3 below.

Figure 1. Showing Gestational age at delivery

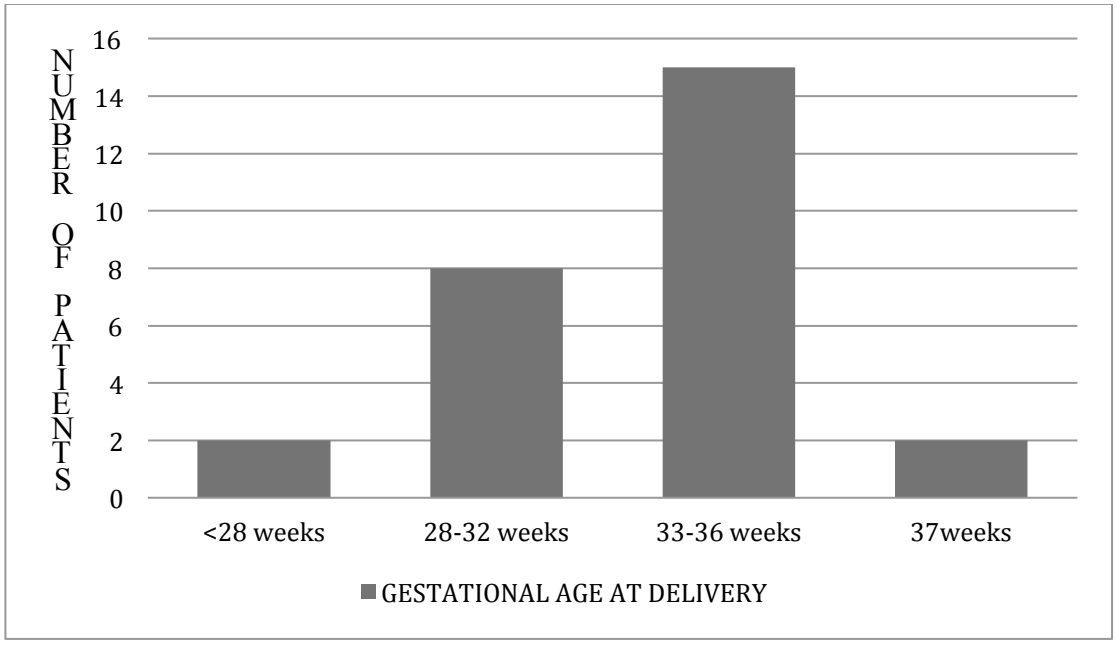

Table 3. Comparing ultrasound findings, surgical findings, histopathology findings and MRI findings

Case number	Ultrasound findings of adherence	MRI findings	Surgical finding of adherence	Histopathology	Final report
1	Present	Placenta Increta	Present	Placenta Increta	Placenta Increta
2	Present	Placenta Accreta	Not present	Not Applicable	Negative
3	Present	Negative	Present	Placenta Accreta	Placenta Accreta
4	Present	Negative	Not present	Not Applicable	Negative
5	Present	Placenta Increta	Present	Placenta Accreta	Placenta Accreta
6	Present	Negative	Not present	Placenta Accreta	Placenta Accreta
7	Not Present	Not Applicable	Present	Placenta Accreta	Placenta Accreta

Table 4. Comparison of feto-maternal outcomes between patients with suspicion of PAS and prenatal ultrasound scanning and patients without suspicion of PAS on prenatal scanning

Variable	**Without PAS**	**With PAS**	**Significance test**	**p-value**
Blood loss in ml (Mean ±SD)	648±59ml	1537±582ml	t=2.7413	0.0098
Hysterectomy Yes No	 (0) 0.0% (24) 100.0%	 (4) 44.44% (5) 55.56%	Fisher Exact test	0.0031
Organ Injury Yes No	 (0) 0.0% (22) 100%	 (3) 42.86% (4) 57.14%	Fisher Exact test	0.0096
Ventilator support postoperatively Yes No	 (0) 0.0% (22) 100.0%	 (2) 33.33% (4) 66.67%	Fisher Exact test	0.005
1-minute Apgar score (Mean ±SD)	7.2±0.4	4.7±1.5	t=2.2252	0.0337
5-minute Apgar score (Mean ±SD)	9.0±0.3	6.6±1.9	t=2.3285	0.0271

Discussion

The incidence of PP varies in the literature from 0.3% to 1.9%. This wide range could be due to differences in risk profiles across different geographical locations. This study found a 0.3% incidence of PP, which falls within the range quoted in the literature. [1]

Advanced maternal age has been found to be associated with an increased risk of PP. [1] In this study, the prevalence of advanced maternal age was (32.7%). This is almost double the prevalence of advanced maternal age in the South African pregnant population (17.5%). [5] The pathophysiology of how advanced maternal age affects normal placental migration is not well understood. [6] A probable cause may be an increase in sclerotic changes in intramyometrial arteries, compromising adequate blood supply to the placenta.

The incidence of prior CS in patients with PP in our study was 27.2%. This relatively high prevalence has been noted in other studies. [7] Several studies from different global regions have shown a 2-fold increase in PP in women with prior CS. [8, 9] There is also a dose response pattern in the risk of PP with increasing numbers of previous CS as shown by Faiz et al. [10] This makes a case for increased efforts to reduce primary CS and to advocate for vaginal birth after previous CS, especially in women without contraindications to vaginal birth. Nearly a third (27.2%) of our patients had a prior miscarriage, this relatively higher incidence has been noted in other studies. [7]

PP was more commonly present among multiparous women (83.6%) a finding similar to that obtained by other authors [1]. The association of multigravida with PP may partially reflect a multigravida woman's likelihood of having had a previous miscarriage, or a previous CS, or increased age. The larger proportion of multiparous patients lessens the complexity of the decision to proceed to a hysterectomy in case of uncontrolled bleeding during surgery.

Globally, the incidence of obesity is rising steadily, and there is a high prevalence of obesity among women of childbearing age**.** [11] More than half (55%) of our patients

had BMI 30Kg/m^2 and above. This can have an impact on the outcomes of these patients as studies have shown an association between obesity and increased maternal Morbidity in PP. [12] This is because, CS in these women, poses surgical and anesthetic challenges.

In more than a third (35.29%) of our patients, PP was found as an incidental finding on ultrasound. We, therefore recommend that the placenta should be routinely assessed during a 20-week scan. This will enable early diagnosis of PP and any associated PAS, and hence adequate time to prepare for any complications and thus reducing morbidity and mortality. There must be a higher index of suspicion in patients with prior CS and previous miscarriage, especially.

Unfortunately, most authors who reported outcomes of PP did not clarify what proportion of deliveries were electively scheduled and therefore performed under controlled circumstances rather than by emergency CS. The problem with emergency delivery is that it may pose associated maternal and neonatal morbidities. This is because mobilization of resources may not be prompt enough to avoid these adverse outcomes. Fortunately, however, more of our patients (53.85%) had scheduled delivery rather than emergency delivery (46.15%). Further studies may be warranted to evaluate to what extent complications are increased with emergency delivery versus scheduled delivery

Significant maternal morbidity was noted in this study, including sepsis, more Intensive Care Unit admissions, hysterectomies, and massive hemorrhage. There was however no maternal death recorded. This could be attributed to the small sample size in this study. This can also be attributed to the MDT approach in the management of these patients, which is shown in the literature to have significant reduction in maternal morbidity and mortality. [13] The team at CHBAH includes a senior surgeon who is the most experienced in the department. Even though consultants perform all the cases, the senior surgeon is always available to assist when complications are encountered in theatre. When there are concerns of placenta adherence, the case is done by the senior surgeon to avoid wasting valuable surgical time if the patient complicates. This approach is used in both elective and emergency cases. Also, preoperative hemoglobin is optimized to at least 12g/dl for all our patients to improve

the perioperative outcomes, as blood loss can be catastrophic and rapid in these patients. Our patients are also counseled and consented for possible blood transfusion. Blood products are always available in theater during the operation with arrangements in place to get more blood products urgently if needed. It is therefore recommended that CS for PP and PAS should only be done in institutions with blood bank facilities

Four (12.12%) of patients had hysterectomies. According to Wu et al. PAS has become the number one reason for emergency postpartum hysterectomy due to the high risk of bleeding in these patients. [14] Because of this consent is always obtained for life-saving hysterectomies for all our patients before surgery. When PAS is suspected, consent is obtained for bladder repair and bowel resection with stoma as well.

The mean gestational age of delivery was 33.84 weeks. According to the CHBAH protocol patients with suspected PAS are electively delivered between 32-34 weeks and patients with PP with no suspicion of PAS are electively delivered at 36 weeks. Even though Infants born preterm are usually at risk for several complications, the mother is regarded as priority and hence the iatrogenic preterm delivery in most of our patients. This resulted in about a third (30.12%) of our babies requiring neonatal intensive care unit admission. We also recommend that patients with PP and PAS should be managed and delivered in institutions with NICU facilities. These patients should be counseled by the neonatologist about the risk of prematurity.

No neonatal deaths were reported in this study although most studies on neonatal outcomes in PP and PAS have demonstrated significant perinatal morbidity. [15] This observation should however be interpreted with caution as neonatal outcomes were only studied for the first 24 hours of life and any neonatal death recorded beyond this period will not be reported in this study. Kalimba et al in 2003 looked at the survival rate of preterm infants at Charlotte Maxeke Johannesburg Academic Hospital, a hospital that sees a similar population of patients as CHBAH. They concluded that majority (79%) of neonatal death in preterm infants happens by the end of the first week of life and therefore 24 hours only is too short a time to determine the actual incidence. [16] Besides, the sample size was small. Further studies with larger numbers and longer follow-up is needed to ascertain the true incidence and long term outcomes in these infants

Although the accuracy of diagnosis of PAS with MRI was low in our study, others have demonstrated very high accuracies. [17] A systemic review from 2015 that analyzed the overall performance of MRI for prenatal diagnosis of PAS had sensitivities ranging from 75-100%. [17] The MRI in the above studies is performed in institutions with remarkable experience in performing and interpreting these images. The poor accuracy of MRI to diagnose PAS in this study may be a reflection of the lack of expertise in interpreting the images and not the modality itself. However, technological advancement now allows for images to be sent to centers of excellence with the appropriate levels of expertise for second opinions

Ultrasound scanning, on the other hand, is widely accepted as the primary diagnostic tool for PP. Most importantly, the utility of ultrasound in diagnosing PAS and predicting outcomes has been demonstrated in this study. Half of the cases suspected to have PAS on ultrasound were eventually confirmed to have PAS. Only One case of PAS was not suspected on prenatal ultrasound. Ebrahim et al. discovered that ultrasound findings such as retroplacental hypervascularity, lack of clear zone, and presence of lacunae (all suggestive of PAS on ultrasound) were associated with increased severity of intrapartum hemorrhage. [18] Maternal hemorrhage, as an important factor in causing maternal and perinatal morbidity, could explain the more severe adverse outcomes in patients with prenatal suspicion of PAS on ultrasound.
Other authors have demonstrated that ultrasound can achieve similar number of true cases of severe PAS, just as MRI. [19] Dwyer et al. went further to show that the ability of MRI or ultrasound to diagnose PAS was not even affected by placental location as suggested by other authors. [20]

Conclusion

Patients with risk factors such as advanced maternal age, previous CS and previous miscarriages should have the placenta routinely accessed by ultrasound in the second trimester. PP and PAS increase the likelihood of maternal and neonatal morbidity. Management of these patients must involve an experienced MDT with blood bank, NICU and Intensive Care Unit facilities available. Ultrasound is a useful tool in evaluating placental implantation and can assist in anticipating severe fetomaternal outcomes in PP and PAS. MRI has a limited clinical value in this setting currently,

and is a scarce and expensive imaging modality, and should not be done routinely. Further research on diagnosis and outcomes in PP and PAS, with higher numbers, is warranted. The strengths of this study are, the protocol remained the same throughout the study period and the same person performed all the ultrasound scans. The limitations include the small number of patients, the retrospective nature of the study, and different doctors interpreting the MRIs

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Appendix A: Approved Research Protocol

Fetomaternal outcomes of patients with placenta previa and accuracy of diagnosis of placenta accreta syndrome at CHBAH

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MMed (Obstetrics and Gynecology)

Supervisors: Dr. Jayshree Jeebodh

Dr. Chrysanthi Georgio

List of abbreviations

AKI	Acute Kidney Injury
APGAR	Activity, Pulse, Grimace, Appearance, Respiration
APH	Ante Partum Hemorrhage
CHBAH	Chris Hani Baragwanath Hospital
CS	Cesarean Section
EBL	Estimated blood loss
Hb	Hemoglobin
HC	High Care
ICU	Intensive Care Unit
IUGR	Intra Uterine Growth Restriction
LBW	Low Birth Weight
MDT	Multidisciplinary Team
MRI	Magnetic Resonance Imaging
NICU	Neonatal Intensive Care Unit
PA	Placenta Accreta
PP	Placenta Previa
PT	Protrombin Time
PVB	Per Vaginal Bleeding
REDCap	Research Electronic Data Capture
SD	Standard Deviation
SGA	Small for Gestational Age
US	Ultrasound

1.0 Introduction and Background

Placenta previa (PP) is when the placenta implants in the lower uterine segment and covers the os partially or wholly. (1)It happens in about 0.3-0.5% of pregnancies (2) and it is an important factor in causing maternal morbidity, prematurity and perinatal mortality due to the possibility of maternal bleeding. (3)

1.1 Problem statement

Fetomaternal morbidity and mortality from PP are immense and puts a lot of burden on health care resources. (4) One in three of every antepartum hemorrhage is caused by PP. (5) The bleeding from PP is of sudden onset, painless, recurrent and causes increased maternal morbidity and mortality due to high possibility of hemorrhagic shock, increased risk of operations interventions and infections. (5) The rate of hysterectomy after cesarean section (CS) for PP is 5.3% (as compared to 0.04% of those without PP), according to a study by Rosengberg et al. in 2010. (4) Placenta previa is also associated with a higher incidence of perinatal morbidity and mortality as a result of prematurity and other associated complications like low birth weight, neonatal infections and birth asphyxia. (5) Most studies have demonstrated a link between PP and severe obstetric bleeding (6) and obstetric bleeding in sub-Saharan Africa is the number one cause of fetal and maternal mortality and morbidity. (7)
Unfortunately, the incidence of PP will continue to increase, giving the rising incidence of CS combined with increasing maternal age. (8)

1.2 Justification

Considering the significant morbidity associated with PP and placenta accreta (PA), the accurate diagnose of PP prenatally is very crucial as it allows both pregnant woman and obstetricians to adequately make room for potential complications. The literature has also shown conflicting reports with regards to fetomaternal outcomes and placenta previa.
Chris Hani Baragwanath Academic Hospital (CHBAH) introduced a new protocol for management of PP/PA from 2018. This protocol includes the use of a multidisciplinary team (MDT) in the management of PP/PA

This study therefore, aims to ascertain accuracies with prenatal diagnosis of PP/PA and its fetomaternal effects in women with PP/PA at CHBAH with the new protocol in place.

2.0 Literature review

2.1 Risk factors

The exact cause of PP is unknown but several risk factors have been reported in association with PP. (9) Important risk factors associated with PP include high maternal age, multiparty, previous cesarean section, previous history of PP, curettage and evacuation of retained products of conception, previous myomectomy, and uterine fibroids. (9-11) Cigarette smoking is also a potential risk factor. (10)

Darios et al. showed in their study that a short interpregnancy interval is linked with an increased risk of PP as well. (12) A study according to Bülent et al. reported that male fetuses increased poor gestational outcomes with PP. (11). Nielsen et al. concluded in their study in 1989 that the risk of PP was 0.25% in an unscarred uterus and 1.22% in patients who have had one or more CS previously. (13) Clark et al. in 1995 also calculated that the risk of PP increased from 0.26% with an unscarred uterus to 10% with at least 4 previous cesarean sections. (14)

Increases in primary cesarean rates, the number of previous cesarean sections, fertility treatments and rates of pregnancy in women more than 34 years have caused a rise in the prevalence and aggressiveness of PP and PA. (4)(11)

2.2 Placenta previa and placenta accrete

Placenta accreta is when there is an invasion of the chorionic villi into myometrial tissue. (15) It is sub classified into accreta, increta, and percreta depending on the depth of penetration into the myometrium.

Placenta accreta involves superficial uterine attachment, placenta increta penetrates the myometrium whiles placenta percreta penetrates through the myometrium and other pelvic organs, usually the bladder. (8)

The increasing rate of PA is being driven by increasing CS rate. This occurs in approximately 1 of 2500 deliveries. (16) The relative risk of PA with PP is 1:2065, which is significantly more than the risk for women without PP(16). The risk for PA

with PP increases drastically with the number of previous CS. The risk for PA is approximately 25% for one previous CS and 40% for two previous CS according at Silver et al. in 2006. (17) This risk further climbs to 67% with four or more CS according to Clark et al. in 1995 (14)

Meanwhile, patients presenting with PP without a previous CS have a 5% risk of developing PA, from Hsu et al. in 2004. (18) The maternal mortality rate associated with PA is 7% and its one of the leading causes of hysterectomy according to Silver et al. in 2006. (18) According to Wu et al, PA has become the number one reason for emergency post partum hysterectomy (19). Prenatal diagnosis may be beneficial with regards to reduction in morbidity and mortality in preparing for delivery. (9)(20) Operation involving PA is a considerable challenge, but study shows maternal morbidity is lowered in women who sought care in tertiary hospitals. (21)

2.3 Radiologic diagnosis of placenta previa and placenta accrete

Admittedly prenatal detection, especially in high-risk pregnant women can drastically improve the outcome by enabling preparation for a possible obstetric emergency. This can result in less maternal morbidity. (22)

Ultrasound (US) is still the primary modality in the assessment of placental implantation but unsurprisingly there has been increased interest in magnetic resonance imaging (MRI) in recent years. (23)(24) Even though MRI will probably never become a screening tool for PA, theoretically, it can help in confirming PA in those diagnosed by US. (25)

Some writers think that MRI is clearly indicated if placenta is posterior and also when US findings are ambiguous. Some schools of thought also say that MRI can better define areas of abnormal placentation, modify levels of invasion, and can ultimately change surgical management and therefore must be used routinely. (16)(26-27)

The problem however with MRI is its use could be limited by its high cost and availability only to major centers, although it has been found to diagnose PP accurately. (28). Ultrasound is relatively cheaper and more widely available and as a result remains the main diagnostic instrument for abnormal placentation. (29)

Prenatal diagnosis of PA is very crucial as well because it's a significant contributor of maternal morbidity and mortality. (30)Various criteria used in identification of placenta accreta on antenatal US examination have been reported as the following;

marked thinning /absence (31) of or obliteration (32) of the retroplacental hypoechoic space (32), thinning, irregularity or focal disruption of the hyperechoic uterine serosa-bladder was complex (32)or of the interface between the posterior bladder wall and the uterus(32), presence of a focal exophytic mass with the same echogenicity as placental lacunae(32), a myometrial thickness < 1mm, disruption of the placental-uterine wall interface(22) , placental lacuna flow(26), prominent subplacental venous complex(26), bladder-uterine serosa interface hypervascularity(26), vessels extending from placenta to bladder(28), vessels bridging from placenta to margin of uterus(27) And vessels crossing interface disruption site inherently (22), Mohammed et al. found that color Doppler US and MRI has the same sensitivities in the diagnosis of PA prenatally. (25)

2.4 Fetomaternal Outcomes

Literature work that explored fetomaternal outcomes in PP are conflicting, whiles Sheiner et al. (33) found a link with PP and preterm delivery, CS and abruptio placenta, they however, could not find any link with intrauterine growth restriction (IUGR). Rosenberg et al. on the other hand (4)found a link between PP and IUGR but not with placenta abruption (12). Yeniel et al. (34) studied only neonatal outcomes and could not find any link between both IUGR and intrauterine demise with PP (34). Nielson et al. found that, patients with previous CS and PP have a 16% risk of having a cesarean hysterectomy from severe bleeding as against 3.6% of patients with PP and with no history of a previous CS. (13) .

Placenta previa also leads to increased incidence of ante partum hemorrhage which leads to maternal shock and its consequences, increased incidence of operative interventions, increased incidence of PPH all posing increased risk of maternal morbidity and mortality (5). In a study on PA published in March 1995 by Makhseed et al, hysterectomy was the end result in 81% of cases, maternal complications affected 31% of cases. This included coagulopathy in 18.8%, bladder injury in 12.5%. Blood transfusion was needed in all the patients (35). According to Jung et al. there was no significant difference in the rates of SGA, stillbirth, neonatal death, perinatal mortality, Apgar scores of less than seven at five minutes and length of NICU stay between the placenta previa group and the control group in their study (36). However Gamal et al. in 2013 found neonatal morbidity in their study to be significant, more

than 28% of newborns were admitted to NICU. They also observed a low1 minute Apgar score, the five minute Apgar score however was improved and only 4.1% had a score less than 7 (37)

2.5 Multidisciplinary team care in placenta previa and placenta accrete

Considering the substantial morbidity associated with PP/PA, its paramount strategies are evaluated and implemented to improve outcomes. A very important strategy is the use of multidisciplinary teams with experience and expertise in management of PP/PA. (21)(38) Eller et al concluded in their study that maternal morbidity was reduced in pregnant women with placenta accreta who were attended to in tertiary hospitals with multidisciplinary teams experienced in the care of patients with PA (21). Despite these clear benefits of reduced maternal morbidity, however, there is no benefit demonstrated with MDT on neonatal outcomes. (39) The MDT approach is the main strategy adopted in the new CHBAH protocol in the management of PP/PA. (Refer Appendix B)

3.0 Study Aims and Objectives

3.1 Aim

This study aims to evaluate fetomaternal outcomes of PP and accuracy of diagnosis of PA among pregnant women at CHBAH from 1st January 2018 to 31st December 2018.

3.2 Objectives

1. To describe the demographic characteristics of patients who present with PP at CHBAH and to evaluate the clinical features and risk factors.
2. To describe the maternal and perinatal outcomes of PP at CHBAH.
3. To compare the prenatal MRI and US's findings with surgical assessment and determine the value of MRI in our setting.

4.0 Methods

4.1 Study setting

The study will be done at Chris Hani Baragwanath Academic Hospital (CHBAH), the largest tertiary hospital in South Africa, with the largest maternity unit in the country. It serves as a referral center for several community health centers from greater Soweto area and from more distant areas, including centers outside the Gauteng province.

4.2 Study design

This will be a retrospective, descriptive study using antenatal and maternal records, patients theatres note, ICU (Intensive Care Unit)/HC (High care) notes, radiology reports, and neonatal records. Histopathology reports of patients who had hysterectomy specimen sent off will also be followed up

4.3 Study population

The study population will include all cases of placenta previa diagnosed and delivered at the maternity unit at CHBAH, from 1 January 2018 to 31 December 2018.

4.4 Data collection

Subjects will be identified through fetal medicine records. The fetal medicine department will provide records of all women who were diagnosed with PP within the period of study. The maternal records of all these patients will be obtained from the records department. Once the records have been obtained, those cases that delivered within 1st January 2018 and 31st December 2018
will be selected as subjects for the study. Data will be abstracted from these patients file using a data collection tool.
Information on maternal demographics, clinical features at presentation, gestational age at presentation, past obstetric history and other risk factors will be abstracted from antenatal health records and records from the fetal medicine department. The following risk factors will be studied: age, previous uterine operation, number of previous CS, previous uterine evacuation or curettage, multiparty, smoking, uterine fibroids and prior history of placenta previa.

Clinical presentation will be grouped as antepartum hemorrhage (APH), Non APH or incidental finding on US and per vaginal bleeding (PVB). APH will be defined as bleeding from the genital tract, from 28 weeks of pregnancy and prior to delivery of the fetus. Any bleeding from the genital tract before 28+0 weeks and prior to the birth of the fetus will be coded as PVB. Data will be collected on the hemoglobin level at diagnosis also.

PP will also be noted, as being major, minor or low lying as per US findings. PP will be defined as implantation of the placenta over or near the internal opening of the cervix after 28+0 weeks of gestation. Major PP will be defined as placenta covering completely the internal os. Minor PP will be defined as placental edge extending to the margin of the internal os, but does not cover it. A low-lying placenta will be a placenta edge within 2cm from the internal os. (33) The location of the placenta will be noted as anterior or posterior. Measurement of placental overlap in major PP will also be studied as well as the presence or absence of US features of morbid adherence. Data will also be collected on subsequent US for those who had more than one US done

Whether or not delivery planning meeting and MDT meeting was held will be studied as well

Information on maternal outcomes will be retrieved from theatre notes of patients, maternity files, ICU/HC notes. The following information will be abstracted: duration of hospital stay from time of diagnosis/presentation until delivery and from time of delivery until discharge, need for blood transfusion pre-operatively, intraoperative and post-operatively, need for ICU/HC admissions, need for extra surgical procedures during CS to prevent or stop bleeding like uterine artery ligation, B Lynch suture, balloon tamponade, and abdominal hysterectomy (total versus subtotal) will be studied.

Uterine artery ligation will be defined as ligation of both uterine arteries during the operation to stop or prevent bleeding.

Need for postoperative ventilation and a need for a relook laparotomy will also be studied. Prolong hospital stay will be defined as 7 or more days stay in hospital postoperative

The following maternal outcomes will be studied as well: postpartum hemorrhage (PPH), hypovolemic shock, coagulopathy, anemia, acute kidney injury (AKI), septicemia and maternal death.

PPH will be defined as estimated blood loss (as stated by the attending physician) of more than 500mL or 1000mls during delivery vaginal delivery and CS respectively. (7)

Hypovolemic shock will be defined as systolic blood pressure of less than 90mmHg in a bleeding patient.

Evidence of coagulopathy in this study will include prolongation of protrombin time (PT) or thrombocytopenia.

Anemia in this study will be defined as hemoglobin level < 10.5g/dl. (40)

Septicemia will be defined as positive blood culture or a persistent tachycardia of more than 100bpm, without any known cause and was managed solely by antibiotic

AKI will be defined as raise in serum creatinine of 5.3mmol/L if the baseline is ≥ 10.8mmol/l or a 50% increase if the baseline is ≤ 10.8mmol/L (41)

The following information will also be abstracted: gestational age at delivery, indication for delivery, estimated blood loss, location of placenta, ureteral injuries, bladder injuries, and bowel injuries, duration of operation (time from skin incision to skin closure). Bladder, bowel, and ureteral injuries will be coded if the attending physicians document them as occurred. Details with regards to the specifics of these injuries will not be ascertained. The rank of the surgeon will also be considered.

Information on fetal/neonatal outcomes will be abstracted from theatres notes, maternal health records, and neonatal records. Neonatal outcome variables will include birth weight, gestational age, stillbirth, neonatal death, small for gestational age (SGA)/ low birth weight (LBW) and neonatal morbidities such as low APGAR score of less than seven at five minutes and need for NICU admission within the first 24 hours. Whereas maternal records throughout the period of hospitalization will be analyzed only the first 24 hours will be considered with regards to the neonates. Stillborn will be defined as all cases of antepartum fetal demise and all cases of intrapartum fetal demise. SGA will be birth weight less than the 10th percentile for the gestational age. (42) LBW will be defined as birth weight of less than 2500g (up to and including 2499g) as per the World Health Organization (WHO). (42)

Surgical findings of the presence or absence of morbid adherence of placenta will be studied. The placenta will be noted as morbidly adherent if the surgeon states so and vice versa. These findings will be compared to MRI findings as reported by the

consultant radiologist and the value of MRI will be determined in our setting. Results of hysterectomy specimen sent for histology will be studied. The type of incision used will also be studied. The data will be captured on Research Electronic Data Capture (REPCAP®)

4.5 Data Analysis

The information extracted and recorded in the data sheet will be entered into Redcap® data management system. The data will then be exported into statistical software for analysis.

Data on continuous variables, which is normally distributed, will be presented as mean with standard deviations and medians

Categorical variables and ordinal variables will be presented, as frequencies and percentages and difference will be assessed by Chi-square test.

4.6 Tools

A data sheet will be used to collate the data (Appendix A)

4.7 Limitations

Because subjects will be identified through the fetal medicine department, patients who present with placenta previa and didn't pass through the fetal medicine department will not be included in this study.

5.0 Ethics

Ethics approval will be obtained from the Human Research Ethics Committee (HREC) of the University of the Witwatersrand. All patients participating will be given a study identification number to ensure anonymity of data. As this is a retrospective study of records, no informed consent will be obtained.

Confidentiality of the information obtained will be ensured and data will be sorted in the Redcap data management system. Data entered into personal computer will only be accessible to the investigator and supervisors and the computer will be password secured.

6.0 Permission from Institution

Approval to conduct the study will also be sought from the Chief Executive Officer at CHBAH. Permission will also be sought from heads of department of Pediatrics, Radiology, ICU, and Pathology.

7.0 Timelines

2018	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Protocol development								X	X	X	X	X
2019	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Submission	X											
Correction		X										
Ethics			X									
Data Collection				X	X	X	X	X				
Analysis									X	X		
Write up											X	
Marking												X
2020	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Corrections	X											

8.0 Funding and budget

All funding cost will be borne by the researcher. No other source of funding is available yet

Item	**Amount**
Printing	R 1000
Travelling cost	R 500
Re-imbursement of biostatistician	R 3000
Publication fee	R 8000
Conference cost	R 10000
Total cost	**R 22500**

9.0 Intension to disseminate

A copy of the final write up will be disseminated to the University of the Witwatersrand and the College of Obstetrics and Gynecology of South Africa. The study will be registered with the National Health Research Database. There is the intention to also publish the research in medical journals and to present at academic meetings.

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Appendix B: Data collecting sheet

Study number_____

Date of data collection_____

Baseline information

Age_____Gravidity_____

Parity_____Height_____Weight_____BMI_____

Risk factors

☐ Uterine fibroids

☐ Previous CSX1

☐ Previous CSX2

☐ Previous CSX3 or more

☐ Previous uterine surgery

☐ Previous uterine curettage/evacuation

☐ Previous history of placenta previa

☐ Smoking

Clinical presentation

Date of admission_____

Gestational age at presentation_____

Clinical presentation

☐ APH ☐ PVB ☐ Incidental findings on US

APH after admission

☐ Yes ☐ No

Total number of bleeding episodes? _____

Hemoglobin level at diagnosis_____

Received transfusion during the antenatal period

☐ Yes ☐ No

Maternal outcomes

Delivery planning meeting held?

☐Yes ☐ No

If yes at what GA_____

MDT meeting held?

☐Yes ☐ No

If yes at what GA_____

Gestational age at delivery_____

Date of delivery_____

Indication for delivery

☐Elective delivery ☐vaginal bleeding ☐PROM☐ Labour☐ Fetal distress ☐ other

_____

Mode of delivery if minor PP or low-lying placenta

☐Emergency CS ☐NVD ☐Assisted vaginal delivery ☐Elective CS

If CS, what was the level of experience of surgeon

☐Consultant ☐Registrar ☐Senior surgeon

If vaginal delivery, who conducted delivery

☐Midwife ☐Intern ☐Registrar ☐Consultant

EBL in vaginal delivery _____

Maternal morbidity

Maternal morbidity	Yes	No
ICU/HC admission		
AKI		
Blood transfusions		
Coagulopathy		
Septicemia		
Relook Laparotomy		
Postoperative ventilation		
Hypovolemic shock		
Visceral injury at operation		
Prolong hospital stay		

Maternal death

☐ Yes ☐ No

If yes, cause of maternal death_____

For patients who had relook, state number_____ of relooks and indications

Relook	Indication	Date
1		

2		
3		
4		
5		

Fetal/neonatal outcomes

Gestational age at delivery_____

Birth weight_____

APGARS

At 1 minute_____ At 5 minute_____

Perinatal morbidity

Morbidity	Yes	No
NICU admissions		
Still Birth		
SGA		

Neonatal death within first 24 hours

☐ Yes ☐ No

US findings

US FINDINGS	1st US	2nd US	3rd US	4th US
Date				
GA				
PP (Y/N)				
Type of PP				
Location of placenta				
Suspicion of PAS (Y/N)				
If PAS suspected, organ involved?				

MRI findings

MRI FINDINGS	Registrar's report	Consultant's report
Date		
GA		
PAS		
If PAS, organ involved?		

Surgical findings

Date of CS_____

Duration of operation_____

Type of surgical incision used

☐Transverse ☐Midline ☐Others, specify_____

Type of previa found

☐Major ☐Minor ☐Low lying

Placenta Accreta

☐Yes ☐No

If percreta, which pelvic organ is involved_____

Visceral injury?

☐Bowel ☐Bladder ☐Ureteral ☐Nil ☐ other, specify_____

Estimated blood loss_____

PPH

☐Yes ☐NO

If yes how was PPH managed

☐Medical management ☐Conservative surgical management ☐emergency Hysterectomy

If hysterectomy preformed, type of hysterectomy performed?

☐Total hysterectomy ☐Sub total hysterectomy

If conservative surgical management, state

☐B lynch suture ☐uterine artery ligation☐Balloon tamponade ☐uterine artery embolization ☐Other, specify_____

Histopathology

Was hysterectomy specimen sent off for histopathology?

☐Yes ☐No

If yes, was PA confirmed

☐Yes ☐No

If yes what type of PA

☐Placenta accreta ☐Placenta increta ☐Placenta percreta

Appendix C: CHBAH protocol in management of placenta praevia/accreta

The MDT at CHBAH comprises the following members; fetal medicine consultant, a senior surgeon, urologist, senior anesthetist, colorectal surgeon and a senior obstetrician.

All cases of confirmed PP form 28 weeks are admitted to hospital. Baseline blood investigations are done and Hemoglobin (Hb) optimized if need be. MRI is requested if there are concerns about morbid adherence. A Delivery planning meeting is individualized for each patient but usually at 32-35 weeks. Fetal medicine consultant, senior surgeon and a senior obstetrician are present at the delivery meeting.

The following decisions are made at the delivery meeting; blood requirement, need for ICU bed post-operative, need for involvement of other disciplines (e.g. urologist, colorectal surgeon, a senior surgeon), type of surgical incision, and the need to present at MDT meeting. Any anticipated difficulty based on the patient's history is discussed and a date is set for elective surgery with the primary surgeon and assistant confirmed. Delivery is at 36 weeks if there are no concerns with morbid adherence. Delivery is however earlier when there are concerns of morbid adherence. It is done between 32-34 weeks. If emergency delivery is required, obstetrician consultant on call usually does the case. A senior surgeon may however be called if needed.

Appendix D: Ethical clearance Certificate

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Dr Michael Nii Armah Hammond

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M190568

NAME: (Principal Investigator)	Dr Michael Nii Armah Hammond
DEPARTMENT:	Obstetrics and Gynaecology Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Fetomaternal outcomes of placenta previa and accuracy of diagnosis of placenta accreta syndrome at Chris Hani Baragwanath Academic Hospital
DATE CONSIDERED:	31/05/2019
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	05/06/2019

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 on the 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 in **May** and will therefore be due in the month of **May** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

Date 16/05/2019

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix E: l Author Guidelines for SAJOG

Guideline word limit: 3 000 words (excluding abstract and bibliography) Research articles describe the background, methods, results and conclusions of an original research study. 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 clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important 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. Where appropriate, sample size calculations should be included to demonstrate that the study is not underpowered. 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. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

- May include up to 6 illustrations or tables
- A max of 20-25 references

Structured abstract

- This should be no more than the 250words, with the following recommended headings
    - Background: why the study is being done and how it relates to other published work
    - Objective: what the study intends to find out
    - Methods: must include study design, number of participants, description of the research tools/instruments, any specific analyses that were done on the data
    - Results: first sentence must be brief population and sample description; outline the results according to 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 data, includes recommendations for future study/actions

- Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors. It should be able to be intelligible to the reader without referral to the main body of the article
- Do not include any reference in the abstracts

Illustrations/photos/scans

• If illustrations submitted have been published elsewhere, the author(s) should provide evidence of consent to republication obtained from the 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 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.

• 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.

• 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.) consecutively as they are referred to in the text.

• Tables must be cell-based (i.e. not constructed with text boxes or tabs) and editable.

• 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.

Do not: Use [Enter] within a row to make ‘new rows’: Rather: Each row of data must have its own proper row: Do not: use separate columns for n and %: Rather: Combine into one column, n (%): Do not: have overlapping categories, e.g.: Rather:

Use <> symbols or numbers that don’t overlap:

References

NB: Only complete, correctly formatted reference lists in Vancouver style will be accepted. If reference manager software is used, the reference list and citations in text are to be unformatted to plain text before submitting..

• 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 the World 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:

o On the Crossref homepage, paste the article title into the ‘Metadata search’ box.

o Look for the correct, matching article in the list of results.

o Click Actions > Cite

o Alongside 'url =' copy the URL between { }.

o Provide as follows, e.g.: https://doi.org/10.7196/07294.937.98x

Some examples:

• Journal references: Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. Stat Med 1998;289(1):350-355. http://dx.doi.org/10.1000/hgjr.182

• Book references: Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101.

• Chapter/section in a book: Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.

• Internet references: World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: WHO, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).

• Legal references

• Government Gazettes:

National Department of Health, South Africa. National Policy for Health Act, 1990 (Act No. 116 of 1990). Free primary health care services. Government Gazette No. 17507:1514. 1996.

In this example, 17507 is the Gazette Number. This is followed by :1514 - this is the notice number in this Gazette.

• Provincial Gazettes:

Gauteng Province, South Africa; Department of Agriculture, Conservation, Environment and Land Affairs. Publication of the Gauteng health care waste management draft regulations. Gauteng Provincial Gazette No. 373:3003, 2003.

• Acts:

South Africa. National Health Act No. 61 of 2003.

• Regulations to an Act:

South Africa. National Health Act of 2003. Regulations: Rendering of clinical forensic medicine services. Government Gazette No. 35099, 2012. (Published under Government Notice R176).

• Bills:

South Africa. Traditional Health Practitioners Bill, No. B66B-2003, 2006.

• Green/white papers:

South Africa. Department of Health Green Paper: National Health Insurance in South Africa. 2011.

• Case law:

Rex v Jopp and Another 1949 (4) SA 11 (N)

Rex v Jopp and Another: Name of the parties concerned

1949: Date of decision (or when the case was heard)

(4): Volume number

SA: SA Law Reports

11: Page or section number

(N): In this case Natal - where the case was heard. Similarly, (C) woud indicate Cape, (G) Gauteng, and so on.

NOTE: no . after the v

• Other references (e.g. reports) should follow the same format: Author(s). Title. Publisher place: Publisher name, year; pages.

• Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'.

• Unpublished observations and personal communications in the text must not appear in the reference list. The full name of the source person must be provided for personal communications e.g. '...(Prof. Michael Jones, personal communication)'.

Appendix F: Turnitin plagiarism report

Appendix G: Plagiarism declaration

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

FACULTY OF HEALTH SCIENCES

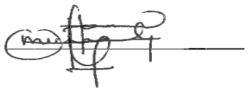
PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I MICHAEL NII ARMAH HAMMOND (Student number: 2069726) am a student registered for the degree of Mmed in the academic year 2021.

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:  Date: 2/02/21

Appendix H: Permission to conduct research from hospital

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE

CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 12th April 2019

TITLE OF PROJECT: Fetomaternal outcomes of patients with placenta previa and accuracy of diagnosis of placenta accreta syndrome at CHBAH.

UNIVERSITY: Witswatersrand

Principal Investigator: Dr MNA Hammond

Department: Obstetrics and Gynaecology

Supervisor : Dr J Jeebodh

Permission Head Department (where research conducted): Yes

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Academic Hospital. The CEO / management of Chris Hani Baragwanath Academic Hospital is accordingly informed and the study is subject to:-

- **Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.**
- The Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- The MAC will be informed of any serious adverse events as soon as they occur
- Permission is granted for the duration of the Ethics Committee Approval.

Recommended
(On behalf of the MAC)
Date: 12/4/2019

Approved/~~Not Approved~~
Hospital Management
Date: 15/04/2019

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

PERMISSION TO CONDUCT RESEARCH AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PRINCIPAL RESEACHER:

FULL NAME: MICHAEL NII ARMAH HAMMOND

DESIGNATION: REGISTRAR

CONTACT NUMBER: 0718462334

EMAIL: NIIAMAHAMMOND@GMAIL.COM

NAME OF SUPERVISOR: DR. JAYSHREE JEEBODH

TITLE OF RESEARC: FETOMATERNAL OUTCOMES OF PATIENTS WITH PLACENTA PREVIA AND ACCURACY OF DIAGNOSIS OF PLACENTA ACCRETA SYNDROME AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

STUDY SITE/S: CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

BRIEF OUTLINE OF METHODOLOGY

THE SUBJECTS FOR THIS STUDY WILL BE OBTAINED FROM THE RECORDS OF FETAL MEDICINE DEPARTMENT. IF INFORMATION WILL THEN BE ABSTRACTED FROM THEIR FILES INCLUDING SURGICAL NOTES, ETC. ONTO A DATA COLLETION TOOL.

PROTOCOL: YES

DATA SHEET: YES

EXPECTED START DATE: 1ST APRIL, 2019 EXPECTED DURATION: FIVE MONTHS

ETHICS CLEARANCE? Y / X / PENDING

CONFLICT OF INTEREST? Y / X DETAILS

COST TO HOSPITAL AND OR PATIENTS? Y / X

SOURCE OF FUNDING: SELF

APPROVAL OF HOD (Y/N)

SIGNATURE	NAME IN PRINT+ DESIGNATION	OFFICAL STAMP+ DATE
	Y Adam	20/03/2019