THE PERIOPERATIVE MANAGEMENT OF CAESAREAN SECTION-RELATED HAEMORRHAGE IN A MATERNAL NEAR-MISS POPULATION: A RETROSPECTIVE STUDY

Rebecca Atebat Iputo

A research report submitted to the Faculty of Health Sciences,

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Johannesburg,

Declaration

I, Rebecca Atebat Iputo, herewith declare that this research report is my own, unaided work. It is being submitted for the degree of Master of Medicine at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

Signed

On this 7th day of 2021 .

Dedication

I dedicate this to both my extended and immediate family. To Teboho and Pula, you have both sacrificed so much to see me through this project, my love and gratitude to you is endless.

Abstract

Background: Maternal near-miss (MNM) is a risk stratification classification for maternal morbidity. The purpose of this study was to describe perioperative care used in the management of this population of women who have undergone caesarean section (CS).

Methods: This was a retrospective, descriptive study at a single tertiary institute over a 1-year period in Johannesburg. Patients enrolled into the study were women who were classified as MNMs who had undergone a CS and had blood loss ≥ 1000 ml during or after delivery.

Results: The primary outcome was the MNM rate for CS deliveries. The median age was 28, with a median parity of 2 (44%), and overall estimated blood loss volume of 1800 ml. The leading cause of haemorrhage was postpartum haemorrhage (87%). Eighteen (17%) of the subjects had a relook surgery for postpartum CS sepsis. Perioperative risk factors for haemorrhage were: parity of 3 ($p = 0.0185$), first (index) CS, antepartum haemorrhage, and multiple interventions to arrest haemorrhage ($p < 0.001$ for all). Management factors associated with blood loss ($p < 0.001$) included a massive transfusion, tranexamic acid use, and a B-Lynch surgical intervention. Management included uterotonic drugs, transfusion blood products, and surgical intervention.

Conclusions: Postpartum haemorrhage was the leading cause of haemorrhage and was aggravated by the presence of antepartum haemorrhage. These patients often require multiple interventions. Future studies should develop a severity scoring index to better identify women at risk, on hospital admission.

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To my supervisors for their dedication, and constant support.

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List of abbreviations

APH:	Antepartum haemorrhage
ASA:	American Society of Anaesthesiologists
CHBAH:	Chris Hani Baragwanath Academic Hospital
CRYO:	Cryoprecipitate
CS:	caesarean section
FFP:	fresh frozen plasma
GA:	general anaesthesia
HREC:	Human Resource Ethics Commission
ICU:	intensive care unit
IQR:	interquartile range
IV:	Intravenous
MNM:	maternal near miss
MTF:	massive transfusion
NMC:	near miss criteria
PLT:	Platelets
PPH:	postpartum haemorrhage
PRBC:	packed red blood cells
SA:	spinal anaesthesia
TXA:	tranexamic acid.
WHO:	World Health Organisation

Submissible article

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Rebecca Iputo[1*], Salome Maswime[2], Palesa Motshabi[1]

1. Department of Anaesthesiology, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand
2. Division of Global Surgery, Department of Surgery, Faculty of Health Sciences, University of Cape Town

***Corresponding author**
Charlotte Maxeke Johannesburg Academic Hospital, Department of Anaesthesiology
7 York Road, Parktown, 2193
0722508526
rebeccaiputo@gmail.com
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Abstract

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Results: The primary outcome was the MNM rate for CS deliveries. The median age was 28, with a median parity of 2 (44%), and overall estimated blood loss volume of 1800 ml. The leading cause of haemorrhage was postpartum haemorrhage (87%). Eighteen (17%) of the subjects had a relook surgery for postpartum CS sepsis. Perioperative risk factors for haemorrhage were: parity of 3 ($p = 0.0185$), first (index) CS, antepartum haemorrhage, and multiple interventions to arrest haemorrhage ($p < 0.001$ for all). Management factors associated with blood loss ($p < 0.001$) included a massive transfusion, tranexamic acid use, and a B-Lynch surgical intervention. Management included uterotonic drugs, transfusion blood products, and surgical intervention.

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Background

According to the World Health Organization (WHO), any health condition attributed to or aggravated by pregnancy and childbirth with negative effects on maternal wellbeing is considered as maternal morbidity. Severe acute maternal morbidity is also referred to as a maternal near-miss (MNM) and has been defined by the WHO as any woman who nearly dies from a complication from pregnancy or within 42 days of delivery or termination of pregnancy.[1]

The MNM classification was first described by Mantel et al [2], who subdivided these criteria into an organ-based system classification (end organ dysfunction) and a management-based system classification (emergency hysterectomy and massive blood transfusion). In their pilot study, women who were severely ill had a 5 fold higher mortality risk. Emergency hysterectomy was the leading cause of MNM, followed by massive transfusion (MTF), which was defined as the need for transfusion of at least five units packed red blood cells (PRBCs) for haemorrhagic shock.[2]. The WHO has since developed a classification with three categories: disease-specific criteria, intervention-based criteria, and Organ System dysfunction.

Caesarean section (CS) delivery has been shown to reduce maternal and neonatal adverse outcomes, but the increased rate of CS delivery in high-income countries has not translated into improvements for maternal outcomes.[3] In South Africa, one-third of obstetric haemorrhage (OH) is linked to CS delivery.[4] OH can be divided into different components such as ante-, intra-, and postpartum haemorrhage and is a growing concern for both obstetricians and anaesthetists. Antepartum haemorrhage (APH) is often an indication for a CS, contributes to significant haemorrhage, and requires management by a multidisciplinary team.

Postpartum haemorrhage (PPH) after a CS accounts for 9.3% and 45.7% of maternal deaths in high- and low-income countries, respectively.[4, 5] Maternal morbidity from OH is therefore a cause for concern, and there is a higher likelihood that more OH occurs intraoperatively during a CS. This puts emphasis on the anaesthetist's role in OH management, which includes medical management through the intraoperative administration of uterotonic drugs,

as well as administration of blood and intravenous fluids during the intraoperative and postoperative resuscitation periods.[6]

In the African Surgical Outcomes Study, African women were 50 times more likely to die from CS-related complications than women in high-income countries.[7] Early recognition of OH by obstetricians and timely medical management by anaesthetists are thus critical to improving outcomes.[4] This study will serve as a quality improvement tool for the management of CS-related obstetric haemorrhage as it will address two knowledge gaps: the quantitative burden of these cases and their clinical management. By identifying deficiencies in management, new strategies in training and skills can be developed and implemented in the future. [8]. This aim of this study was to describe the perioperative management of CS-related haemorrhage in an MNM population.

Methods

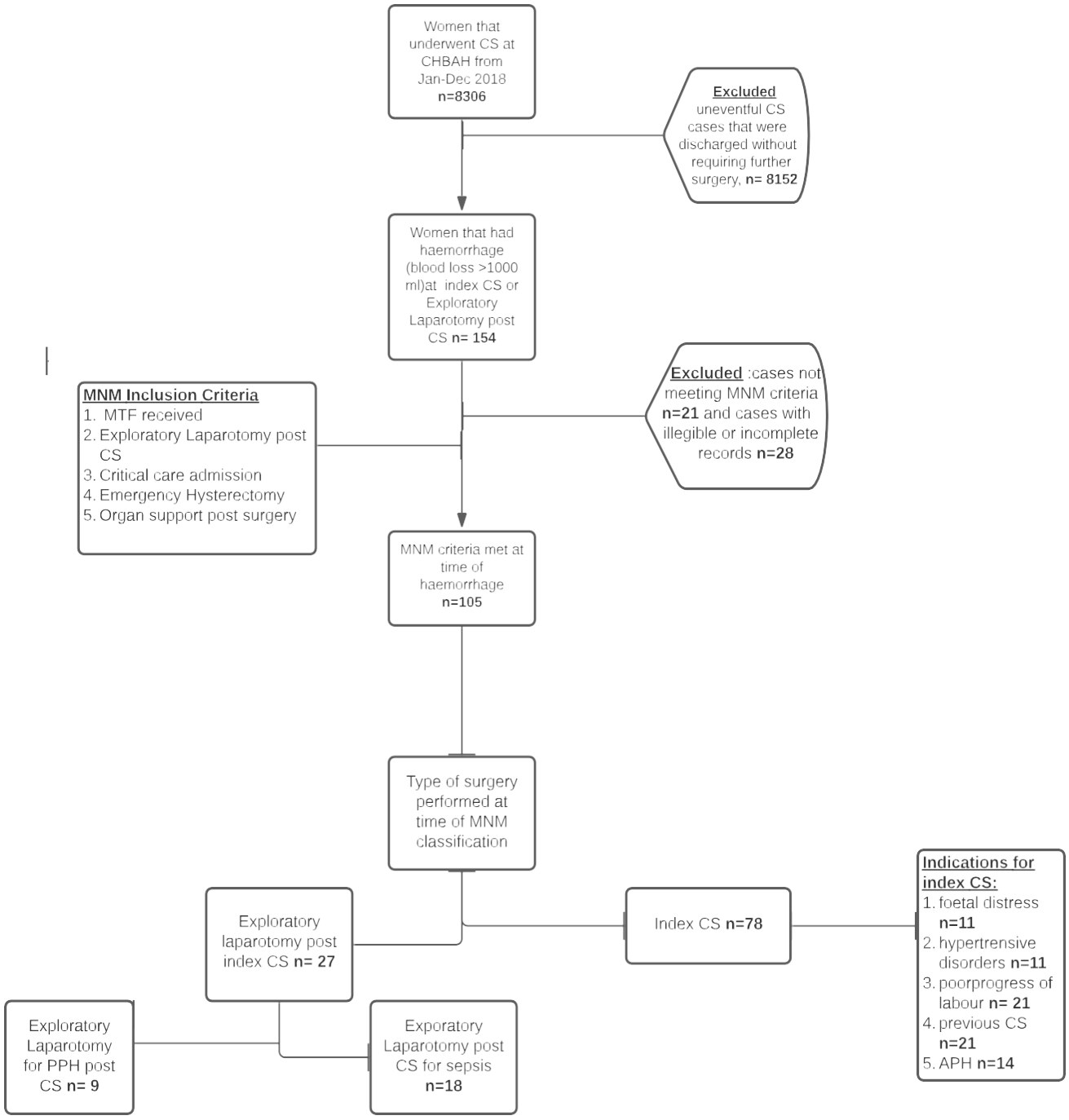
Study design

This was a single centre observational study at the Chris Hani Baragwanath Hospital (CHBAH) maternity theatre complex. CHBAH is a tertiary state hospital attached to the University of the Witwatersrand. It is situated in the township of Soweto and serves a majority African population with a lower to middle income social economical background. It houses approximately 3700 beds, 300 of which are obstetric, with an average of 4500 CSs performed per annum [9]. The study followed a retrospective, contextual, and descriptive research design. It describes the perioperative management of CS-related haemorrhage in a MNM population from 01 January 2018 to 31 December 2018. Approval to conduct the study was granted by the University of Witwatersrand Human Research Ethics Committee (Certificate number M190516).

Sample Population

Data were extracted from the medical records of women who underwent a CS during 2018 and met the criteria for MNM and intra- or postoperative haemorrhage with an estimated

blood loss (EBL) > 1000 ml. The institutional MNM criteria modified from the WHO criteria were used..



Statistical Analysis

Quantitative techniques were employed, and the results were analysed using SAS© version 9.4 (SAS Inc. Cary, NC, USA). Data were observed to be skewed, so nonparametric statistical testing

was used. Descriptive statistics were used to analyse numerical data, and categorical data are reported as frequencies and percentages. Variables that were not normally distributed were analysed using medians and interquartile ranges (IQRs). Statistical significance was set at $P < 0.05$.

Results

A total of 8306 CS were performed at CHBAH in 2018, of which 105 were classified as MNM due to OH after CS (1.26% of all CS done).

The characteristics of the study population (Table I) were a median age of 28 years (IQR 24-40 years), only 20 women had a parity of 1. Most of the women (45%) had an American Society of Anesthesiologists (ASA) classification of 2.We were able to delineate 2 subpopulation groups based on the timing of haemorrhage and MNM classification; women who were identified as MNM at the time CS delivery and women who were identified as MNM at the time of an exploratory laparotomy post CS (EL post CS) The median EBL was 1800 ml (IQR 1200-2100 ml) for all cases combined. The median EBL for women identified as MNM at CS was 2000 ml (IQR 1500-2200) and the median EBL for women identified as MNM at EL post CS was 1200 (IQR 1100-1300).

Table I: Study population characteristics

Variable n = 105		n(%)/Median(IQR)/Median(SD)
Age in years		28 (24-32)
ASA Classification	**1**	40 (38.10)
	2	48 (45.71)
	3	17 (16.19)
Parity		
1		20 (19.15)
2		47 (44.76)
3		24 (22.86)
4		13 (12.38)
Classification as MNN at CS		78 (75.24)
Classification as MNM at EL post CS		27 (24.76)
EBL overall		1800 (1200-2100)
EBL at CS		2000 (1500-2200)
EBL at EL post CS		1200 (1100-1300)
MNM Criteria	**Ventilated**	4 (3.81)
	MTF	20 (19.05)
	Relook	18 (17.14)
	Combination	33 (31.43)
	Other	30 (28.57)

Most (87%) subjects had PPH recorded as the main cause of haemorrhage, and the perioperative factors relating to haemorrhage (Table II) included factors associated with the highest overall EBL, parity of 3 ($p = 0.0185$), first (index) CS ($p < 0.001$), APH as an indication for CS ($p < 0.001$), and a combination of MNM criteria met ($p < 0.001$)

Table II: Perioperative factors and estimated blood loss

Variable		n (%)	Estimated blood loss in ml Mean(SD)/Median(IQR)/n(%)	p value
Age in years	**≤ 27**	50	1500 (1200-2000)	0.0045
	> 27	55	1800 (1300-2250)	
Parity	**1**	20 (19.05)	1450 (1200-1950)	0.0185
	2	47 (44.76)	1600 (1200-200)	
	3	24 (22.86)	2125 (1500-2450)	
	4	13 (12.38)	1800 (1400-2000)	
ASA status	1	40 (38.10)	1550 (1200-2025)	0.8043
	2	48 (45.71)	1800 (1225-2100)	
	3	17 (16.19)	1800 (1300-2250)	
Main cause of haemorrhage	Antepartum	2 (1.9)	1400 (1000 -1800)	0.0002
	Intrapartum	5 (4.76)	1200 (1100 -1300)	
	Postpartum	86 (81.90)	2000 (1500 -2150)	
	Combination	12 (11.43)	2400 (2100 -2500)	
Primary indication of surgery	APH	14 (13.33)	2250 (2000-2500)	< 0.001
	Hypertensive disorder	11 (10.48))	1800 (1200-2000)	
	Foetal distress	11 (10.48)	1300 (1050-2050)	
	Poor progress of labour	21 (20)	2000 (1600-2250)	
	Previous CS	21 (20)	2000 (1600-2100)	
	PPH post CS	9 (8.57)	1250 (1200-1400)	
	Relook -sepsis post CS	18 (17.14)	1175 (1080-1300)	
Timing of surgery	Day	32 (30.48)	1550 (1150-2200))	0.5529
	Night	73 (69.52)	1800 (1250-2050)	
Type of surgery	CS	78 (74.26)	1900 (1400-2200)	< 0.0001
	EL post CS	27 (25.71)	1175 (1100 -1300)	
MNM Criteria	Ventilated	4 (3.81)	1100 (1000-1250)	< 0.001
	Massive transfusion	20 (19.05)	2000 (1400-2275)	
	Relook	18 (17.4)	1175 (1100-1300)	
	Combination	33 (31.43)	2100 (2000-2500)	
	Other	30 (28.57)	1550 (1200-1800)	

Women who bled > 2000 ml had a median age of 30 (Table III), parity of 3, and were undergoing their index CS at the time of MNM classification. The same group of women also had a significantly higher number of multiple interventions such as general anaesthesia (GA), MTF, tranexamic acid (TXA), surgical interventions (particularly balloon tamponade) and intensive care unit (ICU) admission. Women who bled < 2000 ml had a lower parity of 2, MNM classification listed as "other", received less blood products and TXA, and had unclear documentation of which surgical interventions were performed. More of them were admitted in high care postoperatively. The main cause of haemorrhage was PPH in both EBL groups.

Table III: Management strategy by blood loss category

Variable (n)		Blood loss category		p value
		1000–2000 ml n = 77	>2000 ml n = 28	
Age years, median (IQR)		27 (23-31)	30 (27-33)	0.0129
Parity	1	17 (22.08)	3 (10.71)	< 0.001
	2	38 (40.35)	9 (32.14)	
	3	11 (14.29)	13 (46.37)	
	4	10 (12.99)	3 (10.71)	
ASA classification	1	30 (38.96)	10 (35.71)	0.0414
	2	35 (45.45)	13 (46.43)	
	3	12 (15.58)	5 (17.86)	
Indication for surgery	CS -Hypertensive disorder	10 (12.99)	1 (3.57)	< 0.0001
	CS - Foetal distress	8 (10.39)	3 (10.71)	
	CS-Poor progress of labour	13 (16.88)	8 (28.57)	
	APH	4 (5.19)	10 (35.71)	
	EL for PPH	9 (11.69)	-	
	EL for sepsis	18 (23.38)	-	
	CS-Previous CS	15 (19.48)	6 (21.43)	
MNM Criteria	Ventilated	4 (5.19)	-	< 0.001
	Massive transfusion	13 (16.88)	7 (25)	
	Relook	18 (23.38)	-	
	Combination	14 (18.8)	19 (67.86)	
	Other	28 (36.36)	2 (7.14)	
Main cause of Haemorrhage	Antepartum	2 (2.60)	-	< 0.0001
	Postpartum	67 (87.01)	19 (67.86)	
	Intrapartum	5 (6.49)	-	
	Combination	3 (3.90)	9 (32.14)	
***Anaesthetic technique**	Spinal	22 (28.57)	1(4)	0.0003
	General anaesthesia	37 (48.05)	11 (44)	
	Conversion	18 (23.38)	13 (52)	
Uterotonic agents	Oxytocin	42 (56)	11 (39.29)	0.0573
	Oxytocin/Ergometrine	33 (44)	17 (60.71)	
Tranexamic acid use	Yes	43 (55.84)	25 (89.29)	0.0008
	No	34 (44.16)	3 (10.71)	
[#]Blood products	PRC only	35 (55.56)	2 (7.14)	< 0.0001
	PLT only	1 (1.59)	-	
	PRC + FFP	12 (19.05)	4 (14.29)	
	PRC + FFP + PLT	11 (17.46)	18 (64.29)	
	PRC + PLT	4 (6.35)	1 (3.57)	
	PRC + FFP + PLT + cryoprecipitate	-	39 (10.71)	
Surgical intervention	B-Lynch procedure	10 (12.99)	4 (14.81)	< 0.0001
	Balloon tamponade	6 (7.79)	12 (44.44)	
	Hysterectomy	2 (2.60)	5 (18.52)	
	None documented	32 (41.56)	5 (18.52)	
	Other	27 (35.06)	1 (3.71)	

Management factors that were significantly associated with blood loss (Table IV) included conversion to GA from spinal anaesthesia (SA) ($p = 0.007$), MTF ($p < 0.001$), TXA use ($p < 0.001$) and surgical interventions such as B lynch and balloon tamponade ($p < 0.001$).

Table IV: Management strategies related to EBL

Variable		n (%)	EBL in ml Mean(SD)/Median(IQR) n(%)	p value
Anaesthetic technique	Spinal	23 (22.55)	1400 (1100-1800)	0.0007
	GA	48 (47.06)	1400 (1175-2000)	
	Conversion	31 (30.390)	2000 (1500-2300)	
Blood product administration	PLT only	1(1.1)	1500 (1500-1500)	< 0.001
	PRBC only	37 (40.66)	1500 (1150-1800)	
	PRBC + FFP	16 (17.58)	1500 (1200-2050)	
	PRBC + PLT	5 (5.49)	1300 (1200-2000)	
	PRBC + FFP + PLT	29 (31.87)	2200 (2000-2300)	
	PRBC + FFP + PLT + cryoprecipitate	3(3.3)	2600 (2500-2700)	
IV fluids	Crystalloids only	66 (64.71)	1600 (1200-2100)	0.1329
	Crystalloids and colloids	36 (35.29)	2000 (1350-2100)	
Tranexamic acid use	Yes	68 (64.76)	2000 (1300-2225)	0.0003
	No	37 (35.24)	1300 (1150-1800)	
Uterotonic drugs	Oxytocin	53 (51.46)	1800 (1200-2000)	0.1657
	Oxytocin/ergometrine combination	50 (48.54)	1800 (1400-2200)	
Surgical intervention	B-Lynch procedure	14 (13.46)	2000 (1800-2100)	< 0.0001
	Balloon tamponade	18 (17.31)	2200 (1900-2300)	
	Hysterectomy	7 (6.73)	2200 (1200-2500)	
	Other	37 (35.58)	1300 (1150-2000)	
	Not documented	28 (26.92)	1400 (1100-1650)	
Outcome	ICU	9 (8.57)	2200 (1500-2500)	0.1158
	High care	96 (91.43)	1650 (1200-2000)	

There was a significant association (p <0.001) of GA, surgical intervention (particularly hysterectomy), blood product administration, and ICU admission among women who met more than one MNM criteria (Table V). The EL post CS procedures and those listed as MNM due to other criteria received fewer types of blood products (mainly PRBCs), often had unclear documentation of surgical intervention, and were all admitted to high care. There was no significant association for uterotonic drugs, IV fluid, or TXA in the EL post CS group and CSgroup of women.

Table V: Management strategies by MNM criteria

	Variable (n)	Ventilated (4)	MTF (20)	EL post CS (18)	Combination (33)	Other (30)	p value
Anaesthetic technique	Spinal	-	-	-	3 (15)	19 (63.33)	< 0.0001
	GA	4 (100)	12 (60)	18 (100)	17 (56.67)	3 (10)	
	Conversion	-	5 (25)	-	13 (43.33)	11 (36.67)	
Blood product administration	PRBC only	1 (33.33)	1 (5.26	14 (100)	-	21 (95.45)	< 0.0001
	PLT only	-	-	-	1 (3.03)	-	
	PRBC + FFP	-	9 (47.37)	-	6 (18.18)	1 (4.55)	
	PRBC + FFP+PLT	-	7 (36.84)	-	22 (66.67)	-	
	PRBC + PLT	2 (66.67)	2 (10.53)	-	1 (3.03)	-	
	PRBC + FFP + PLT + CRYO		-	-	3 (9.09)	-	
IV fluids	Crystalloids only	3 (75)	14 (70)	11 (64.71)	20 (60.61)	18 (64.29)	0.954
	Crystalloids and colloids	1 (25)	6 (30)	6 (35.29	13 (39.39)	10 (35.71)	
Tranexamic acid use	Yes	3 (75)	15 (75)	9 (50)	26 (78.79)	15 (50)	0.0710
	No	1 (25)	5 (25)	9 (50)	7 (21.21)	15 (50)	
Uterotonic drugs	Oxytocin	4 (100)	12 (63.16)	12 (66.67)	16 (50)	9 (30)	0.0171
	Oxytocin/ergometrine	-	7 (36.84)	6 (33.33)	16 (50)	21 (70)	
Surgical intervention	B-Lynch procedure	-	4 (21.05)	-	6 (18.18)	4 (13.33)	< 0.0001
	Balloon tamponade	-	4 (21.05)	1 (5.56)	11 (33.33)	2 (6.67)	
	Hysterectomy	-	-	-	6 (18.18)	1 (3.33)	
	Other	4 (100)	4 (21.05)	5 (27.78)	10 (30.30)	14 946.67)	
	Not documented	-	7 (36.84)	12 (66.67)	-	9 (30)	
Outcome	ICU	1 (25)	-	-	8 (25)	-	< 0.0001
	High care	3 (75)	20 (100)	18 (100)	25 (75)	30 (100)	

14 frequencies missing*

Discussion

In this study we described a population of women who were classified as MNM due to bleeding during and after CS and identified APH as the leading risk factor. A third of the women required a subsequent laparotomy. More women had GA than SA, and there more women received medical interventions and blood transfusions compared to surgical interventions to arrest haemorrhage. Other interventions included high care for almost all the women or ICU admission. Our overall MNM rate for CS was 1.26% during the study period.

A modified near-miss classification was adopted by the clinical team. Although the WHO criteria for near-miss is the most widely accepted, it is not feasible to apply in certain settings. The incidence of MNM depends on the criteria considered, which has resulted in a broad spectrum of global findings as they are affected by socioeconomic factors such as referral network integrity, health care infrastructure, and resource availability. The various criteria differ in both specificity and sensitivity. The WHO criteria require fewer laboratory resources, and their use is encouraged as the gold standard because they are easy and cost-effective to assess and are based on the accumulative knowledge of experts.[10]

Many of the women in our study had a risk factor for bleeding (APH, GA, high parity). Efforts to improve the prediction of severe maternal morbidity led to the use of an additional scoring system, a severe morbidity index score given on admission can identify risk factors that readily accessible at the time of admission.[11]

For a substantial number of subjects, the MNM classification is based on the attending clinician's judgement, which is adapted from what is described by WHO. Most women who meet the conventional MNM criteria described by WHO, usually meet other criteria. This group ofwomen were noted to bleed more, undergo more interventions, require more blood product administration, often received GA, and were all admitted to the ICU.

On the basis of ASA classification, 47% of patients were considered ASA II, implying systemic disease without target organ damage.[12] However, we did not find a significant relationship between ASA classification and disease morbidity. This risk stratification model has been criticized as it is observer dependent and leaves ample room for misinterpretation; although it may give a good indication of preoperative health status, it is not a good indicator of postoperative mortality.[13]

This study population had a median age of 28 and median parity of 2. Notably, the APH group included older and more multiparous women, which corroborates the observation of a higher incidence of morbidity with advancing age and parity. Similar sociodemographic data were reported in Brazil (20-29 years) and France with a mean age of 30.5 years.[10]

A high proportion of women had an emergency CS for foetal distress or poor progress. One-third (33%) of women were classified as MNM based on more than one criterion, and 31% had foetal distress as an indication for CS. Factors such as maternal age and comorbid conditions reportedly contribute to the development of foetal distress and thus increase the need for CS delivery.[14]Although not a particularly old population, most of the women (62%) had comorbidities based on the ASA classification of II and above.[12]

Appropriate anaesthetic management of critically ill patients depends on the nature of the presenting illness and the ability to maintain airway reflexes, coagulation status, and haemodynamic dependence on sympathetic drive.[15] Patients who received GA—and especially those who were converted from SA to GA—had significantly higher intraoperative blood loss than those who only received SA. GA is usually associated with a higher blood loss than SA, but the need for blood transfusion is not necessarily greater.[16] One group suggested that the increased need for transfusion is related to the underlying disease process (APH, pre-eclampsia, and placenta praevia/accreta) that preclude the use of neuroaxial anaesthesia techniques. APH is a risk factor for intraoperative haemodynamic instability; this is the case for both abruptio placentae and placenta praevia, that are well described causes of APH.[17] In the case of hypertensive disorders, either thrombocytopaenia or altered consciousness/seizures may be evident at presentation. These two scenarios of

haemodynamic instability and thrombocytopaenia would contraindicate a neuroaxial anaesthetic technique.[18]

Blood loss was visually estimated by anaesthetists in our study. This is subjective and observer dependent, but despite this, most women with high EBL required an intervention either to arrest the bleeding or for organ support. APH remains a leading contributor to blood loss when more objective estimates are used, such perioperative transfusion need.[19,20]. APH is defined as significant vaginal bleeding from the second trimester of pregnancy.[16] It is caused by placental or peri placental bleeding and is a documented contributor to maternal and foetal morbidity and mortality.[21] It is important to note that GA is frequently performed in the patients with APH and has been reported to be a cause of uterine atony, which increases the likelihood of haemorrhage.[19] In our study, women who had their first CS had more intraoperative blood loss with GA, but those undergoing EL post CS (also frequently done under GA) did not have similar (higher) blood loss estimates. This suggests that the anaesthetic technique exerts an effect but is not a major contributor to blood loss. A comparative study of types of anaesthesia for CS found similar safety profiles for GA and SA, with choice largely dependent on patient needs and medical conditions.[22]

The uterotonic drugs used in this study were limited to oxytocin and oxytocin/ergometrine combinations, and the type of drug did not significantly influence blood loss. Jin et al [23] ranked carbetocin as the most effective drug in PPH management and prevention followed by the combination of ergometrine and oxytocin; both regimens were superior to oxytocin alone. Resource constraints precluded the use of carbetocin in our study, and ergometrine is contraindicated in hypertensive women. Pregnancy-induced hypertension is a well-described risk factor for APH (especially abruptio placentae),[24] which increases the likelihood of APH because platelet dysfunction on the hypertensive disease spectrum further aggravates bleeding risk.

The pathology of obstetric haemorrhage resembles that of severe trauma, so a MTF protocol with FFP/PRC concentrate ratios of 1:1 has been recommended for its management.[25] Various MTF definitions exist, and the most popular is the need for replacement of half the total blood volume within 1 hour or an equivalent of 4 PRC concentrate transfusions in that time period. In the present study, only 20% and 3% of the women received an MTF and cryoprecipitate, respectively. The current consensus in the literature is that fibrinogen levels should be measured and regarding cryoprecipitate and fibrinogen should only be given if levels are < 200 mg/dl.[25] This is often impossible in resource-constrained environments.

Surgical interventions are employed when pharmacological management alone fails. No conservative surgery technique has been described as superior above any other, but hysterectomy is a last line for protracted bleeding.[26] The present study found surgical intervention rates of 17% for a uterine balloon tamponade and 14% for haemostatic suture (B- Lynch), compared to a 6% rate for hysterectomy.

Limitations

This was a retrospective study and was therefore limited by the quality and completeness of hospital records. Maternal deaths were not included in the study, and the true maternal near-miss rate of the population was not calculated; this data would have given us the proportion of maternal near-misses related to CS versus non-CS related surgeries. These findings are specific to our environment and may not be generalized on a global scale

Strengths

This study sought to understand MNM management during and after CS using data from anaesthetic charts. The results clarified which intraoperative interventions were carried out. This helps identify which population of women are at risk of severe maternal morbidity.

Conclusion

PPH is the leading cause of haemorrhage after CS in the MNM population, and it is aggravated if preceded by antepartum haemorrhage. Women with severe morbidity have risk factors for bleeding, and multiple interventions are needed to arrest the haemorrhage and achieve haemodynamic stability. There is a need for a more standardised and accurate scoring system to identify patients at risk at a much earlier stage of disease process.

Disclaimers

Acknowledgements: To my two supervisors, Prof Maswime and Dr Motshabi for their dedication, commitment, and support. Thank you to my biostatistician, Mpendulo. Thank you to Drs Mlandu and Naidoo in the Department of Obstetrics for assistance with data collection and to Prof Adam for allowing the study to be done. Thank you to Dr Nel for assistance with data collection and Dr Lines for allowing the study to be done.

Declaration conflict of interest: None to declare

Funding source: None.

Ethics declaration: I, Rebecca Atebat Iputo declare that this research report is my own work. It is being submitted for the degree of Masters in Medicine in the branch of Anaesthesiology in the University of Witwatersrand, Johannesburg. It has not been submitted for any degree or examination before at any University.

ORCID IDs:

Dr RA Iputo: https://orcid.org/0000-0001-5705-2045

Prof Salome Maswime: https://orcid.org/0000-0003-4013-5164

Dr Palesa Motshabi: https://orcid.org/0000-0001-9990-6336

References

1. Donati S, Senatore S, Ronconi A. Obstetric near-miss cases among women admitted to intensive care units in Italy. Acta Obstet Gynecol Scand. 2012;91(4):452-7. DOI:10.1111/j.1600-0412.2012.01352.x

2. Mantel GD, Buchmann E, Rees H, Pattinson RC. Severe acute maternal morbidity: a pilot study of a definition for a near-miss. Br J Obstet Gynaecol. 1998;105(9):985-90

3. Kallianidis AF, Schutte JM, van Roosmalen J, van den Akker T. Maternal mortality after cesarean section in the Netherlands. Eur J Obstet Gynecol Reprod Biol. 2018;229:148-52. DOI:10.1016/j.ejogrb.2018.08.586

4. Biccard BM, Alphonsus CS, Bishop DG, Cronje L, Kluyts HL, Kusel B, et al. National priorities for perioperative research in South Africa. S Afr Med J. 2016;106(5):58-9. DOI:10.7196/SAMJ.2016.v106i5.10269

5. Tuncalp O, Hindin MJ, Souza JP, Chou D, Say L. The prevalence of maternal near miss: a systematic review. Bjog. 2012;119(6):653-61. DOI:10.1111/j.1471-0528.2012.03294.x

6. Say L, Pattinson R, Gulmezoglu A. WHO systematic review of maternal morbidity and mortality: the prevalence of severe acute maternal morbidity (near miss). BioMed Central Reproductive Health. 2004;1(1):3. DOI: 10.1186/1471-2288-4-16

7. Bishop D, Dyer RA, Maswime S, Rodseth RN, van Dyk D, Kluyts HL, et al. Maternal and neonatal outcomes after caesarean delivery in the African Surgical Outcomes Study: a 7-day prospective observational cohort study. Lancet Glob Health. 2019;7(4):e513-e22. DOI:10.1016/s2214-109x(19)30036-1

8. Hysong SJ, Best RG, Pugh JA. Audit and feedback and clinical practice guideline adherence: making feedback actionable. Implement Sci. 2006;1:9. DOI:10.1186/1748-5908-1-9

9. Chris Hani Baragwanath Hospital website. Chris Hani Baragwanath Hospital. Available from: https://www.chrishanibaragwanathhospital.co.za/contact South Africa, Johannesburg [Accessed 5 May 2021].

10. Monte AS, Teles LMR, Oriá MOB, Carvalho FHC, Brown H, Damasceno AKC. Comparison between near miss criteria in a maternal intensive care unit. Rev Esc Enferm USP. 2018;52:e03404. DOI:10.1590/s1980-220x2017038703404

11. M MK, Naik G. Maternal near miss: reaching the last mile. J Obstet Gynaecol.

2020:1-9. DOI:10.1080/01443615.2020.1820467
12. Mayhew D, Mendonca V, Murthy BVS. A review of ASA physical status – historical perspectives and modern developments. Anaesthesia. 2019;74(3):373-9. DOI:https://doi.org/10.1111/anae.14569
13. Sankar A, Johnson SR, Beattie WS, Tait G, Wijeysundera DN. Reliability of the American Society of Anesthesiologists physical status scale in clinical practice. Br J Anaesth. 2014;113(3):424-32. DOI:10.1093/bja/aeu100
14. Senanayake H, Piccoli M, Valente EP, Businelli C, Mohamed R, Fernando R, et al. Implementation of the WHO manual for Robson classification: an example from Sri Lanka using a local database for developing quality improvement recommendations. BMJ Open. 2019;9(2):e027317. DOI:10.1136/bmjopen-2018-027317
15. Rout CC. Anaesthesia and analgesia for the critically ill parturient. Best Pract Res Clin Obstet Gynaecol. 2001;15(4):507-22. DOI:10.1053/beog.2001.0197
16. Heesen M, Hofmann T, Klöhr S, Rossaint R, van de Velde M, Deprest J, et al. Is general anaesthesia for caesarean section associated with postpartum haemorrhage? Systematic review and meta-analysis. Acta Anaesthesiol Scand. 2013;57(9):1092-102. DOI:10.1111/aas.12178
17. Gallos I, Williams H, Price M, Pickering K, Merriel A, Tobias A, et al. Uterotonic drugs to prevent postpartum haemorrhage: a network meta-analysis. Health Technol Assess. 2019;23(9):1-356. DOI:10.3310/hta23090
18. Roberts I, Shakur H, Afolabi A, Brohi K, Coats T, Dewan Y, et al. The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial. Lancet. 2011;377(9771):1096-101, 101.e1-2. DOI:10.1016/s0140-6736(11)60278-x
19. Phillips JM, van den Anker JN, Ahmadzia HK. Next Generation Medical Management of Postpartum Hemorrhage. Curr Pharm Des. 2019;25(5):549-55. DOI:10.2174/1381612825666190320155337
20. Rothermel LD, Lipman JM. Estimation of blood loss is inaccurate and unreliable. Surgery. 2016;160(4):946-53. DOI:10.1016/j.surg.2016.06.006
21. Fadl SA, Linnau KF, Dighe MK. Placental abruption and hemorrhage-review of imaging appearance. Emerg Radiol. 2019;26(1):87-97. DOI:10.1007/s10140-018-1638-3
22. Tafish R, El Aish KIA, Madi W. General versus spinal anaesthesia for caesarean section: a quasi-controlled trial. Lancet. 2018;391 Suppl 2:S33.

DOI:10.1016/s0140-6736(18)30399-4
23. Jin B, Du Y, Zhang F, Zhang K, Wang L, Cui L. Carbetocin for the prevention of postpartum hemorrhage: a systematic review and meta-analysis of randomized controlled trials. J Matern Fetal Neonatal Med. 2016;29(3):400-7. DOI:10.3109/14767058.2014.1002394
24. Takai IU, Sayyadi BM, Galadanci HS. Antepartum Hemorrhage: A Retrospective Analysis from a Northern Nigerian Teaching Hospital. Int J Appl Basic Med Res. 2017;7(2):112-6. DOI:10.4103/2229-516x.205819
25. The L. Stemming the global caesarean section epidemic. Lancet. 2018;392(10155):1279. DOI:10.1016/s0140-6736(18)32394-8
26. Sentilhes L, Winer N, Azria E, Sénat M, Ray C, Vardon D, et al. Tranexamic acid for the prevention of postpartum hemorrhage after vaginal delivery: the TRAAP trial. Am J Obstet Gynecol. 2018;218. DOI:10.1016/j.ajog.2017.10.412

Appendices

Appendix 1: Proposal

The perioperative management of caesarean section related haemorrhage in a maternal near miss population: a retrospective study

Rebecca Iputo

1519621

Supervisor: Palesa Motshabi
Co-supervisor: Salome Maswime

1. Introduction and problem statement

Introduction

According to the World Health Organisation (WHO), maternal morbidity is any health condition attributed to or aggravated by pregnancy and childbirth with negative effects on maternal wellbeing. Severe acute maternal morbidity, also referred to as a maternal near-miss has been defined by WHO as any woman who nearly dies from a complication from pregnancy or within 42 days of delivery or termination of pregnancy (1).The concept of a maternal near-miss may serve as a surrogate for evaluating the quality of obstetric care as when compared to maternal mortalities they provide a larger pool of data to study and determine better ways of management (2). Globally, the major causes of a maternal near-miss include; hypertensive disorders in pregnancy, sepsis, obstetric haemorrhage, anaemia and obstructed labour (3).

Although caesarean sections have been shown to reduce maternal and neonatal adverse outcomes, the excessive use of caesarean sections in high income countries has not been equally met with an improvement in maternal outcomes (4). Obstetric haemorrhage, which has various components such as antepartum, intrapartum and postpartum haemorrhage is a growing concern that is important to both obstetricians and anaesthetists. While antepartum haemorrhage is an indication for a caesarean section and thus requires management by both an anaesthetist and obstetrician, postpartum haemorrhage accounts for 9.3% of maternal mortalities in high income countries and 45.7% in low income countries (5). There is evidence that obstetric haemorrhage is the leading cause of maternal mortality globally, and also that one third of obstetric haemorrhage cases in South Africa are related to caesarean sections (6). Therefore, maternal morbidity from obstetric haemorrhage is a cause for concern, and there is a likelihood that more obstetric haemorrhage occurs intrapartum during a caesarean section. Obstetric haemorrhage is a growing area of interest in Anaesthesiology. The role of the anaesthetist includes the medical management of obstetric haemorrhage through the administration of uterotonic drugs intraoperatively, as well as administration of blood and intravenous fluids during the intraoperative and postoperative resuscitation period (2, 7, 8)

The WHO has specific guidelines for the management and prevention of obstetric haemorrhage, but globally there are variations in its definition as well as varying emphasis on various components of the guidelines, with some guidelines placing an emphasis more on surgical interventions than pharmacological measures (9). The South African guidelines, developed through the Essential Steps in Managing Obstetric Emergencies (ESMOE) training programme, has been incorporated into modules with practice drills and simulations used to keep clinicians up to date with best clinical practices(10).

Problem Statement

Access to caesarean section has improved in much of the world. However, there has been an unacceptably high mortality rate from caesarean section related haemorrhage especially in low- and middle-income countries. Early recognition of haemorrhage by obstetricians and timely medical management of obstetric haemorrhage by anaesthetists is thus critical to improving outcomes (11). There is a paucity of data on the role of the anaesthetist in the intraoperative management of obstetric haemorrhage.

Caesarean section rates are on the increase in both high and low income countries (12). A caesarean section delivery poses a greater risk for maternal morbidity than vaginal delivery (4, 6). Obstetric haemorrhage is one of the leading cause of maternal morbidity and mortality in South Africa (6). A growing proportion of obstetric haemorrhage will be encountered intraoperatively and its management should thus be improved on.

2. Aim

The aim of this study is to describe the intraoperative medical management of caesarean section related haemorrhage in a maternal near-miss population.

3. Objectives

The objectives of this study are to:

- determine the maternal near-miss rate from caesarean section related obstetric haemorrhage in the study institution
- describe the use of drugs, blood and intravenous fluid replacement given intraoperatively for women with caesarean section related obstetric haemorrhage
- determine the conditions related to these maternal near-miss cases.

4. Research assumptions

The following definitions will be used in the study**.**

Anaesthetist: is any qualified doctor working in the Department of Anaesthesiology including interns, medical officers, registrars and consultants**.**

Medical officer: is a qualified doctor practising in the Department of Anaesthesiology under specialist supervision**.** Medical officers with more than 10 years of experience are career medical officers and are regarded as consultants.

Registrar: is a qualified doctor who is registered with the Health Professional Council of South Africa as a trainee anaesthetist**.**

Consultant: is a specialist anaesthetist or career medical officer**.**

Elective caesarean section: A caesarean section performed under non urgent conditions at a chosen date that has been agreed upon by both patient and obstetrician (13).

Emergency caesarean section: A caesarean section performed when there is either foetal or maternal compromise, which may or may not be a threat to life (13).

Maternal near-miss: A woman who survives a life threatening condition within 42 days of childbirth or termination of pregnancy (14). In this study, a maternal near-miss has been

identified by the department of Obstetrics and Gynaecology and a list of maternal near-miss cases who had caesarean sections will be requested from this department and their corresponding anaesthetic charts will be reviewed.

Perioperative haemorrhage: This will include all obstetric haemorrhage that is managed by the anaesthetist intraoperatively, that may be either antepartum, intrapartum, or postpartum.

Intrapartum haemorrhage: Blood loss that occurs during delivery in theatre

Postpartum haemorrhage: postpartum blood loss of more than 500mL

Antepartum haemorrhage: All blood loss that occurs prior to delivery.

Day: From 07h00 to 16h00

Night: From 16h01 to 06h59

Weekday: Monday 07h00 to Friday 16h00

Weekend: Friday 16h01 to Monday 06h59

Medical management: This will include all fluids, blood products, uterotonic drugs, inotropic drugs as well as tranexamic acid administered intraoperatively by the anaesthetist.

Massive transfusion: All patients that receive at least 4 units of blood intraoperatively after a caesarean section.

Dialysed patients: All patients that are initiated on dialysis after a caesarean section.

Ventilated patients: All patients that cannot be extubated and require postoperative ventilation after a caesarean section.

5. Demarcation of study field

The study will be conducted in the Department of Anaesthesiology and the Department of Obstetrics and Gynaecology at Chris Hani Baragwanath Hospital (CHBAH). CHBAH is a 2888 bed central hospital that is affiliated with the Faculty of Health Sciences at the University of the Witwatersrand. According to departmental statistics there are approximately 500 caesarean sections performed per a month.

6. Ethical considerations

Approval to conduct the study will be obtained from both the Human Research Ethics Committee (Medical) and the Graduate Studies Committee of the University of the Witwatersrand. Permission to conduct the study will be requested from the Medical Advisory Committee at CHBAH (Appendix A). Approval to access stored documents will be requested from the Head of Department of Obstetrics and Gynaecology (Appendix B) and the Head of Department of Anaesthesiology at CHBAH (Appendix C).
This is a retrospective study and patient anonymity will be maintained on the data collection sheet. A study number will be allocated to each near miss patient. Patient names and hospital numbers with corresponding study numbers will be recorded and filed separately. In order to ensure confidentiality, only the researcher and supervisors will have access to raw data.

All data will be stored securely for 6 years after the completion of the study.

This study will be conducted according to the principles of the Declaration of Helsinki (15)and the South African Guidelines for Good Clinical Practice (16).

7. Data collection

7.1Research design

A retrospective, contextual, descriptive research design will be followed in this study.
A retrospective study measures variables that have occurred in the past (17). This study will obtain information from previously completed anaesthetic records.
A contextual study is one that focuses on a specific group, also referred to as a "small scale world" (18). This study is contextual as it will be undertaken at CHBAH maternity theatre.
A descriptive study is one in which phenomena are described or the relationship between variables are examined with no attempt to manipulate the variables (17). This study will describe the management of caesarean section related haemorrhage.

27.2Study population

The study population will be anaesthetic records of patients who had caesarean section related near miss at CHBAH and a list of all maternal near-miss cases provided by the Department of Obstetrics and Gynaecology from their mortality and morbidity database.

7.3 Study sample

Sample method

In this study a retrospective consecutive sampling method will be used. Convenience sampling is when the most readily accessible participants or units are chosen in a study and consecutive sampling is a form of convenience sampling where every available participant or unit within an accessible population is chosen (19).

This study will use a retrospective consecutive sampling method as all the anaesthetic records of maternal near miss cases from the obstetric theatre will be used to collect data.

Sample size

A period sample with no sampling strategy will be used, including all women who had a caesarean section related near-miss event at CHBAH from the period of 1 January 2018 to 31 December 2018. This is approximately 190 cases. A list of all the near-miss events during this time will be provided by the secretary of the Department of Obstetrics and Gynaecology. The criteria used to classify a near-miss in this department include:

- All patients requiring ventilation after surgery
- All patients requiring dialysis after surgery
- All patients that receive a massive transfusion
- All patients who receive inotropes during and after surgery
- All patients that require an ICU admission after surgery.

Inclusion and exclusion criteria

The anaesthetic records of all patients who had a caesarean section related near miss from 1 January 2018 to 31 December 2018 will be included in this study.

Illegible records will be excluded from this study.

7.4 Collection of data

Once the study has been approved, data will be collected and recorded on a Microsoft Excel spreadsheet.

The CHBAH obstetric and anaesthesia departments will provide information about the total number of near miss cases that had caesarean sections during the study period as well as the patients names and hospital numbers. Each near miss patient will be allocated a study number.

The CHBAH anaesthetic records for caesarean sections that were near miss cases will be evaluated to determine the number of obstetric haemorrhages encountered as well as medical management undertaken intraoperatively.

The data collection sheet (Appendix C) will include various information:

- Total number of caesarean sections done from 1 January 2018 to 31 December 2018
- ASA classification
- parity, age, race
- elective vs emergency caesarean section
- timing of the caesarean section
- anaesthetic technique
- cause of maternal near-miss
- presence of obstetric haemorrhage and subsequent medical management thereof including drugs (uterotonic, inotropes, tranexamic acid), intravenous fluid and blood product administration.
- surgical intervention for bleeding

Data capturing will be done in both the Department of Obstetrics and Gynaecology and the Department of Anaesthesiology at CHBAH. Data will be captured by the researcher within these departments and no records will be removed from the hospital premises.

7.5 Data analysis

Data will be captured onto a Microsoft Excel spreadsheet and then imported into a statistical program. Data will be analysed in consultation with a bio-statistician. Descriptive statistics will be used to analyse numerical data. Categorical data will be analysed using frequencies

and percentages. Normally distributed continuous variables will be presented using means and standard deviations whereas those that are not normally distributed will presented using medians and interquartile ranges. In this study statistical significance will be indicated by a p-value of < 0.05 and a confidence interval of 95%.

8. Significance of the study

A near-miss audit is an important healthcare quality improvement tool which facilitates the measuring and the improvement of clinical practices (20). This study will serve as a quality improvement tool for the management of caesarean section related obstetric haemorrhage as it will address two knowledge gaps, one being the quantitative burden of these cases and the other being how these cases are managed.
Through the identification of deficiencies in management, new strategies in training and skills development may then be implemented in future (21).

9. Validity and reliability of the study

The validity of a study implies how accurately the study reflects the variables being measured and the reliability is the degree of consistency and repeatability of the technique used to obtain a measurement (22).
Various steps will be taken to ensure validity and reliability in this study:

- An appropriate research design will be used
- A single researcher will collect data
- Every tenth entry into a Microsoft Excel spreadsheet will be checked for accuracy.

10. Potential limitations of the study

Study limitations are characteristics of the design or methodology of a study that negatively influence the interpretation of the findings of the study (22). The findings in this study may not be representative of findings of similar studies done elsewhere

because this is a contextual study where the population is limited to maternity theatre patients who underwent a caesarean section at CHBAH.

This is a retrospective study and is thus limited by the quality and completeness of information recorded, as there is a reliance on adequately completed records.

11. Project outline

Entity	Mar 2019	May 2019	June 2019	July 2019	Aug 2019	Sept 2019	Oct 2019	Nov 2019	Feb 2020
Proposal and Literature Review									
Proposal Submission									
Ethics approval									
Postgraduate Approval									
Data Collection									
Data Analysis									
Draft Article									
Submission									

12. Financial plan

The Department of Anaesthesiology will bear the cost of printing and paper for the study.

	Price per page	Number of pages	Copies	Total
Proposal	R1	20	6	R120
Postgraduate form	R1	2	6	R12
Completed report	R1	100	4	R400
			Grand total	R532

13. References

1. Donati S, Senatore S, Ronconi A. Obstetric near-miss cases among women admitted to intensive care units in Italy. Acta Obstet Gynecol Scand. 2012;91(4):452-7.DOI:10.1111/j.1600-0412.2012.01352.x

2. Kilpatrick SJ. Understanding Severe Maternal Morbidity: Hospital-based Review. Clin Obstet Gynecol. 2018;61(2):340-6.DOI:10.1097/grf.0000000000000351

3. Small MJ, Allen TK, Brown HL. Global disparities in maternal morbidity and mortality. Semin Perinatol. 2017;41(5):318-22.DOI:10.1053/j.semperi.2017.04.009

4. Kallianidis AF, Schutte JM, van Roosmalen J, van den Akker T. Maternal mortality after cesarean section in the Netherlands. Eur J Obstet Gynecol Reprod Biol. 2018;229:148-52.DOI:10.1016/j.ejogrb.2018.08.586

5. Say L, Chou D, Gemmill A, Tuncalp O, Moller AB, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health. 2014;2(6):e323-33.DOI:10.1016/s2214-109x(14)70227-x

6. Biccard BM, Alphonsus CS, Bishop DG, Cronje L, Kluyts HL, Kusel B, et al. National priorities for perioperative research in South Africa. S Afr Med J. 2016;106(5):58-9.DOI:10.7196/SAMJ.2016.v106i5.10269

7. Oladapo OT, Iyaniwura CA, Sule-Odu AO. Quality of antenatal services at the primary care level in southwest Nigeria. Afr J Reprod Health. 2008;12(3):71-92

8. Tuncalp O, Hindin MJ, Souza JP, Chou D, Say L. The prevalence of maternal near miss: a systematic review. Bjog. 2012;119(6):653-61.DOI:10.1111/j.1471-0528.2012.03294.x

9. Dahlke JD, Mendez-Figueroa H, Maggio L, Hauspurg AK, Sperling JD, Chauhan SP, et al. Prevention and management of postpartum hemorrhage: a comparison of 4 national guidelines. Am J Obstet Gynecol. 2015;213(1):76.e1-.e10.DOI:10.1016/j.ajog.2015.02.023

10. Bergh A-M, Baloyi S, Pattinson R. What is the impact of multi-professional emergency obstetric and neonatal care training? 2015;29.DOI:10.1016/j.bpobgyn.2015.03.017

11. Collis R, Guasch E. Managing major obstetric haemorrhage: Pharmacotherapy and transfusion. Best Pract Res Clin Anaesthesiol.

2017;31(1):107-24.DOI:10.1016/j.bpa.2017.02.001
12. Ryan GA, Nicholson SM, Morrison JJ. Vaginal birth after caesarean section: Current status and where to from here? Eur J Obstet Gynecol Reprod Biol. 2018;224:52-7.DOI:10.1016/j.ejogrb.2018.02.011
13. Lucas DN, Yentis SM, Kinsella SM, Holdcroft A, May AE, Wee M, et al. Urgency of caesarean section: a new classification. J R Soc Med. 2000;93(7):346-50.DOI:10.1177/014107680009300703
14. Madeiro AP, Rufino AC, Lacerda EZ, Brasil LG. Incidence and determinants of severe maternal morbidity: a transversal study in a referral hospital in Teresina, Piaui, Brazil. BMC Pregnancy Childbirth. 2015;15:210.DOI:10.1186/s12884-015-0648-3
15. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects 2013 [updated Nov 27. 2013/10/22:[2191-4].DOI:10.1001/jama.2013.281053
16. Guidelines for good clinical practice in the conduct of clinical trials with human participants in South Africa. 2nd ed. Pretoria, South Africa: Department of health; 2006.
17. Brink H. Fundamentals of research methodology for health care professionals. 2nd ed. Cape Town, South Africa: Juta; 2006.
18. Strydom H, Fouche C, Poggenpoel M, Schurink E. Research at grass roots. Pretoria, South Africa: Van Schaik; 1998.
19. Endacott R, Botti M. Clinical research 3: Sample selection. Accid Emerg Nurs. 2007;15(4):234-8.DOI:10.1016/j.aaen.2006.12.006
20. Esposito P, Dal Canton A. Clinical audit, a valuable tool to improve quality of care: General methodology and applications in nephrology. World J Nephrol. 2014;3(4):249-55.DOI:10.5527/wjn.v3.i4.249
21. Hysong SJ, Best RG, Pugh JA. Audit and feedback and clinical practice guideline adherence: making feedback actionable. Implement Sci. 2006;1:9.DOI:10.1186/1748-5908-1-9
22. Burns N, Grove S. Understanding nursing research. Philadelphia: Saunders; 2003.

Appendix 2: Ethics clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr R Iputo

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M190516

NAME: (Principal Investigator)	Dr R Iputo
DEPARTMENT:	School of Clinical Medicine Department of Anaesthesiology Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	The perioperative management of caesarean section related haemorrhage in a maternal near-miss population - A retrospective study
DATE CONSIDERED:	2019/05/31
DECISION:	Approved unconditionally
CONDITIONS:	Change of study title noted on 2019/07/18
SUPERVISOR:	Drs P Motshabi and S Maswime
APPROVED BY:	CB Penny Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2019/06/07

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

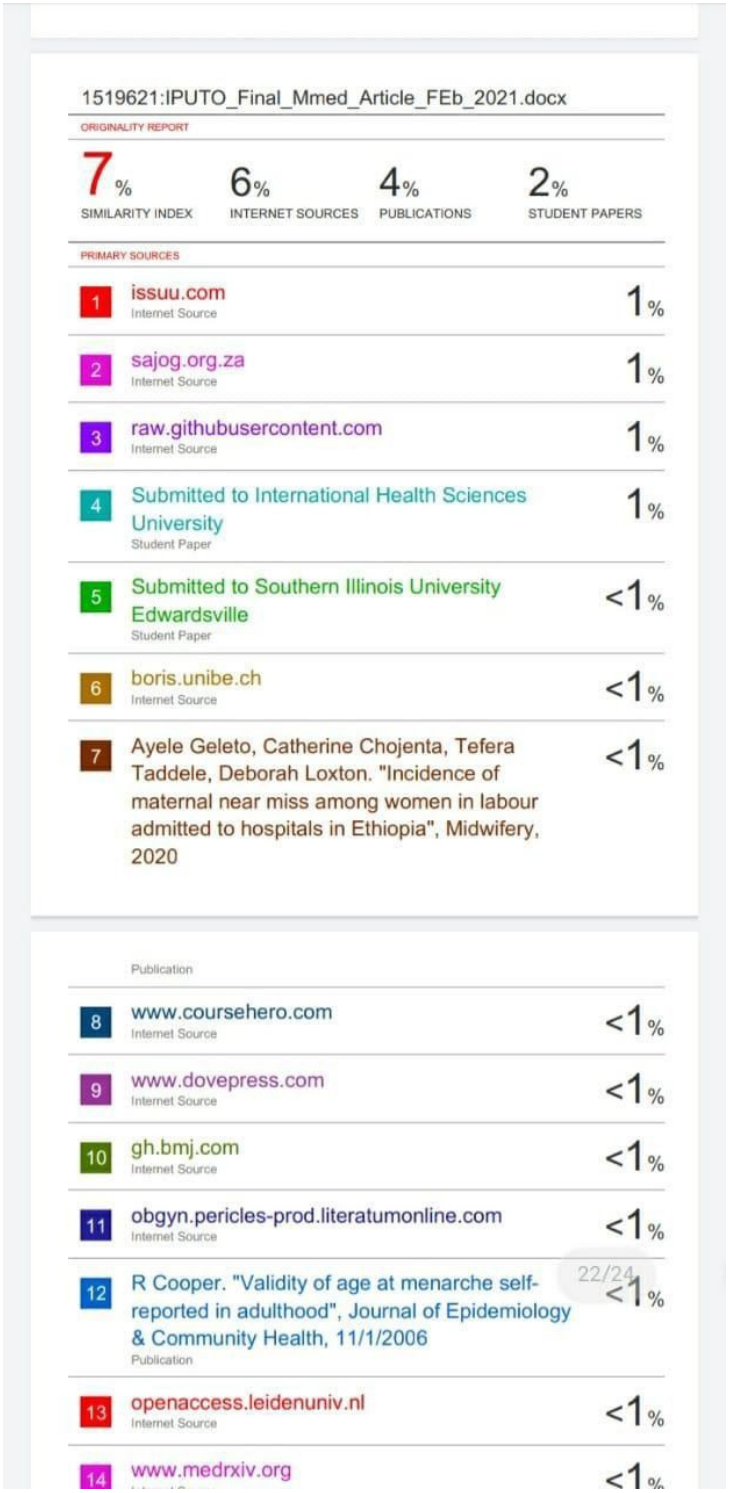
DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
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 submit details to the Committee. I **agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **May** and will therefore reports and re-certification will be due early 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 _____

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES

Appendix 3: Plagiarism/ Turnitin report cover page



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Appendix 4: Permission letter from HOD obstetrics at Chris Hani Baragwanath Academic Hospital

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

OBSTETRICS AND GYNAECOLOGY
School of Clinical Medicine

Department of Obstetrics and Gynaecology
Chris Hani Baragwanath Academic Hospital, PO Bertsham 2013, South Africa. Telephone: t 27 11 933 8156

Date: - 02 May 2019

RE: The anaesthetics management of caesarean section related haemorrhage in a maternal near miss population: retrospective study

To whom it may concern,

Permission is hereby granted to Dr Iputo to perform her study in the department of Obstetrics and Gynaecology. She will be using data from anesthetic notes as described on the data sheet. This permission is subject to Human Research Ethics Committee approval and approval from the CEO at Chris Hani Baragwanath Academic Hospital.

Thank you

Professor Y. Adam
Clinical Head and Adjunct Professor
Obstetrics & Gynaecology Department
Chris Hani Baragwanath Academic Hospital
The University of the Witwatersrand
Date: 02 May 2019

Faculty of Health Sciences
Johannesburg Hospital I Private Bag X39, Johannesburg, South Africa I **T** +27 11 488 3179 I **F** +27 11 643 2522 I www.wits.ac.za

Appendix 5: Postgraduate approval letter

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

09 July 2019
Person No: 1519621
PAG

Dr R Iputo
Unit 103
Savuti Sands
Naivasha Rd
Sunninghill
2191
South Africa

Dear Dr Rebecca Iputo

Master of Medicine: Approval of Title

We have pleasure in advising that your proposal entitled *The perioperative management of caesarean section related haemorrhage in a material near-miss population: a retrospective study.* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

Appendix 6: Permission letter HOD Anaesthesia Chris Hani Baragwanath Academic Hospital

05/04/2019

Dear Dr lputo

Permission is granted to access the records that you require to conduct your retrospective study on patients after caesarean section at the Chris Hani Baragwanath Academic Hospital for the period 1 January 2018 to 31 December 2018.

Permission is granted subject to you obtaining the relevant permission from the Wits Human Research Ethics Committee and Wits Post Graduate Committee before starting your data collection.

I wish you all the success with your study.

Dr D Lines Acting HOD

Department of Anaesthesiology

Chris Hani Baragwanath Academic Hospital

Appendix 7: Data collection sheet

General Information

Total number of maternal near miss cases:	
Total number of caesarean sections related near miss cases:	
Total number of caesarean section related haemorrhage cases:	

Data Collection Sheet

Study number:	
Age:	
Race:	
Parity:	
ASA classification	
Indication for caesarean section:	
Timing of caesarean section:	• Day • Night
Estimated Blood Loss (ml):	
Cause of near-miss:	• Antepartum haemorrhage • Postpartum haemorrhage • Intrapartum haemorrhage • Other
Obstetric haemorrhage medical management:	**Uterotonic Drugs, dose:** • Oxytocin, dose: • Oxytocin/Ergometrine, dose: • Misoprostol, dose: • Prostaglandin F2a, dose: **Blood products, no units:** • Packed red cells, units: • Fresh frozen plasma, units: • Platelets, units:

	• Cryoprecipitate, units: **Intravenous Fluids:** • Crystalloids, units: • Colloids, units: **Inotropes:** • Adrenaline, maximum dose: • Dobutamine, maximum dose: **Vasopressors:** • Phenylephrine, maximum dose: • Ephedrine, maximum dose: **Tranexamic Acid** • Yes, dose: • No
Anaesthetic technique	• Spinal • General • Epidural • Conversion, reason:
Surgical Intervention	• B – Lynch procedure • Balloon Tamponade • Hysterectomy • None • Other
Outcome	ICU admission, reason: High Care admission, reason: Other

Appendix: Journal guidelines to author

South African Journal of Anaesthesia and Analgesia author guidelines:

Keywords

All articles should include keywords. Up to five words or short phrases should be used. Use terms from the Medical Subject Headings (MeSH) of Index Medicus when available and appropriate. Key words are used to index the article and may be published with the abstract.

Acknowledgements

In a separate section, acknowledge any financial support received or possible conflict of interest. This section may also be used to acknowledge substantial contributions to the research or preparation of the manuscript made by persons other than the authors.

References

Cite references in numerical order in the text, in superscript format (Format> Font> Click superscript). Please do not use brackets or do not use the footnote function of MS Word.

In the References section, references must be typed double-spaced and numbered consecutively in the order in which they are cited, not alphabetically.

The style for references should follow the format set forth in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (http://www.icmje.org) prepared by the International Committee of Medical Journal Editors.

Abbreviations for journal titles should follow Index Medicus format. Authors are responsible for the accuracy of all references. Personal communications and unpublished data should not

be referenced. If essential, such material should be incorporated in the appropriate place in the text.

List all authors when there are six or fewer; when there are seven or more, list the first three, then "; et al."; When citing URLs to web documents, place in the reference list, and use the following format: Authors of document (if available). Title of document (if available).URL (Accessed [date]).

The following are sample references:

1. Jun BC, Song SW, Park CS, Lee DH, Cho KJ, Cho JH. The analysis of maxillary sinus aeration according to aging process: volume assessment by 3-dimensional reconstruction by high-resolutional CT scanning. Otolaryngol Head Neck Surg. 2005 Mar;132(3):429-34.

2. Polgreen PM, Diekema DJ, Vandeberg J, Wiblin RT, Chen YY, David S, et al. Risk factors for groin wound infection after femoral artery catheterization: a case-control study. Infect Control HospEpidemiol [Internet]. 2006 Jan [cited 2007 Jan5]; 27(1):34-7. Available from: http://www.journals.uchicago.edu/ICHE/journal/issues/v27n1/2004069/2004069.web.pdf.

More sample references can be found at:
http://www.nlm.nih.gov/bsd/uniform_requirements.html"

Tables

Tables should be self-explanatory, clearly organised, and supplemental to the text of the manuscript. Each table should include a clear descriptive title on top and numbered in Roman numerals (I, II, etc) in order of its appearance as called out in text. Tables must be inserted in the correct position in the text. Authors should place explanatory matter in footnotes, not in the heading. Explain in footnotes all non-standard abbreviations.

For footnotes use the following symbols, in sequence: *, †, ‡, §, ‖, **, ††, ‡‡

Figures

All figures must be inserted in the appropriate position of the electronic document. Symbols, lettering, and numbering (in Arabic numerals e.g. 1, 2, etc. in order of appearance in the text) should be placed below the figure, clear and large enough to remain legible after the figure has been reduced. Figures must have clear descriptive titles.

Photographs and images

If photographs of patients are used, either the subject should not be identifiable or use of the picture should be authorised by an enclosed written permission from the subject. The position of photographs and images should be clearly indicated in the text. Electronic images should be saved as either jpeg or gif files. All photographs should be scanned at a high resolution (300dpi, print optimised). Please number the images appropriately.

Permission

Permission should be obtained from the author and publisher for the use of quotes, illustrations, tables, and other materials taken from previously published works, which are not in the public domain. The author is responsible for the payment of any copyright fee(s) if these have not been waived. The letters of permission should accompany the manuscript.

The original source(s) should be mentioned in the figure legend or as a footnote to a table.

Review and action

Manuscripts are initially examined by the editorial staff and are usually sent to independent reviewers who are not informed of the identity of the author(s). When publication in its original form is not recommended, the reviewers' comments (without the identity of the reviewer being disclosed) may be passed to the first author and may include suggested revisions. Manuscripts not approved for publication will not be returned.

Ethical considerations

Papers based on original research must adhere to the Declaration of Helsinki on "; Ethical Principles for Medical Research Involving Human Subjects"; and must specify from which recognised ethics committee approval for the research was obtained.

Conflict of interest

Authors must declare all financial contributions to their work or other forms of conflict of interest, which may prevent them from executing and publishing unbiased research. [Conflict of interest exists when an author (or the author's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her opinions or actions.]* *Modified from: Davidoff F, et al. Sponsorship, Authorship, and Accountability. (Editorial) JAMA 2001: 286(10). The following declaration may be used if appropriate: "I declare that I have no financial or personal relationship(s) which may have inappropriately influenced me in writing this paper."

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All submissions must be made online at www.sajaa.co.za and correspondence regarding manuscripts should be addressed to:

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Note: Ensure that the article ID [reference] number is included in the subject of your email correspondence.

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All manuscripts will be processed online. Submissions by post or by e-mail must be accompanied by a signed copy of the following indemnity and copyright form. CLICK HERE to download and save it to your computer.

Tips on Preparing your manuscript

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biomedical journals” at www.icmje.org

2. Please consult the guide on Vancouver referencing methods

at: http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=citmed.TOC&depth=2

3. The submission must be in UK English, typed in Microsoft Word or RTF

with no double spaces after the full stops, double paragraph spacing, font size10 and font type: Times New Roman

4. All author details (Full names, Qualifications and affiliation) must be

provided.

5. The full contact details of corresponding author (Tel, fax, e-mail, postal

address) must be on the manuscript.

6. There must be an abstract and keywords.

7. References must strictly be in Vancouver format. (Reference numbers must

be strictly numerical and be typed in superscript, not be in brackets and must be placed AFTER the full stop or comma.)

8. It must be clear where every figure and table should be placed in the text. If

possible, tables and figures must be placed in the text where appropriate. If too large or impractical, they may be featured at the end of the manuscript or uploaded as separate supplementary files.

9. All photographs must be at 300dpi and clearly marked according to the figure numbers in the text. (Figure 1, Table II, etc.)

10. All numbers below ten, without percentages or units, must be written in words

11. Figure numbers: Arabic, table numbers: Roman <="" uk="" in="" proficient="" expert="" a="" by="" reviewed="" be=""must="">

Submission Preparation Checklist

As part of the submission process, authors are required to check offtheir submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

1. This manuscript has currently only been submitted to SAJAAand has not been published previously.

2. This work is original and all third party contributions (images,ideas and results) have been duly attributed to the originator(s).

3. Permission to publish licensed material (tables, figures, graphs) has been obtained and the letter of approval andproof of payment for royalties have been submitted as supplementary files.

4. The submitting/corresponding author is duly authorised toherewith assign copyright to the South African Society of Anaesthesiologists (SASA).

5. All co-authors have made significant contributions to themanuscript to qualify as co-authors.

6. Ethics committee approval has been obtained for originalstudies and is clearly stated in the methodology.

7. A conflict of interest statement has been included whereappropriate.

8. The submission adheres to the instructions to authors interms of all technical aspects of the manuscript.

9. Plagiarism The submitting author acknowledges that the Editorial Board reserves the right to use plagiarism detectionsoftware on any submitted material.

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