DIAGNOSIS IN WOMEN SUSPECTED OF PULMONARY EMBOLISM AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL – A RETROSPECTIVE REVIEW

This is a research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfillment of the requirements for the degree

of

Masters of Medicine in Obstetrics and Gynaecology

Dr SM Gqola

Student number: 0701953E

Supervisors: Prof Y Adam, Dr L Mbodi

NOVEMBER 2023

Johannesburg

TABLE OF CONTENTS

DEDICATION

This research report is dedicated to my loving spouse Ms Phumla Ngubane, my mother Mrs Liziwe Gqola and my family at large.

DECLARATION

I **Dr SISEKO GQOLA** student number **0701953E** as a postgraduate student registered for a MMed at the University of the Witwatersrand declare the following:

- I am aware that plagiarism is the use of someone else's work without their permission and or without acknowledging the original source.
- I am aware that plagiarism is wrong.
- I confirm that this written work is my own work except where I have stated 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 if I have failed to acknowledge the ideas or writing of others.

I declare that this research report is my own work. It is being submitted in partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Obstetrics and Gynaecology, at the University of Witwatersrand, Johannesburg. This work has not been submitted for any degree or examination at this or any other University.

Name Dr Siseko Gqola

Signed……SG……20/11/ 2023

CONTRIBUTION LETTER

Dear Sir / Madam

This letter serves to confirm the author's contributions to the submission of the paper. I confirm that with the guidance of the supervisors, I worked through the protocol, collected data and initiated the write-up of the research findings and the draft of the final manuscript.

My supervisors assisted with topic selection, data analysis, interpretation of the results and review of the final draft.

Yours sincerely

Dr Siseko Gqola

Signed……SG……20/11/ 2023

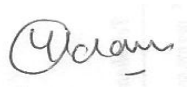
DECLARATION: STUDENT'S CONTRIBUTION TO THE ARTICLE AND AGREEMENT OF CO-AUTHORS

I **SISEKO GQOLA** Student Number **0701953E** declare that this Thesis/Dissertation/Research Report is my own work and that I contributed adequately towards research findings published in the article(s) stated below which are included in my Thesis/Dissertation/Research Report.

Signature of Student ……SG…….

Date……20/11/ 2023…….

Name of Primary Supervisor: ……. **Prof YASMIN ADAM**……

Signature of Primary Supervisor…… 

Date……20/11/ 2023……....

Agreement by co-authors: By signing this declaration, the co-authors listed below agree to the use of the article(s) by the student as part of his/her Thesis/Dissertation/Research Report. In cases where the student is not the 1st author of the published article, the primary supervisor must explain (under comments) why the student is entitled to use the paper for his/her degree purposes.

Article 1: Title: **Diagnosis in women suspected of pulmonary embolism at Chris Hani Baragwanath Academic Hospital – A retrospective review**

Authors	**Name**	**Signature**	**Date**
1st author	Siseko Gqola	**SG**	20/11/ 2023
2nd author	Yasmin Adam		20/11/ 2023
3rd author	Langanani Mbodi		20/11/ 2023

PRESENTATION AND OR PUBLICATION ARISING FROM THE STUDY

Presentation: Not presented.

Publication: We will be submitting the manuscript for consideration for publication in the South African Journal of Obstetrics and Gynaecology (SAJOG).

ABSTRACT

Pulmonary embolism accounts for 3.6% of maternal deaths in South Africa and 9.2% of all pregnancy-related deaths in the United States. This cross-sectional descriptive study sought to identify clinical factors and investigations used in pregnant or postpartum women who presented with suspected pulmonary embolism. Pulmonary embolism (PE) is often one of the conditions that are considered in the differential diagnosis of women attending/admitted at Chris Hani Baragwanath Academic Hospital Obstetric High Care Unit. Women investigated with Computed tomography pulmonary angiogram (CTPA) and/or Ventilation/perfusion (VQ) scans from July 1, 2018, to June 30, 2019, were included. STATA version 14.2 was used for data analysis of the variables.

The prevalence of PE was 9.4%. The mean age was 28.2 years (SD+-5.8). Most women, 126 (69.6%), were post-partum and 10 (7.9%) of those diagnosed and treated for PE. There were 81.7% women were delivered by caesarean section and 7.7% of them diagnosed with PE. Hundred (55.2%) women who had a CTPA or VQ scan were symptomatic, and the asymptomatic women had other clinical features suspicious of PE including persistent tachycardia of unknown cause. This was one of the indications for investigation in 159 (87.8%) women. Five (2.8%) women were diagnosed with deep vein thrombosis (DVT) on compressions ultrasound (CUS). Of the 181 scans (CTPA and VQ) done, 12 reports had features suggestive of Pulmonary Embolism.

Pulmonary embolism is a rare, but severe condition. It is therefore important to diagnose and treat appropriately.

ACKNOWLEDGEMENTS

I would like to express my heartfelt gratitude to my supervisors, Prof. Yasmin Adam and Dr Langanani Mbodi for their supervision, guidance and support. Thank you for all the patience in reviewing my work and allowing time to improve. You have been supportive of my career goals and worked actively to provide me with protected academic time to pursue those goals.

I am thankful to the department of Obstetrics and Gynaecology, Radiology and Nuclear Medicine at Chris Hani Baragwanath Academic Hospital for all the support.

I am grateful to all of those with whom I have had the pleasure to work with during data collection, a special mention to Ms Asanda Oyiya.

A special thanks to my loving partner and great friend Ms Phumla Ngubane for her patience and support throughout the course of this project. I would also not forget to thank my sister Ms Bomikazi Gqola for the great help in reviewing my work. Thank you all.

List of Abbreviations

ALT	Alanine transaminase
AST	Aspartate Aminotransferase
AKI	Acute kidney injury
CHBAH	Chris Hani Baragwanath Academic Hospital
CRP	C-reactive protein
CTPA	Computed tomography pulmonary angiogram
CXR	Chest x-ray
DVT	Deep vein thrombosis
ECG	Electrocardiogram
HCA	High Care area
HIV	Human Immunodeficiency Virus
IQR	Interquartile range
LMWH	Low molecular weight heparin
MOU	Midwife obstetric unit
PE	Pulmonary embolism
RCOG	Royal College of Obstetricians and Gynaecologists
SA	South Africa
VTE	Venous thromboembolism
WHO	World Health Organisation
VQ scan	Ventilation perfusion scan

List of Figures

Description **Pages**

List of Tables

Description **Page(s)**

JOURNAL ARTICLE

Diagnosis in women suspected of pulmonary embolism at Chris Hani Baragwanath Academic Hospital – A retrospective review

Siseko Gqola[1,3*], Langanani Mbodi[1,3], Yasmin Adam[2,3]

[1]Department of Obstetrics and Gynaecology, Charlotte Maxeke Johannesburg Academic Hospital.

[2] Department of Obstetrics and Gynaecology, Chris Hani Baragwanath Academic Hospital.

[3]Department of Obstetrics and Gynaecology, University of Witwatersrand.

[*]Corresponding author: 076 392 7940 sisekogqola@yahoo.com

Balboa Park, Oakdene Park drive, Oakdene, Johannesburg, 2190.

ABSTRACT

Pulmonary embolism accounts for 3.6% of maternal deaths in South Africa and 9.2% of all pregnancy-related deaths in the United States. This cross-sectional descriptive study sought to identify clinical factors and investigations used in pregnant or postpartum women who presented with suspected pulmonary embolism. Pulmonary embolism (PE) is often one of the conditions that are considered in the differential diagnosis of women attending/admitted at Chris Hani Baragwanath Academic Hospital Obstetric High Care Unit. Women investigated with Computed tomography pulmonary angiogram (CTPA) and/or Ventilation/perfusion (VQ) scans from July 1, 2018, to June 30, 2019, were included. STATA version 14.2 was used for data analysis of the variables.

The prevalence of PE was 9.4%. The mean age was 28.2 years (SD+-5.8). Most women, 126 (69.6%), were post-partum and 10 (7.9%) of those diagnosed and treated for PE. There were 81.7% women were delivered by caesarean section and 7.7% of them diagnosed with PE. Hundred (55.2%) women who had a CTPA or VQ scan were symptomatic, and the asymptomatic women had other clinical features suspicious of PE including persistent tachycardia of unknown cause. This was one of the indications for investigation in 159 (87.8%) women. Five (2.8%) women were diagnosed with deep vein thrombosis (DVT) on compressions ultrasound (CUS). Of the 181 scans (CTPA and VQ) done, 12 reports had features suggestive of Pulmonary Embolism.

Pulmonary embolism is a rare, but life-threatening condition which should be diagnosed and treated.

Keywords: Pregnancy, Pulmonary embolism, Diagnosis of Pulmonary Embolism, Venous Thromboembolism, CTPA, VQ scan.

Word count – Abstract 236

Manuscript

Introduction

Venous thromboembolism (VTE) is a rare but a life- threatening condition [1]. Pulmonary embolism (PE) during pregnancy, intra-partum and in the post-partum period is amongst the leading cause of maternal mortality globally but not in South Africa (SA) [2]. PE accounts for 3.6% of maternal deaths in SA and 9.2% of all pregnancy related deaths in the US [3]. The proportion of maternal deaths in SA from PE is on the rise with 1.9%, 3%, 3.6% in 2002-2004, 2014-2016, 2017-2019 triennia respectively [6-8].

According to World health organization (WHO), embolism was responsible for 3.1% of all maternal deaths worldwide between January 2003 and December 2012 [4]. A systemic review summarizing epidemiology of VTE in African populations, noted that the risk of PE was high after surgery in persons with high co-morbidities. The incidence of DVT ranged between 2.4% and 9.6% in post-operative patients. PE ranges between 0.14% and 61.5% in medical patients, with mortality rate of PE between 40% and 69.5% [5].

PE may present with non-specific symptoms which may mimic the physiological changes of pregnancy making diagnosis difficult [9]. There are also other medical conditions such as cardiac, respiratory and infective disorders which present with similar symptoms to PE [10].

The symptoms of PE may be non-specific, present with acute respiratory symptoms or more infrequently syncope and arterial hypotension with haemodynamic instability [11]. When there is a suspicion of PE, it needs to be confirmed with a computed tomography pulmonary angiography (CTPA) and/or ventilation/ perfusion (VQ) scan [12]. These modalities involve exposure to ionizing radiation and contrast media [13, 14]. Therefore, consent should be sought when these are performed. Recently algorithms using clinical parameters and blood tests were studied in order to decide whether a CTPA should be performed. It was shown that using an algorithm (with D-Dimer and clinical suspicion of a PE) a CTPA was avoided in the diagnosis of PE in 32%-65% of pregnant patients with suspected PE [15].

Clinical probability tests are not used at the CHBAH tertiary maternity unit. In instances where DVT is diagnosed, treatment should be commenced and no further investigation is necessary [12]. Compression ultrasonography (CUS) of the leg should be performed if there are any signs and symptoms of DVT. The sensitivity of whole leg CUS is 79% and specificity of 84% with low specificity for PE [16]. Normal compression ultrasonography should be followed by a CTPA or a VQ scan should there be clinical suspicion of PE [13]. Extensive research by Shahir *et al*, 2010 comparing CTPA versus VQ scanning demonstrates

that both have equivalent clinical negative predictive value (99% CTPA; 100% VQ scan) and image quality in pregnant patients [17].

CHBAH is a tertiary hospital with seven bedded High Care Area (HCA). PE is often one of the conditions that are considered in the differential diagnosis of many of the women admitted. Women that are admitted to the HCA are at risk of PE. The prevalence of PE in this setting is unknown. The clinical factors that prod doctors to order a CTPA are unknown.

The aim of the study was to characterize women with a PE and those suspected of having a PE in the Department of O&G at CHBAH from the 1st July 2018 to the 30th June 2019. The objectives were to identify clinical factors and investigations used in pregnant or postpartum women who presented with suspected pulmonary embolism.

Methodology

Study design and population

This was a retrospective record review. A sample size was not calculated. There were 18 989 deliveries in the unit during the year of study and 2987 (15.7%) were admitted to the high care obstetric unit. The study population was all women who had a CTPA/VQ scan. PE is diagnosed by CTPA in the presence of filling defects in pulmonary arteries or images suggesting pulmonary micro-embolism interpreted by certified experienced radiologists. A VQ scan is a nuclear test that uses a perfusion scan to delineate the blood flow distribution and ventilation scan to measure airflow distribution in the lungs.

Identification of VTE cases

We reviewed the medical notes of women who had a CTPA and/or VQ scan between 1st July 2018 and 30th June 2019. The data that were extracted were demographic information, clinical findings (history and examination at presentation), laboratory tests (FBC, D-dimer, CRP, Urea & Electrolytes), pregnancy information (booking blood results, gestational age, type of delivery and complications).

Data collection and hospital record review criteria for VTE diagnosis

There were 135 reports from the Nuclear Medicine Department's VQ scans and 46 CTPA reports from the Radiology Department. Forty reports were excluded because files could not be found and 4 files were further excluded due to missing data.

Data analysis

Data were recorded on a data sheet, and then put into an Excel Spreadsheet. The data was analyzed using STATA version 14.2 (StataCorp, 4905 Lakeway Drive, College Station, Texas 77845 USA). Categorical variables were described using frequencies and percentages. Continuous variables will be described using means (with SD) and medians (with IQR and ranges).

Ethics

Permission to perform the study was obtained from the clinical departments; Obstetrics & Gynaecology, Radiology and Nuclear Medicine. Permission from the CEO of CHBAH was obtained. Ethics approval for the study was obtained from the Human Research ethics Committee (Medical) at the University of the Witwatersrand (No. M191177).

Results

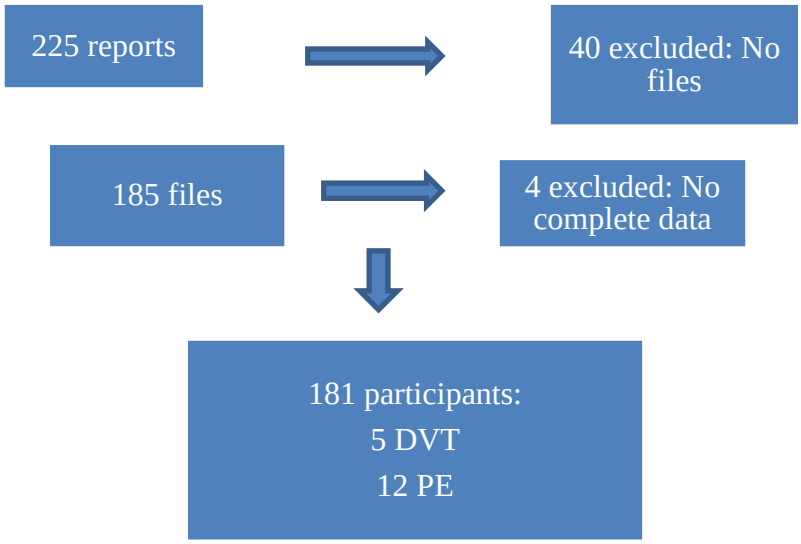


Figure 1. Description of the inclusion, exclusion and final number of files analyzed.

There were 135 women who were investigated with VQ scan and 46 women who were investigated using CTPA. There were 12 (6.6%) women diagnosed as having features of PE, 6/46 (13%) were diagnosed using CTPA and 6/135 (4.4%) with VQ scan. There were 5

(2.8%) women diagnosed with DVT. Table 1 is a summary of the women who were diagnosed as having a PE.

Table 1: Description of baseline characteristics of the 12 women diagnosed with Pulmonary Embolism (n=17)

Variable	
Mean Age (SD)	27 (±7.8)
Median Parity (range)	3 (1 -4)
Pregnancy period at diagnosis	
• Antepartum	7 (41.2%)
• Postpartum	10 (58.8%)
HIV status	
• Positive	5 (29.4%)
• Median VL (range)	6300 (n= 5 (148-45 500)
Medical co-morbidity	
• Hypertensive disorder of pregnancy	7 (41.2%)
• Anaemia	4 (23.5%)
• Pneumonia	2 (11.8%)
• Cardiomyopathy	1 (5.9%)
• Type 2 diabetes	1 (5.9%)
• None	2 (11.8%)
CXR abnormal	7 (41.2%) CTPA 6, VQ 1
Symptomatic*	17 (100%)
Median CRP, (range)	67 (4-309)
Median D-dimer	5.5mg/L
Delivery (Postpartum women)	
• Caesarean section	8 (80%)
• Normal vaginal	2 (20%)

*Symptoms – were respiratory

Baseline characteristics of all women investigated for a PE

Most women (126/181 (69.6%)) investigated for PE were in the post-partum period. Of those in the antenatal period 39/55 (70.1%) were in the third trimester and 13/55 (23.6%) were in the second trimester. The mean age was 28.24 years (SD±6.6). The median gestation at delivery was at 38 (IQR- 35-39; range 20-41). The median parity of the women was 2 (IQR- 1-3; range 1-6). There were 43 (23.75%) women who were HIV positive. Of these women,

34 had their CD4 counts recorded and the median CD4 count was 432 cells/mm^3 (IQR-285-747; range 126-1035) and median viral load of 14 014 copies (IQR 350-34 540; <20-45 500) in 37 women. The median booking haemoglobin was 12g/dl (IQR 11-12; range 8.3-14.6). There were 6 (3.3%) women with a Rhesus blood group that was negative. All the women had a negative syphilis (RPR) test. The median weight (n=80) was 71.5kg (IQR 58-85; range (30-140). The median BMI (n=79) was 30 kg/m2(IQR 24-35; 17-52). There were 6 (3.31%) women with a poor obstetric history. There were 28 (15.47%) women that had a previous caesarean delivery. Eight (3.7%) women had a multiple pregnancy; 86 (47.51%) women had hypertensive disorders of pregnancy (pre-eclampsia- 44 (51.16%), Chronic hypertension – 11 (12.79%), gestational hypertension -31 (36.04%). There were 37 (20.44%) women with anaemia. Sepsis was diagnosed in 35 (19.34%) women. There were 17 (9.39%) women who were diagnosed with a respiratory illness and 12 (6.63%) with a cardiac illness. There were 103 (n=126 (81.7%) women who were delivered by caesarean section and the other 23 (n=126 (18.3%) delivered vaginally. Twelve (n=103 (11.65%)) women had a relook laparotomy after caesarean delivery and 8 (n=103 (7.77%)) ended up having a hysterectomy. The mean estimated blood loss recorded at caesarean section was 578.6 ml (SD± 421.4). 1 (0.55 %) was reported to have had primary post-partum haemorrhage at caesarean delivery. Table 2 and Table 3 give a description of demographic baseline characteristics, medical and surgical co-morbidity respectively.

Table 2: Baseline characteristics of the participants (N=181)

Variable	
Age, mean (SD)	28 (±6.6)
Median gravidity (IQR; range)	2 (1-5; 1-6)
Median parity (IQR; range)	2 (1-3; 1-6)
Gestation at delivery, median (IQR; range)	38 (35-39; 20-41)
Time during pregnancy n (%)	
• 1st trimester	3 (7.2)
• 2nd trimester	13 (7.6)
• 3rd trimester	39 (21.1)
• Post-partum	126 (69.6)
HIV status n (%)	
• Positive	43 (24)
• Negative	138 (76)
Median CD4 count (IQR; range)	432 (n=34 (285-747; 126-1 035)
Median Viral load (IQR; range)	14 014 (n=37 (350-34 540; <20-45 500)
Median Hb at booking, (IQR; range)	12 (11-12; 8.3 14.6)
Median Body Mass Index, (IQR; range)	30 (n=79 (24-35;17-52)

Table 3: Descriptions of medical and surgical co-morbidity (N=181)

Variable	N (%)
Hypertensive disorder of pregnancy	86 (47.5)
Anaemia	37 (20.4)
Previous caesarean section	28 (15.5)
Multiple pregnancy	8 (3.7)
Cardiac disease	12 (6.6)
Respiratory illness	17 (9.4)
Relook laparotomy	12 (11.6)
Hysterectomy	8 (7.7)
Sepsis	35 (19.3)

*Some women had more than 1 co-morbidity

Clinical characteristics of the participants

More than half 100 (55.2%) were symptomatic whilst there were 81 (44.75%) who were asymptomatic. The asymptomatic women had other clinical features suspicious of PE. The symptomatic women presented features of one or more of the following symptoms. There was 94/100 (94%) who presented with shortness of breath, 14/100 (14 %) with cough, 25/100 (25 %) with chest pain, 12/100 (12 %) with leg swelling and 3/100 (3 %) had acute collapse. There were 159 women who had a tachycardia of unknown cause leading to investigation for PE at presentation, with median heart rate of 125 bpm (IQR 120-129; range (78-148).

Table 4: Description of clinical symptoms of those who were diagnosed with a PE (N=17)

N=17	N (%)
Shortness of breath	17(100)
Chest pains	2 (11.7)
Cough/haemoptysis	2(11.7)
Collapse	1(5.9)
Leg swelling	7(41.2) (5 DVT, 2 no DVT)

*Symptoms – were respiratory

Features of the diagnostic investigations

There are several tests that were done to assist clinicians in the diagnosis of PE. The median Hb for the patients at the time of investigation was 10.6g/dl (IQR 9.5-11.9; range 6.9-14.6).

The median D-dimer was 1.77mg/L (n=140, IQR 1.06-4.79; range 0.2-17.6). When categorized, women with D-dimer level < 0.5 were 13, those between 0.5 – 1 were 16 and majority of women had their d-dimer >1 at 111.

On the ECG report or prints, sinus tachycardia was the dominant feature in the interpretation of the ECG 60/90 (66.6 %). There were 23 (12.7%) women who had an abnormal chest radiography (CXR). Table 5 outlines the summary of clinical features and diagnostic investigations data results.

Table 5: Clinical features and diagnostic investigations (N=181)

Variable	**N (%)**
Symptomatic	100 (55)
Asymptomatic	81 (45)
Shortness of breath	94/100 (94)
Coughing	14/100 (14)
Chest pains	25/100 (25)
Leg swelling	12/100 (12)
Collapse	3/100 (3)
Median Hb (IQR; range)	10.6mg/L (9.5-11.9; range 6.9-14.6).
AKI	9 (5)
CRP, median (IQR: range)	106mg/L
White cell count, median (IQR; range)	14
D-dimer (n=140)	
• < 0.mg/L	13
• 0 – 1mg/L	16
• > 1mg/L	111
D-dimer, median ((IQR; range)	1.8mg/L (1.1-4.8; 0.2-17.6)
Abnormal CXR	23 (12.7)
Duplex compression US	5 (2.8)
Positive CTPA	6 (3.3)
Positive VQ scan	6 (3.3)

Discussion

There were 9.4% of women who had a proven VTE in our study. A study published in Lancet in 1999 on thrombosis in pregnancy reported that in patients who are investigated for PE, less than 10% will have a positive finding [3].

Our results showed that clinical suspicion for PE differed between the trimester and pregnancy period in women who are investigated. The finding of 68.11% who were in the post-partum period correlates with what is reported in literature where more than half of

pregnancy-related VTE occurred during the postpartum [18]. The mean age of the overall women who were suspected of PE and those in whom the diagnosis was confirmed did not differ (27 years versus 29 years). Perhaps this represents the age group where most women delivered in this hospital and not necessarily the age group where PE suspicion is high or diagnosis is confirmed.

Recent surgery is associated with an increased risk of PE [19]. In our study 103 of the 126 (82%) women that were post-partum had a caesarean delivery. The incidence of caesarean section at CHBAH in 2018 was at 44% [8]. In 2019, a South African study concluded that drivers for the initiation of VTE prophylaxis included pre-eclampsia, caesarean delivery, and immobility [20]. In our study, 8 of the 17 women (47.1%) who had VTE were delivered by caesarean section.

One in five people in South Africa aged between 15 and 49 years is believed to be infected with HIV [21]. There were 43 women that tested positive for HIV in our study. HIV has been studied and shown to have a moderate risk for hyper coagulation with an increase in some clotting factors and reduced function of natural anti-fibrinolytics [22]. In our study 5 of the 17 women with VTE were HIV positive. There were 39 women who were HIV positive that were not diagnosed with PE. HIV positivity was not shown to increase the risk of thrombosis when assessing the general study population.

There were only 15 women with medical co-morbid diseases in the study. This again shows that the existence of co-morbid medical conditions did not increase the risk to be investigated for PE as well as the actual diagnosis of PE. However, our study was of the convenience sample limited to those women admitted at the High Care setting.

The measured median D-dimer was raised in all women with a VTE and those whom did not have the diagnosis. The presence of a clinical suspicion of a PE and a raised D-Dimer is an indication for PE investigation [23]. D-dimer results are significantly influenced by medical conditions, post-operative state and by pregnancy as it is a by-product of the blood clotting and breakdown process that can be measured [24].

The value of CRP was higher in those treated for puerperal sepsis. Some serum biomarkers were collected as these may be deranged in patients with pre-eclampsia. Liver dysfunction and acute kidney injury was seen in those with severe features of pre-eclampsia. Seven (3.8%) women had a placenta abruption and 9 (5%) women had acute kidney injury in the

group diagnosed and due to complicated pre-eclampsia.

All women in our study had a CXR done and the 6 women who were diagnosed with PE through CTPA had abnormal CXR reported. Only 1 woman who was diagnosed through the VQ scan had an abnormal CXR. All CXR investigations for those with DVT were normal. The diagnosis of PE in pregnancy and during the post-partum period poses a challenge. Recent clinical guidelines identify compression venous ultrasound as the best way to diagnose deep venous thrombosis in pregnancy and CTPA as the best way to diagnose pulmonary embolism in pregnancy [25]. There were 46 women that had CTPA and 135 VQ scan in our study. CTPA and VQ scan results reported negative features for PE in 40/46 (86.9%) and 129/135 (95.5%) respectively.

One woman died who was investigated for PE and had a confirmed PE on CTPA and post-mortem. PE is a cause of death in 3.6%-10% (US and SA) Based on clinical suspicion, a large number of patients are likely going to be initiated on a therapeutic anticoagulation. However, imaging will only diagnose or confirm a few of those patients as having a PE. Most clinicians will opt to continue with treatment for PE and keep these patients in High Care setting because of the associated mortality with PE. We need to strike a balance between preventing deaths from PE and avoiding over diagnosis.

Limitations of the study

Due to the retrospective nature of the study, there was missing information from the file which affected the final results. These include missing information from the Antenatal cards.

The poor filing system and difficulty in accessing hardcopy files resulted in the retrieval of fewer files than expected.

Conclusion:

Pulmonary embolism is a rare, but severe condition. It is therefore important to diagnose and treat appropriately.

Conflict of interest

The authors declare no conflict of interest

References

1. Practice bulletin no. 123: Thromboembolism in pregnancy. Obstet Gynecol. 2011 Sep; 118(3):718-729. doi: 10.1097/AOG.0b013e3182310c4c.
2. ISTH Steering Committee for World Thrombosis Day. Thrombosis: a major contributor to the global disease burden. J Thromb Haemost. 2014 Oct; 12(10):1580-90. doi:10.1111/jth.12698.
3. Greer IA. Thrombosis in pregnancy: maternal and fetal issues. Lancet. 1999 Apr 10;353(9160):1258-65. doi: 10.1016/S0140-6736(98)10265-9.
4. Say L, Chou D, Gemmill A et al. Global causes of maternal death: a WHO systematic analysis. *Lancet Glob Health* 2014; 2: e323–33. http://dx.doi.org/10.1016/S2214-109X(14)70227-X.
5. Danwang C, Temgoua MN, Agbor VN et al. Epidemiology of venous thromboembolism in Africa: a systematic review. J Thromb Haemost. 2017 Sep; 15(9):1770-1781. doi: 10.1111/jth.13769. Epub 2017 Aug 10. PMID: 28796427.
6. National Committee on Confidential Enquiries into Maternal Deaths (South Africa). South Africa Saving Mothers 2002-2004. Pretoria, South Africa: Department of Health (South Africa), 2006.
7. National Committee on Confidential Enquiries into Maternal Deaths. Saving Mothers 2014 - 2016: Seventh Triennial Report on Confidential Enquiries into Maternal Deaths in South Africa: Executive Summary. Pretoria: National Department of Health, 2018.
8. National Department of Health, South Africa. Saving Mothers 2017: Annual Report on Confidential Inquiries into Matenal Death in South Africa. Pretoria: NDoH, 2017.
9. Konstantinides SV, Torbicki A, Agnelli G. ESC Guidelines on the diagnosis and management of acute pulmonary embolism. European Heart Journal (2014)35, 3033–3080. doi:10.1093/eurheartj/ehu283
10. Pollack CV, Schreiber D, Goldhaber SZ et al. Clinical characteristics, management, and outcomes of patients diagnosed with acute pulmonary embolism in the emergency department: initial report of EMPEROR (Multi-center Emergency Medicine Pulmonary Embolism in the Real World Registry). J Am Coll Cardiol2011;57(6):700 – 706
11. Thames MD, Alpert JS, Dalen JE. Syncope in patients with pulmonary embolism. JAMA. 1977 Dec 5; 238(23):2509-11. PMID: 578884.

12. Royal College of Obstetricians and Gynaecologists. *Thromboembolic Disease in Pregnancy and the Puerperium: Acute Management. Green-top Guideline No. 37b*. London: *RCOG* 2015.
13. Chung JK, Broga DW, Sethi NN et al. Female Breast Radiation Exposure During CT Pulmonary Angiography. *Am J Roentgenol*. 2005;185(5):1228–33. DOI:10.2214/AJR.04.0770
14. Webb JAW, Thomsen HS, Morcos SK et al. The use of iodinated and gadolinium contrast media during pregnancy and lactation. *Eur Radiol.* 2005;15(6):1234–40. DOI 10.1007/s00330-004-2583-y
15. Van der Pol LM, Tromeur C, Bistervels IM et al. Pregnancy-Adapted YEARS Algorithm for Diagnosis of Suspected Pulmonary Embolism. N Engl J Med. 2019 Mar 21; 380(12):1139-1149. doi: 10.1056/NEJMoa1813865.
16. Da Costa Rodrigues J, Alzuphar S, Combescure C et al. Diagnostic characteristics of lower limb venous compression ultrasonography in suspected pulmonary embolism: a meta-analysis. J Thromb Haemost. 2016 Sep; 14(9):1765-72. doi: 10.1111/jth.13407.
17. Shahir K, Goodman LR, Tali A et al. Pulmonary embolism in pregnancy: CT pulmonary angiography versus perfusion scanning. *Am J Roentgenol* 2010;195(3):214–20. DOI: 10.2214/AJR.09.3506.
18. Liu S, Rouleau J, Joseph KS et al. Epidemiology of pregnancy-associated venous thromboembolism: a population-based study in Canada. J Obstet Gynaecol Can. 2009 Jul; 31(7):611-620. doi: 10.1016/S1701-2163(16)34240-2.
19. Clark SL, Belfort MA, Dildy GA et al. Maternal death in the 21st century: causes, prevention, and relationship to cesarean delivery. Am J Obstet Gynecol. 2008 Jul; 199(1):36.e1-5; discussion 91-2. E7-11. doi: 10.1016/j.ajog.2008.03.007.
20. Naidoo P, Mothilal R, Snyman LC. Assessment and management of venous thrombo-embolism risk during pregnancy and the puerperium (SAVE): The South African cohort. S Afr Med J. 2019 Feb 26; 109(3):186-192. doi: 10.7196/SAMJ. 2019.v109i3.13487.
21. Eyal A, Veller M. HIV and venous thrombotic events. S Afr J Surg. 2009 May;47(2):54-6. PMID: 19626781.
22. Funderburg NT, Lederman MM. Coagulation and morbidity in treated HIV infection. Thromb Res. 2014 May;133 Suppl 1(0 1):S21-4. doi: 10.1016/j.thromres.2014.03.012. PMID: 24759134; PMCID: PMC4021706

23. To MS, Hunt BJ, Nelson-Piercy C. A negative D-dimer does not exclude venous thromboembolism (VTE) in pregnancy. *J Obstet Gynaecol*. 2008;28(2):222-223. doi:10.1080/01443610801915975.
24. Sikora-Skrabaka M, Skrabaka D, Ruggeri P et al. D-dimer value in the diagnosis of pulmonary embolism – may it exclude only? J Thoracic Disease. 2019: 11 (3):664-672. Doi: 10.21037/jtd.2019.02.88.
25. Rosenberg V.A, and Lockwood, C.J. Thromboembolism in pregnancy. *Obstet Gynecol Clin North Am*. 2007Sep;34(3):484-500.

APPENDIX A: Approved Research Protocol

DIAGNOSIS IN WOMEN SUSPECTED OF PULMONARY EMBOLISM AT CHBAH – A RETROSPECTIVE REVIEW.

Name: **Siseko Gqola**

Student Number: **0701953E**

Supervisor:

Prof. Y. Adam: BSc (Durban), MBBCh (Wits), FCOG (SA), MSc (Wits).

Co-supervisors:

Dr G. Rubin: MBBCh (Wits), DA (SA), FCRad (Diag) (SA), MMed (Wits).

Dr L. Mbodi: Dip Nurs(VNC), MBChB (Medunsa), Dip.Obst (SA), FCOG (SA), MMed (Wits), MSc (Wits), Cert. Gynae Oncology (SA).

Contents

Abbreviations

ATS/ STR - American Thoracic Society and the Society of Thoracic Radiology

CHBAH – Chris Hani Baragwanath Academic Hospital

CTPA - Computed tomography pulmonary angiogram

CXR – Chest x-ray

DVT – Deep vein thrombosis

ECG - Electrocardiogram

HCA - High care area

HIV- Human immunodeficiency virus

LMWH - Low molecular weight heparins

MOU _ Midwife obstetric unit

PE – Pulmonary embolism

SA - South Africa

VTE – Venous thromboembolism

VQ scan - Ventilation/perfusion scan

Diagnosis in women suspected of pulmonary embolism at CHBAH – a retrospective review.

1. Background

Introduction:

Pregnancy is associated with physiologic and anatomical changes that can have a significant risk of thromboembolism. Pulmonary embolism (PE) is a life-threatening condition that continues to pose a challenge in the diagnosis process globally (1). It is in the top 10 of the maternal causes of death in South Africa (SA) and there is a concern with death from embolism reported at 3% between 2014 -2016 (2).

Thromboembolism is also associated with a high morbidity (1). Post thrombotic syndromes are one of the long term complications, patients who had recovered from deep vein thrombosis (DVT) still experience symptoms (3).

The signs and symptoms are non-specific and often similar to pregnancy symptoms of swelling of legs, dyspnoea and tachycardia. It is often not the most favoured diagnosis with pneumonia, TB, HIV related lung disease and sepsis being part of the differential diagnosis (3). The use of clinical decision algorithms together with D-Dimer levels have shown different sensitivity and specificity in pregnant women making computed tomography pulmonary angiogram (CTPA's) or Ventilation/Perfusion (VQ) scans the most reliable tests in pregnancy (4).

The Wells score (see Appendix A) and Geneva score (see Appendix B) are the commonly used probability tests which have been shown to be effective in non-pregnant women. These tests are clinical prediction rules that can be used to determine the pre-test probability of a diagnosis of pulmonary embolus, using risk factors and clinical features. These tests are not used to triage patients at Chris Hani Baragwanath Academic Hospital (CHBAH) obstetrics unit, making CTPA and VQ scan the tests most often used in women without a proven DVT.

CTPA and VQ scanning are the gold standard for making the diagnosis of a PE. CTPA is a diagnostic test that uses computed tomography angiography to obtain an image of the pulmonary vessels and the VQ scan is a nuclear medicine scan that uses radio-active material to examine ventilation and perfusion of the lungs (4). However, these two radiological tests

are best in non-pregnant patients. There are challenges with interpretation of these studies during pregnancy due to the physiological changes of pregnancy (5).These tests also pose a risk because of ionising radiation and the contrast media to the mother and the foetus (5).

CHBAH is a tertiary hospital that delivers approximately 20 000 women/ year. Women are referred to this hospital from four midwife obstetrics unit (MOU's), a district hospital and two regional hospitals. In this study we propose to assess the clinical parameters that are used to consider these tests and also to describe the findings and incidence of thromboembolism

Literature review

1.1 Venous thromboembolism (VTE)

DVT and PE are collectively referred to as VTE. The risk of VTE is considered higher during pregnancy and the puerperium (13). Deep vein thrombosis (DVT) accounts for most of the cases of pregnancy-associated VTE with two most common presenting symptoms of pain and swelling of the lower extremities (6).

1.2 Pulmonary embolus

Definition

Pulmonary embolism is defined as a blood clot in the lung pulmonary arterial tree. The blood clot may develop in the leg, pelvic or arm veins, then breaks off from the vein wall travelling through the heart into the lung arteries (1).

A massive PE is dangerous and is one that can cause haemodynamic instability.

Epidemiology

The overall rate of VTE in and around pregnancy (including both pregnancy and the post-partum) is 107 per 100 000 per year (3).The prevalence of DVT in pregnant and post-partum women in Africa varies in between 448 per 100 000 per year and 380 per 100 000 per year in 2003 respectively (7). It is higher in patients in the intensive care unit and those diagnosed with Tuberculosis. Pulmonary embolism has its prevalence at 1.4% in one study that reviewed the prevalence of pulmonary embolus in pregnant and post-partum women (7).

PE during pregnancy, intra-partum and in the post-partum is among the leading causes of maternal morbidity and mortality globally but not in South Africa (SA) (8). Some studies have shown similar risks in the different trimesters and other have shown an increase in the third trimester and post-partum, and with an increase further post-partum (11.9 fold) (3).

Sultan et al reported an absolute rate of VTE roughly similar in the first, second trimester and the late post-partum period with incidence rate of 30, 40 and 35 per 100 000 per year respectively (3). The rate of VTE was higher in the third trimester and peaked in the early post-partum of 6.1 fold and 22 fold increase in risk respectively (3).

Embolism as a direct cause of death accounted for more deaths than its global average in southeastern Asia (12.1%) and eastern Asia (11.5%) (8).The rate of maternal causes of deaths from embolism reported in the different triennial reports of the confidential inquiry into maternal deaths of SA was 1.9% (2002-2004), 1.9% (2008-2010), 2.3% (2012-2013) and 3% (2014-2015) (9-12).Reflecting a significant rise in death from embolism in SA.

Risk factors

The most important individual risk factors for VTE in pregnancy are personal history of thrombosis and the presence of a thrombophilia (13). The risk of recurrent VTE is increased in pregnancy and about close to a quarter of all cases of VTE in pregnancy are recurrent events (13). The risk of VTE is higher in pregnancy and the risk factors within a pregnancy are previous VTE, thrombophilia, autoimmune disease, malignancy, immobility, surgery, age and obesity (14). Caesarean delivery had a fourfold risk of VTE than following vaginal delivery (15). Caesarean delivery, particularly when complicated by post-delivery haemorrhage or infection, as well as any of the medical factors complicating pregnancy such as obesity, hypertension, autoimmune disease, heart disease, sickle cell disease and preeclampsia increase risk of VTE especially PE post-partum (13). Pre-pregnancy, antenatal and post-partum risk assessment is key.

Pathophysiology

Venous stasis, vascular injury and hypercoagulable states (Virchow triad) are all responsible for the increased risk of VTE in pregnancy. Venous stasis due to pressure on the inferior vena cava increased secondary to the mechanical interference by the gravid uterus. This interference is greatest in the supine position. Vascular injury from medical conditions or any other risk factor of vasculopathy are added risks (16). Changes in the normal functioning of the coagulation system, with fibrinogen, Factor VII, Factor VIII, Factor X and Von Willebrand factor are increased in pregnancy. There are no changes in procoagulants Factor II, Factor V and Factor IX and in anticoagulants Protein C and Anti-thrombin. There appears to be a decrease in anticoagulant Protein S (16). Inherited thrombophilia's also contribute to the development of VTE in pregnancy (17).

Human immunodeficiency virus (HIV) infection has been recognised as a pro-thrombotic condition (18).The use of protease inhibitors has been associated with thrombosis in how it interferes with hepatic metabolism, association with lipodystrophy and the HIV-positive patients with fat redistribution (19).

Clinical features

The clinical features associated with thromboembolism evaluation of suspected PE in pregnancy include shortness of breath, pleuritic chest pain, hypoxemia, tachycardia, leg swelling and to a lesser extent haemoptysis, syncope, cough, unexplained hypotension and may present with any type of chest pain or discomfort (20).

Diagnosis

Previously there has been challenges with research in diagnostic evaluation of pregnant women with suspected PE. In 2018 a prospective study was done to validate a diagnostic strategy in pregnant women suspected of PE. This diagnostic strategy based on assessment of clinical probability, D-dimer measurement, compression ultrasound and CTPA can safely rule out PE (30).

The diagnostic workup for suspected PE starts with an evaluation for peripheral DVT. Diagnosis of DVT is done by performing bilateral venous compression ultrasound of lower extremities. A venogram may be done if the ultrasound results are unclear. This radiological investigation uses an injection of a contrast-dye and fluoroscopy to take

pictures of the leg veins. It is not recommended in pregnancy due to contrast usage (20).

It is recommended that a chest x-ray (CXR) as the first radiation-associated procedure in the imaging work-up in pregnancy is done (20). It is not useful in the diagnosis of pulmonary embolism but useful in excluding other causes such as pneumonia, pulmonary oedema and pneumothorax (4).An enlarged pulmonary artery, regional oligaemia and in patients with pulmonary infarction, a peripherally located wedge-shaped opacity may be seen. The sensitivity and positive predictive values of these features on CXR is quite low (4).

The most frequent abnormalities on ECG consistent with acute PE are sinus tachycardia, S1Q3T3 pattern, right bundle branch block and T wave inversion in precordial leads (21).

Royal college of obstetricians and gynaecology (RCOG) recommend that in a normal CXR, a VQ scan should be the next imaging test rather than CTPA. When CXR is abnormal a CTPA should be done as it may diagnose other lung pathologies (20).

Alternative or repeat testing should be carried out where VQ scan or CTPA is normal but clinical suspicion of PE remains. In patients with a non-diagnostic VQ scan in whom a decision is made to further investigate, a CTPA is recommended (20).

1.3 Investigations with pre-test probability assessment

Pre-test probability tools in the general population are used to determine the likelihood of a PE. Wells and Geneva scores are the commonly used probability tests which have been shown to be effective in non-pregnant women (22). These tests are clinical prediction rules that can be used to determine the pre-test probability of a diagnosis of pulmonary embolus using risk factors and clinical features. These tests can then further guide the diagnostic approach toward imaging or D-dimer testing (22). These existing rules do not consider pregnancy and pregnancy related risk factors.

1.4 Role of D-dimers and compression duplex ultrasound

D-dimer is a fibrin degrading product that is detected in the blood following blood clot degradation.

In pregnancy and post-partum

In pregnancy a progressive rise in D-dimer levels with advancing gestation is noted with levels becoming high abnormal at term and in the postnatal period (23). D-dimer testing should be performed with caution in the investigation of acute VTE in pregnancy (23). It may not be used to rule out PE but the greatest advantage to its characteristics are its negative predictive value as a diagnostic testing tool (24).

The American Thoracic Society and the Society of Thoracic Radiology (ATS/STR) recommend bilateral venous compression ultrasound of the lower extremities only in patients presenting with signs and symptoms of DVT, but recommend proceeding to imaging of the chest in all other patients (20).

1.5. CTPA

The guidelines from the ATS/STR recommend using CTPA only in patients and those pregnant with no signs or symptoms of DVT or with an abnormal CXR (20).

The CTPA is readily available during both in and after hour services, minimally invasive and fast. It can reveal other possible causes of the symptoms and signs (4). CTPA is either positive/diagnostic, negative/non-diagnostic and/or inconclusive/indeterminate. CTPA has high sensitivity and specificity demonstrating 83% and 96% respectively using clinical prediction rules (4).

VQ scan after an indeterminate CTPA

There is little literature pertaining to VQ scans performed after indeterminate CTPA (25).There is very low incidence of PE diagnosed on VQ imaging after a suboptimal CTPA, most suboptimal CTPA may rule out central PE (26).

1.6 Ventilation/Perfusion scan

The likelihood of detecting PE by VQ scan in pregnant women is reported similar to that in non-pregnant, age- and sex-matched patients (5).The VQ scan is preferred particularly in renal failure, contrast material allergies, young women and patients who cannot fit in the CT scanner. Cost and availability of the machine may be an issue for certain institutions. They are interpreted along with a correlative chest radiograph performed within 12-24 hours (4).

A peripheral wedge-shaped perfusion defect in a lobar, segmental or sub-segmental distribution without a corresponding ventilation defect raises the concern for the presence of PE.

CTPA after intermediate probability VQ scan

Any decision made to proceed to CTPA in patients with an intermediate probability VQ scan should be made with a clear understanding that CTPA has limited accuracy in the diagnosis of PE outside the central pulmonary arteries and their branches (27). However with improved technological developments, CTPA may improve with time and guidelines may change (27). Extensive research into comparison of CTPA versus VQ scanning show that both have equivalent clinical negative predictive value (99% CTPA; 100% for VQ scan) and image quality in the care of pregnant patients (25).

1.7 Exposure to ionising radiation and contrast agents

The technologic advances in CT scan have had a dramatic impact on the diagnosis and management of almost all patients with complex thoracic and cardio-pulmonary disease, including pulmonary thromboembolism (28).

CTPA delivers a minimum of radiation dose of 2.0 rad (20 mGy) to the breasts of an average-sized woman. The potential latent carcinogenic effects of such radiation exposure at this time remains unknown (28).

Foetal exposure to ionizing radiation is demonstrated to be lower with CTPA compared to the VQ scan whilst maternal exposure is higher with CTPA when compared to VQ scan (5).

The radiologist and the clinicians need to work together to develop better selection criteria of patients for CTPA. Reduce the radiation exposure of patients and shield the eyes, thyroid gland, and female breasts whenever possible (28).

Foetal exposure to iodinated contrast medium and any associated iodide is likely to be short-lived. Depression of foetal thyroid function is the most important potential harmful effect (29).

2. The research problem

CHBAH is a tertiary hospital with a seven bedded High care area (HCA). There were no deaths due to VTE in the last three years. VTE is often one of the conditions that are

considered in the differential diagnosis of many of these women. The caesarean section rate has increased from 35% in 2011 to 45% in 2019 reflecting the fact that the number of high risk women has increased. Overall obesity and diabetes, two other risk factors for VTE has also increased in the population that is served at CHBAH. The number of radiological examinations to exclude PE has increased over the past few years, with at least one VQ scan or CTPA being requested every week

This study was developed to describe these women being investigated. Findings from the study will help with understanding data, which could mean that policies need to be reviewed with the current work-up strategies.

The first step is to evaluate the current data that we have. This will open up further research into the work up, diagnosis and management of PE at CHBAH. Audit information is very important for the obstetrician and gynaecologist, radiologist, medical and critical care teams.

3. The main objective.

The aim is to describe the clinical factors and investigations in pregnant or postpartum women who were suspected of having a PE who were admitted to the department of Obstetrics, CHBAH in July 2018 to June 2019.

Specific Objectives

- To describe the socio-demographic and clinical factors in these women
- To determine the prevalence of PE
- To identify the clinical reasons for performing a VQ scan or a CTPA
- To describe the findings of the VQ scan and the CTPA.

4. Methodology

4.1. Setting

The study will take place at CHBAH in the Department of Obstetrics &Gynaecology. It is a tertiary academic hospital in Soweto, Johannesburg which performs approximately 23 000 deliveries a year. The hospital is a referral hospital for 56 local clinics, 7 MOU's and 1 district hospital. It is also a referral hospital for 2 regional hospitals in Gauteng and 2 in the North West province.

4.2 Study population

All women who are pregnant or who have had a pregnancy in the last 42 days that have had a CTPA or a VQ scan.

4.3 Sample size

All patients investigated at the radiology department from 01 July 2018 – 30 June 2019. This is a descriptive study and a sample size was therefore not calculated. The researchers are a expecting a number of 50 patients.

4.4 Study design

Cross-sectional retrospective study.

Data management:

4.5 Data collection

The registers in the Department of radiology and the Maternity HCA will be used to identify women who have had any of these tests from 01 July 2018- 30 June 2019. The maternity records will then be requested from the records Department. The demographics, pregnancy related factors and reasons for the investigation will be recorded. The final diagnosis for the woman's signs and symptoms will be recorded (eg pneumonia, pregnancy related sepsis, etc). The original CTPA/VQ scan will be used to extract information on the tests. There is a list kept by the administrative team in the radiology department where and all monthly requests are recorded. The list is categorised into each department the request had been sent from.

Variables that will be extracted: age, parity, weight, height, MUAC, history of smoking, HIV (including CD4 and ART use), booking haemoglobin, blood group, trimester that the test was performed, D-Dimer, final diagnosis, reason for investigation, co-morbidities, blood loss at delivery and some biochemical work up.

All reports and findings of the CTPA and VQ scan were reported in the final report by a radiologist.

Data sheet include in Appendix C.

4.6 Data analysis

Data will be recorded on a data sheet, then put into an Excel Spreadsheet. The data will be exported to Strata version 14.2 for analysis. All categorical variables will be described using frequencies and percentages. All continuous variables will be

described using means (and SD) and medians (and IQR with ranges)

4.7 Limitations

- Missing information from the file.
- Lost files

5. Ethics

Access permission from the clinical departments – Obstetrics & Gynaecology and Radiology will be obtained. Permission from the CEO of CHBAH will be obtained. An application to the Human Research Ethics Committee (HREC) of The University of the Witwatersrand will be made. All patients participating in the study will be given a study number to ensure anonymity of data and all data will be stored electronically, with a key or code available only to the primary researcher. The patient hospital number will be recorded because we have to obtain records from different departments. This will be kept separately in a secure place.

6. Funding

The study will not need funding. The cost of printing and the use of the computer will be borne by the researcher

7. Permission from institution

Permission will be sought from the chief executive officer (CEO) of CHBAH to conduct the study at CHBAH.

8. Timeline

a. Ethics application will be made on 25 October 2019
b. Participants will be recruited and data collected over a four month period between 01 November 2019 – 29 February 2020
c. Data analysis will be performed over 01 March 2020 – 30 April 2020
d. The write up will be done from 01 May 2020 – 31 August 2020

9. Intention to disseminate

A copy of the write-up will be disseminated to the College of Obstetrics and Gynaecology of South Africa and a copy will be submitted to The University of the Witwatersrand. There is also an intention to submit the research to publish in medical journals and for presentation at academic meetings.

10. Conflict of interest

There are no conflicts of interest

References

1. Scott. JR. Thromboembolism in pregnancy: Practice Bulletin guidelines. *Obstertrics and Gynaecology* 2011;118(3):718–29. DOI:10.1097/AOG.0b013e3182310c4c. [Access 26/04/2019]
2. Pattinson RC, ed. Saving Mothers: Fifth report on Confidential Enquiries into Maternal Deaths in South Africa 2014 - 2016. Pretoria: National Department of Health, 2017. [accessed 28/04/2019]
3. Greer IA. Thrombosis in pregnancy: maternal and fetal issues. Lancet. 1999 Apr 10;353(9160):1258-65. doi: 10.1016/S0140-6736(98)10265-9.
4. Sultan AA, West J, Tata LJ, Fleming KM, Nelson-Piercy C. Risk of first venous thromboembolism in and around pregnancy: a population-based cohort study. *British Journal of Haematology* 2011;156;366-373. doi:10.1111/j.1365-2141.2011.08956.x [accessed 26/04/2019]
5. Moore AJE, Wachsmann J, Camarthy MR, Panjikaran L, Tanabe Y, Rajiah P. Imaging of acute pulmonary embolism: an update. *CardiovascDiagnTher.* 2018;8(3):225-243. http://dx.doi.org/10.21037/cdt.2017.12.01
6. Harris BS, Bishop KC, Kuller JA. Radiologic Aspects of the Diagnosis of Pulmonary Embolism in Pregnancy. *Clin Obs Gynecol* 2018;61(2):219– DOI:10.1097/GRF.0000000000000366 [Accessed 05/05/2019]
7. Saha P, Black S, Breen K, Patel A, Modarai B, Smith A. Contemporary management of acute and chronic deep venous thrombosis. British Medical Bulletin, 2016, 117:107–120. DOI: 10.1093/bmb/ldw006 [Accessed 28/04/2019]

8. Danwang C, Temgoua MN, Agbor VN, Tankeu AT, Noubiap JJ. Epidemiology of venous thromboembolism in Africa: a systematic review. *J ThrombHaemost* 2017; 15: 1770–81. DOI: 10.1111/jth.13769 [Accesed 26/04/2019]
9. Say L, Chou D, Gemmil A, Daniels J, Temmerman M. Global causes of maternal death: a WHO systematic analysis. *Lancet Glob Health* 2014;2: e323–33. http://dx.doi.org/10.1016/S2214-109X(14)70227-X
10. Moodley J, ed. Saving Mothers: Third report on Confidential Enquiries into Maternal Deaths in South Africa 2002 - 2004. Pretoria: National Department of Health, 2006.
11. Moodley J, ed. Saving Mothers: Fourth report on Confidential Enquiries into Maternal Deaths in South Africa 2005 - 2007. Pretoria: National Department of Health, 2009.
12. Moodley J, ed. Saving Mothers: Fifth report on Confidential Enquiries into Maternal Deaths in South Africa 2008 - 2010. Pretoria: National Department of Health, 2012.
13. Moodley J, ed. Saving Mothers: Sixth report on Confidential Enquiries into Maternal Deaths in South Africa 2011 - 2013. Pretoria: National Department of Health, 2015.
14. Royal College of Obstetricians and Gynaecologists. Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium. Green-top Guideline No. 37a. London: *RCOG* 2015. [Accessed 05/05/2019]
15. Balillari G, Londero AP, Brenner B, Nauffal D, Del Molino F. Recurrence of venous thromboembolism in patients with recent gestational deep vein thrombosis or pulmonary embolism: Findings from a RIETE Registrty. *European Journal of Internal Medicine* 2016;32;53–59. http://dx.doi.org/10.1016/j.ejim.2016.02.013
16. Blondon M, Casini A, Hoppe KK, Boehlen F, Righini M, Smith NL. Risks of Venous Thromboembolism After Cesarean Sections: A Meta-Analysis. *Chest* 2016 Sep;150(3):572-96. doi:10.1016/j [Accessed 14/06/2019]
17. Virkus RA, Lokkergaard O, Lidegaard O, Nielsen AL. Risk factors for venous thromboembolism in 1.3 million pregnancies. A nationwide prospective cohort. *PLoS ONE* 9(5): e96495. doi:10.1371/journal.pone.0096495 [Accessed 04/05/2019]
18. Dado CD, Levinson AT, Bourjeily G. Pregnancy and Pulmonary Embolism. *Clin Chest* Med 2018;39:525–537. https://doi.org/10.1016/j.ccm.2018.04.007
19. Harling G, Moyo S, McGovern ME, Mabaso M, Marra G, Rehle T. National South African HIV prevalence estimates robust despite substantialtestnon-participation. *S Afr Med J* 2017;107(7);590-594. DOI:10.7196/SAMJ.2017.v107i7.11207. [Accessed 14/06/2019]

20. Bibas M, Biava G, Antinori A. HIV-Associated Venous Thromboembolism. *Mediterr J Hematol Infect Dis* 2011, 3:e2011030. DOI 10.4084/MJHID.2011.030 [Accessed 14/06/2019]
21. Leung AN, Bull MT, Lockwood CJ, Boiselle PB. An official American Thoracic Society/Society of Thoracic Radiology clinical practice guideline: Evaluation of suspected pulmonary embolism in pregnancy. *Am J Respir Crit Care Med*. 2011;184(10):1200–8. DOi: 10.1164/rccm.201108-1575ST [Accessed 04/05/2019]
22. Calvo-Romero JM1, Lima-Rodriguez EM. Electrocardiographic adnormalities in acute pulmonary embolism. *Eur J Gen Med* 2005; 2(4):150-152. [05/06/2019]
23. Royal College of Obstetricians and Gynaecologists.Thromboembolic Disease in Pregnancy and the Puerperium: Acute Management. Green-top Guideline No. 37b. London: *RCOG* 2015.n [Accessed 04/04/2019]
24. Choi H, Krishnamoorthy D. The diagnostic utility of D-dimer and other clinical variables in pregnant and post-partum patients with suspected acute pulmonary embolism. *International Journal of Emergency Medicine* (2018)11:10. https://doi.org/10.1186/s12245-018-0169-8
25. To MS, Hunt BJ, Nelson-Piercy C. A negative D-dimer does not exclude venous thromboembolism (VTE) in pregnancy, *Journal of Obstetrics and Gynaecology* 2008;28(2), 222-223. DOI: 10.1080/01443610801915975 [Accessed 23/06/2019]
26. Shahir K, Goodman LR, Tali A, Thorsen KM, Hellman RS. Pulmonary embolism in pregnancy: CT pulmonary angiography versus perfusion scanning. *Am J Roentgenol* 2010;195(3):214–20. DOI: 10.2214/AJR.09.3506. [Accessed 20/06/2019]
27. Curtis BR, Cox M, Poplawski M, Lyshchik A. Low yield of ventilation and perfusion imaging for the evaluation of pulmonary embolism after indeterminate CT pulmonary angiography. *Emerg Radiol*. 2017;24(5):525–30. DOI: 10.1007/s10140-017-1503-9 [Accessed 20/06/2019]
28. Stone E, Roach P, Bernard E, Briggs G, Faulder K. Use of computed tomography pulmonary angiography in the diagnosis of pulmonary embolism in patients with an intermediate probability ventilation/perfusion scan. *Intern Med J*. 2003;33(3):74–8. [Accessed 04/06/2019]
29. Chung JK, Broga DW, Sethi NN, Camacho MA, Parker MS, Hui FK. Female Breast Radiation Exposure During CT Pulmonary Angiography. *Am J Roentgenol*. 2005;185(5):1228–33. DOI:10.2214/AJR.04.0770 [Accessed 05/06/2019]

30. Webb JAW, Thomsen HS, Morcos SK, Almén T, Aspelin P, Bellin MF, et al. The use of iodinated and gadolinium contrast media during pregnancy and lactation. *Eur Radiol.* 2005;15(6):1234–40. DOI 10.1007/s00330-004-2583-y [Accessed 05/06/2019]
31. Righini M, Robert-Ebadi H, Elias A, et al. Diagnosis of Pulmonary Embolism During Pregnancy: A Multicenter Prospective Management Outcome Study. Ann Intern Med. 2018;169:766 – 773. DOI:10.7326/M18-1670 [Accessed 22 September 2019]

Appendix A – Wells score

PREDICTOR	SCORE
Clinical signs and symptoms of DVT(minimum of leg swelling and pain with palpation of deep veins)	+3
An alternative diagnosis is less likely than PE	+3
Heart rate greater then 100	+1.5
Immobilization at least 3 days and surgery in the previous 4 weeks	+1.5
Previous PE/DVT	+1.5
Haemoptysis	+1
Malignancy	+1
TOTAL	/12.5

RISK OF PE	ASSOCIATED SCORE
Low (3% risk of PE)	<2
Moderate (28%)	2 – 6
High (78%)	>6

RISK OF PE	ASSOCIATED SCORE
Unlikely (5.1- 7.8%) rate of PE	<4
Likely (approx. 40%)	>4

Wells PS, Anderson DR, Rodger M, Ginsberg JS, Kearon C, Gent M, et al. Derivation of a Simple Clinical Model to Categorize Patients Probability of Pulmonary Embolism-Increasing the Models Utility with the SimpliRED Ddimer. *Thromb Haemost*. 2000; 83(3): 416-20.

Appendix B – Geneva score

VARIABLE	REVISED GENEVA	SIMPLIFIED REVISED GENEVA
Age > 65	1	1
Previous DVT\PE	3	1
Recent surgery or fracture (<4/52)	2	1
Active malignancy	2	1
Unilateral lower limb pain	3	1
Haemoptysis	2	1
Pain on lower limb deep vein palpation or unilateral oedema	4	1
Pulse 75 – 94 beats per minute >95 beats per minute	 3 5	 1 2

*In the revised Geneva score patients are divided into three risk groups:

- Patients scoring 0 to 3 are considered low risk
- Patients scoring 4 to 10 are considered moderate risk
- Patients scoring 11 to 25 are at high risk of PE

**In the simplified revised Geneva score patients are divided into:

- Patients scoring 0 to 2 are low risk (or PE unlikely)
- Patients scoring3 and more are high risk (or PE likely)

*Le Gal G, Righini M, Roy PM, et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. Annals of Internal Medicine. 2006; 144(3):165-171.

**Klok FA, Mos, ICM, Nijkeuter M et al: Simplification of the Revised Geneva Score for Assessing Clinical Probability of Pulmonary Embolism. Arch Intern Med. 2008;168(19):2131-2136

Appendix C – Data Sheet

Allocated Study number	

Demographics data

Age …….

Gravidity…… Parity: Before current pregnancy……..

Post-partum……..

Gestational age: At event…….....

At delivery…….

Referral status: Home/ Clinic/ Hospital

Booked/ Unbooked

Rhesus…… RPR…… HIV: Positive/ Negative/ Unknown

If positive:

ARVs…….

CD4 count……. VL……

Hb: Booking…….. Weight: …….

Height…… BMI……..

At event……

……..

Problem list:

……..

……..

Past and present history data

Past obstetrics history

Year	Gestation	Mode of delivery: CS/ NVD	Outcome: Alive/ Misc/Stillbirth/ ENND

Past medical history……
……

Past surgical History……
……

Smoking: Yes/ No/ Not specified

Alcohol: Yes/ No/ Not specified

Family History……..

Current obstetrics co-morbidity……
……

Pregnancy: Singleton/ Twins

Other complications……
……

Presenting features data

Symptomatic/ Asymptomatic

If symptomatic: Shortness of breathe

Coughing and or Hemoptysis

Chest pain

Collapse

Leg swelling

Other……
……

Heart rate: At booking……..

At event……..

Blood pressure: At Booking……..

At event:……

Respiratory rate: ……

Oxygen saturation:……..

Temperature: ……

Chest: Normal/ Abnormal

Where Abnormal

specify……..

CVS: Normal/ Abnormal

Where Abnormal

specify……..

DVT signs: Present/ Not present

Diagnostic data

D-dimer: Actual value……..

Not done

Hb…… Urea……. Cr…….. AST……. ALT……..

Chest X-ray: Normal/ Abnormal

Where Abnormal

specify……..

ECG: Normal/ Abnormal

Where Abnormal

specify……..

CTPA done: Non-diagnostic/ Negative

Diagnostic/ Positive

Indeterminate

VQ scan if done: High probability

Low probability

Indeterminate probability

Delivery data

Mode of delivery: NVD/ CS

Estimated blood loss……..

Outcome: Alive/ Stillbirth/ ENND

Number of days post-partum……

Final outcome of patient

Discharged/ Death

APPENDIX B: Ethics clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Siseko Gqola

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M191177

NAME: (Principal Investigator)	Dr Siseko Gqola
DEPARTMENT:	Obstetrics and Gynaecology Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Diagnosis in women suspected of pulmonary embolism at CHBAH - a retrospective study
DATE CONSIDERED:	29/11/2019
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Grace Ruben and Dr Langanani Mbodi
APPROVED BY:	Dr Nitien Naran, Co-Chair, HREC (Medical)
DATE OF APPROVAL:	07/01/2020

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

Principal Investigator Signature

Date 28/1/2020

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX C: Letter of approval from CHBAH CEO

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE

CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 25th October 2019

TITLE OF PROJECT:

Diagnosis in women suspected of Pulmonary Embolism at CHBAH – A Retrospective Review

UNIVERSITY: Witswatersrand

Principal Investigator: Siseko Gqola

Department: Obstetrics and Gynaecology

Supervisor : Prof Y Adam

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: 25/10/2019

Approved/~~Not Approved~~
Hospital Management
Date: 25/10/2019

APPENDIX D: Letter of approval from Nuclear medicine and CT scan department

Division of Nuclear Medicine

WITS SCHOOL OF CLINICAL MEDICINE

Division of Nuclear Medicine, Department of Radiation Sciences. WITS Health Sciences Facul
7 York Road, Parktown, 2193, South Africa.
Telephone: +27 11 488-3500 Fax: +27 11 488-3501 E-mail: vangumw@medicine.wits.ac.

17th June 2020

Dr Siseke Gqola
CHBAH in the Department of Obstetrics &Gynaecology

RE: Permission to access Nuclear Medicine archive for perfusion/ventilation imaging for the MMed study- Dr Siseko Gqola N0 **0701953E**

Dear Dr Siseko

You are grated the permission to access nuclear medicine reports 'archive at the Chris Hani Baragwanath academic Hospital only for the purpose of completing relevant data on you MMed project titled: **Diagnosis in women suspected of pulmonary embolism at CHBAH – a retrospective review.**

Dr K. Purbhoo who is in charge of the clinical activities has been informed and will assist in facilitation this access.

Should the project result in publication of your work then the following should be considered and already discussed with your supervisors.

1. Nuclear medicine should be acknowledged if data from the perfusion/ventilation scans just add some trivial contribution to the emerging paper.
2. However, if data from nuclear medicine will substantially contribute to write the paper then nuclear medicine should co-author the paper, respecting all requirements for such.

Kind Regards,

Prof Vangu
MD, MMed, MSc, Cert exec MBA, PhD
Cert Fundamentals of Clinical and Translational Research (Harvard)
Chief Specialist and Head Radiation Sciences (University of the Witwatersrand)
Head Nuclear Medicine-CM Johannesburg Academic and CH Bara Hospitals
Office: +2711 4883500; Fax: +2711 4883501; Mobile: +2783 2670004

Cc: Dr K. Purbhoo

REQUEST FOR PERMISSION TO ACCESS THE PACS SOFTWARE

15 October 2019

To: Head of Department Radiology
Chris Hani Baragwanath Academic Hospital
Soweto

From: Dr Siseko Gqola
Registrar
Chris Hani Baragwanath Academic Hospital
Department of Obstetrics and Gynaecology

Greetings,

I am conducting a research as part of the preparation for MMed requirements for the speciality in Obstetrics and Gynaecology. My research topic is **Diagnosis in women suspected of pulmonary embolism at Chris Hani Baragwanath Academic Hospital.**

My research will be a cross sectional retrospective study. I will be collecting data from files of all women who were pregnant or who have had a pregnancy in the last 42 days that have had a CTPA or a VQ scan. Between 01 July 2018 to 30 June 2019.

I am kindly requesting permission to access data on the PACS software. I will be assisted by my supervisor Dr Grace Rubin. No patients will be interviewed. We expect 60-80 patients in this time period

Ethics Approval: Pending

Accompanying this letter is the Research Protocol and the data collection sheet.

Regards

Dr Siseko Gqola

..... Date 22/10/2019.

Head of Department: Prof Yasmin Adam

HOD: _____. Date: 25/10/2019.

Permission to access the PACS software at CHBAH: Granted ~~Refused~~

Clinical head of department: _____. Date: 29/10/2019.

APPENDIX E: Plagiarism declaration

Plagiarism declaration for written work

I…….. student number…….. as a postgraduate student registered for a MMed at the University of the Witwatersrand declare the following:

- I am aware that plagiarism is the use of someone else's work without their permission and or without acknowledging the original source.
- I am aware plagiarism is wrong.
- I confirm that this written work is my own work except where I have stated 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 if I have failed to acknowledge the ideas or writing of others.

Signature ……...

Date

PLEGIARISM DECLARATION

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I _____ (Student number: _____) am a student

registered for the degree of _____ in the academic year _____.

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: _____

APPENDIX F: SOUTH AFRICAN JOURNAL OF OBSTETRICS AND GYNAECOLOGY GUIDLEINES

Author Guidelines

Author Guidelines

Please view the Author Tutorial for guidance on how to submit on Editorial Manager.

To submit a manuscript, please proceed to the SAJOG Editorial Manager website: http://www.editorialmanager.com/sajog

To access and submit an article already in production, please see the guidelines here.

Author Guidelines

Please take the time to familiarise yourself with the policies and processes below. If you still have any questions, please do not hesitate to ask our editorial staff (tel.: +27 (0)21 532 1281, email: submissions@samedical.org).

Article Processing Charges

All articles published in the South African Journal of Obstetrics & Gynaecology are open access and freely available online upon publication. This is made possible by applying a business model to offset the costs of peer review management, copyediting, design and production, by charging an article-processing charge (APC) of R2 729.50 (ex vat) for short articles and R5 459 (ex vat) for full-length articles published. The charge applies only to articles submitted after 1 Jan 2020. The APC is standard and does not vary based on length, colour, figures, or other elements.

When submitting a Research article to the SAJOG, the submitting author must agree to pay the APC should the article be accepted for publication. The APC is payable when your manuscript is editorially accepted and before production commences for publication. The submitting author will be notified that payment is due and given details on the available methods of payment. Prompt payment is advised; the article will not enter production until

payment is received.
Queries can be directed to claudian@samedical.org

Authorship

Named authors must consent to publication. Authorship should be based on: (i) substantial contribution to conceptualisation, design, analysis and interpretation of data; (ii) drafting or critical revision of important scientific content; or (iii) approval of the version to be published. These conditions must all be met for an individual to be included as an author (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org)

If authors' names are added or deleted after submission of an article, or the order of the names is changed, all authors must agree to this in writing.

Please note that co-authors will be requested to verify their contribution upon submission. Non-verification may lead to delays in the processing of submissions.

Conflicts of interest

Conflicts of interest can derive from any kind of relationship or association that may influence authors' or reviewers' opinions about the subject matter of a paper. The existence of a conflict – whether actual, perceived or potential – does not preclude publication of an article. However, we aim to ensure that, in such cases, readers have all the information they need to enable them to make an informed assessment about a publication's message and conclusions. We require that both authors and reviewers declare all sources of support for their research, any personal or financial relationships (including honoraria, speaking fees, gifts received, etc) with relevant individuals or organisations connected to the topic of the paper, and any association with a product or subject that may constitute a real, perceived or potential conflict of interest. If you are unsure whether a specific relationship constitutes a conflict, please contact the editorial team for advice. If a conflict remains undisclosed and is later brought to the attention of the editorial team, it will be considered a serious issue prompting an investigation with the possibility of retraction.

Research ethics committee approval

Authors must provide evidence of Research Ethics Committee approval of the research where relevant. Ensure the correct, full ethics committee name and reference number is included in the manuscript.
If the study was carried out using data from provincial healthcare facilities or required active

data collection through facility visits or staff interviews, approval should be sought from the relevant provincial authorities. For South African authors, please refer to the guidelines for submission to the National Health Research Database. Research involving human subjects must be conducted according to the principles outlined in the Declaration of Helsinki. Please refer to the National Department of Health's guideline on Ethics in Health research: principles, processes and structures to ensure that the appropriate requirements for conducting research have been met, and that the HPCSA's General Ethical Guidelines for Health Researchers have been adhered to.

Protection of rights to privacy

Research Participants

Information that would enable identification of individual research participants should not be published in written descriptions, photographs, radiographs and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) has given informed written consent for publication and distribution. We further recommend that the published article is disseminated not only to the involved researchers but also to the patients/participants from whom the data was drawn. Refer to Protection of Research Participants. The signed consent form should be submitted with the manuscript to enable verification by the editorial team.

Other individuals

Any individual who is identifiable in an image must provide written agreement that the image may be used in that context in the SAJOG.

Copyright notice

Material submitted for publication in the SAJOG is accepted provided it has not been published or submitted for publication elsewhere. Please inform the editorial team if the main findings of your paper have been presented at a conference and published in abstract form, to avoid copyright infringement. The SAJOG does not hold itself responsible for statements made by the authors. The corresponding author should also indicate if the research forms part of a postgraduate short report, dissertation or thesis.

Previously published images

If an image/figure has been previously published, permission to reproduce or alter it must be

obtained by the authors from the original publisher and the figure legend must give full credit to the original source. This credit should be accompanied by a letter indicating that permission to reproduce the image has been granted to the author/s. This letter should be uploaded as a supplementary file during submission.

Privacy statement

The SAJOG is committed to protecting the privacy of its website and submission system users. The names, personal particulars and email addresses entered on the website or submission system will not be made available to any third party without the user's permission or due process. By registering to use the website or submission system, users consent to receive communication from the SAJOG or its publisher SAMA on matters relating to the journal or associated publications. Queries about privacy may be directed to publishing@samedical.org.

Ethnic/race classification

Use of racial or ethnicity classifications in research is fraught with problems. If you choose to use a research design that involves classification of participants based on race or ethnicity, or discuss issues with reference to such classifications, please ensure that you include a detailed rationale for doing so, ensure that the categories you describe are carefully defined, and that socioeconomic, cultural and lifestyle variables that may underlie perceived racial disparities are appropriately controlled for. Please also clearly specify whether race or ethnicity is classified as reported by the patient (self-identifying) or as perceived by the investigators. Please note that it is not appropriate to use self-reported or investigator-assigned racial or ethnic categories for genetic studies.

Continuing Professional Development (CPD)

SAJOG is an HPCSA-accredited service provider of CPD materials. Principal authors can earn up to 15 CPD continuing education units (CEUs) for publishing an article; co-authors are eligible to earn up to 5 CEUs; and reviewers of articles can earn 3 CEUs. Each month, SAJOG also publishes a CPD-accredited questionnaire relating to the academic content of the journal. Successful completion of the questionnaire with a pass rate of 70% will earn the reader 3 CEUs. Administration of our CPD programme is managed by Medical Practice Consulting. To complete questionnaires and obtain certificates, please visit MRP Consulting

Manuscript preparation

Preparing an article for anonymous review

To ensure a fair and unbiased review process, all submissions are to include an anonymised version of the manuscript. The exceptions to this requirement are Correspondence, Book reviews and Obituary submissions.

Submitting a manuscript that needs additional blinding can slow down your review process, so please be sure to follow these simple guidelines as much as possible:
• An anonymous version should not contain any author, affiliation or particular institutional details that will enable identification.
• Please remove title page, acknowledgements, contact details, funding grants to a named person, and any running headers of author names.
• Mask self-citations by referring to your own work in third person.

General article format/layout
Submitted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction prior to being sent for review, which will delay publication.

General:
• Manuscripts must be written in UK English (this includes spelling).
• The manuscript must be in Microsoft Word or RTF document format. Text must be 1.5 line spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes). Pages and lines should be numbered consecutively.
• Please make your article concise, even if it is below the word limit.
• Qualifications, full affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
• Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
• Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
• Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
• Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the only exception. Please DO NOT use fill, format lines and so on.

SAJOG is a general specialist obstetrics and gynaecology journal, therefore for articles involving genetics, it is the responsibility of authors to apply the following:

- Please ensure that all genes are in italics, and proteins/enzymes/hormones are not.
- Ensure that all genes are presented in the correct case e.g. TP53 not Tp53.

** NB: Copyeditors cannot be expected to pick up and correct errors with respect to the above, although they will raise queries where concerned.

- Define all genes, proteins and related shorthand terms at first mention, e.g. '188del11' can be glossed as 'an 11 bp deletion at nucleotide 188.'
- Use the latest approved gene or protein symbol as appropriate:

o Human Gene Mapping Workshop (HGMW): genetic notations and symbols
o HUGO Gene Nomenclature Committee: approved gene symbols and nomenclature
o OMIM: Online Mendelian Inheritance in Man (MIM) nomenclature and instructions
o Bennet et al. Standardized human pedigree nomenclature: Update and assessment of the recommendations of the National Society of Genetic Counsellors. J Genet Counsel 2008; 17:424-433: standard human pedigree nomenclature.

Preparation notes by article type

Research

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 - 25references

Structured abstract

• This should be no more than 250words, with the following recommended headings:

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

o Objectives: what the study intends to find out

o Methods: must include study design, number of participants, description of the research tools/instruments, any specific analyses that were done on the data.

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

o Conclusion: must be supported by the data, include recommendations for further 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 references in the abstracts.

Here is an example of a good abstract.

Scientific letters/short reports

These are shorter length, scholarly research articles of no more than 1500 words, and include case reports.

Guideline word limit: 1 500 words

• Abstract: Structured, of about 150 words, with the following recommended headings: Background, Objectives, Methods, Results, and Conclusion.

• May include only one illustration or table

• A maximum of 8 references

Editorials

Guideline word limit: 1 000 words

These opinion or comment articles are usually commissioned but we are happy to consider and peer review unsolicited editorials. Editorials should be accessible and interesting to readers without specialist knowledge of the subject under discussion and should have an

element of topicality (why is a comment on this issue relevant now?) There should be a clear message to the piece, supported by evidence.
Please make clear the type of evidence that supports each key statement, e.g.:
• expert opinion
• personal clinical experience
• observational studies
• trials
• systematic reviews.

Review articles
Review articles should always be discussed with the Editor prior to submission.

Guideline word limit: 4 000 words
These are welcome but should be either commissioned or discussed with the Editor before submission. A review article should provide a clear, up-to-date account of the topic and be aimed at non-specialist hospital doctors and general practitioners. They should be aligned to practice in South and/or sub-Saharan Africa and not a précis of reviews published in the international literature
Please ensure that your article includes:
• Abstract: unstructured, of about 100-150 words, explaining the review and why it is important
• Methods: Outline the sources and selection methods, including search strategy and keywords used for identifying references from online bibliographic databases. Discuss the quality of evidence.
• When writing: clarify the evidence you used for key statements and the strength of the evidence. Do not present statements or opinions without such evidence, or if you have to, say that there is little or no evidence and that this is opinion. Avoid specialist jargon and abbreviations and provide advice specific to southern Africa.
• Personal details: Please supply your qualifications, position and affiliations and MP number (used for CPD points); address, telephone number and fax number, and your e-mail address; and a short personal profile (50 words) and a few words about your current fields of interest.

Correspondence (Letters to the Editor)
Guideline word limit: 400 words
Letters to the editor should relate either to a paper or article published by the SAJOG or to a

topical issue of particular relevance to the journal's readership

• May include only one illustration or table

• Must include a correspondence address.

Obituaries

Guideline word limit: 400 words

Should be offered within the first year of the practitioner's death and may be accompanied by a photograph.

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)'.

From submission to acceptance

Submission and peer-review

To submit an article:

• Please ensure that you have prepared your manuscript in line with the SAJOG requirements.

• All submissions should be submitted via Editorial Manager

• The following are required for your submission to be complete:

o Anonymous manuscript (unless otherwise stated)

o Author Agreement form

o Manuscript

o Any supplementary files: figures, datasets, patient consent form, permissions for published images, etc.

• Once the submission has been successfully processed on Editorial Manager, it will undergo a technical check by the Editorial Office before it will be assigned to an editor who will

handle the review process. If the author guidelines have not been appropriately followed, the manuscript may be sent back to the author for correcting.

Peer Review Process

All manuscripts are reviewed initially by the Editor-in-Chief and only those that meet the scientific and editorial standards of the journal and fit within the aims and scope of the journal, will be sent for external peer review. Each manuscript is reviewed by two reviewers selected on the basis of their expertise in the field. A double-blind review process is followed at SAJOG.

Authors are expected to receive feedback from reviewers and an editorial decision within approximately 6 weeks of submission. The time period of the entire review process may vary however depending upon the quality of the manuscript submitted, reviewers' responses and the time taken by the authors to submit the revised manuscript.

Manuscripts from review may be accepted, rejected or returned to the author for revision or resubmission for review. Authors will be directed to submit revised manuscripts within two months of receiving the editor's decision and are requested to submit a point by point response to the reviewers' comments. Manuscripts which authors are requested to revise and resubmit will be sent for a second round of peer review, often to the original set of reviewers. All final decisions on a manuscript are at the Editor's discretion

Production process

The following process should usually take between 4 - 6 weeks:

1. An accepted manuscript is passed to a Managing Editor to assign to a copyeditor (CE).
2. The CE copyedits in Word, working on house style, format, spelling/grammar/punctuation, sense and consistency, and preparation for typesetting.
3. If the CE has an author queries, he/she will contact the corresponding author and send them the copyedited Word doc, asking them to solve the queries by means of track changes or comment boxes.
4. The authors are typically asked to respond within 1-3 days. Any comments/changes must be clearly indicated e.g., by means of track changes. Do not work in the original manuscript - work in the copyedited file sent to you and make your changes clear.
5. The CE will finalise the article and then it will be typeset.
6. Once typeset, the CE will send a PDF of the file to the authors to complete their final check, while simultaneously sending to the 2nd-eye proofreader.
7. The authors are typically asked to complete their final check and sign-off within 1-2 days.

No major additional changes can be accommodated at this point.
8. The CE implements the authors' and proofreader's mark-ups, finalises the file, and prepares it for the upcoming issue.

Changing contact details or authorship
Please notify the Editorial Department of any contact detail changes, including email, to facilitate communication.

Errata and retractions

Errata

Should you become aware of an error or inaccuracy in yours or someone else's contribution after it has been published, please inform us as soon as possible via an email to publishing@samedical.org,including the following details:

• Journal, volume and issue in which published
• Article title and authors
• Description of error and details of where it appears in the published article
• Full detail of proposed correction and rationale

We will investigate the issue and provide feedback. If appropriate, we will correct the web version immediately, and will publish an erratum in the next issue. All investigations will be conducted in accordance with guidelines provided by the Committee on Publication Ethics (COPE).

Retractions

Retraction of an article is the prerogative of either the original authors or the editorial team of SAMA. Should you wish to withdraw your article before publication, we need a signed statement from all the authors.

Should you wish to retract your published article, all authors have to agree in writing before publication of the retraction.
Send an email to publishing@samedical.orgincluding the following details:

• Journal, volume and issue to which article was submitted/in which article was published
• Article title and authors
• Description of reason for withdrawal/retraction.

We will make a decision on a case-by-case basis upon review by the editorial committee in line with international best practices. Comprehensive feedback will be communicated with

the authors with regard to the process. In case where there is any suspected fraud or professional misconduct, we will follow due process as recommended by the Committee on Publication Ethics (COPE), and in liaison with any relevant institutions.

When a retraction is published, it will be linked to the original article.

Submission Preparation Checklist

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

Named authors consent to publication and meet the requirements of authorship as set out by the journal.

The submission has not been previously published, nor is it before another journal for consideration.

The text complies with the stylistic and bibliographic requirements in **Author Guidelines**.

The research was approved by a Research Ethics Committee (if applicable)

The authors are aware of the page fee costs associated with their submission. Please see **Author Guidelines** for more information.

Copyright Notice

Copyright of published material remains in the Authors' name. This allows authors to use their work for their own non-commercial purposes without seeking permission from the Publisher, subject to properly acknowledging the Journal as the original place of publication.

Authors are free to copy, print and distribute their articles, in full or in part, for teaching activities, and to deposit or include their work in their own personal or institutional database or on-line website. Authors are requested to inform the Journal/Publishers of their desire/intention to include their work in a thesis or dissertation or to republish their work in any derivative form (but not for commercial use).

Material submitted for publication in the *SAJOG* is accepted provided it has not been published or submitted for publication elsewhere. Please inform the editorial team if the main findings of your paper have been presented at a conference and published in abstract form, to avoid copyright infringement.

Privacy Statement

The *SAJOG* is committed to protecting the privacy of the users of this journal website. The names, personal particulars and email addresses entered in this website will be used only for the stated purposes of this journal and will not be made available to third parties without the user's permission or due process. Users consent to receive communication from the *SAJOG* for the stated purposes of the journal. Queries with regard to privacy may be directed to publishing@hmpg.co.za.

APPENDIX G: LETTER TO THE EDITOR

Dr Siseko Gqola

Department of Obstetrics and Gynaecology

Charlotte Maxeke Johannesburg Academic Hospital & University of Witwatersrand

7 Yolk Road

Parktown

Johannesburg

2193

Dr William Edridge

Editor-In-Chief

South African Journal of Obstetrics and Gynaecology

31 March 2023

Dear Dr Edridge

We would like to submit an original research article titled "**Diagnosis in women suspected of pulmonary embolism at Chris Hani Baragwanath Academic Hospital – A retrospective review"** for consideration for publication in your journal, *South African Journal of Obstetrics and Gynaecology.* The article is authored by S Gqola (Primary investigator), Y Adam, and L Mbodi as co-authors. This study is part of the research undertaken in partial fulfilment of the conditions for the Master of Medicine.

The authors declare that this article is original and that no funding for this research and no known conflict of interest.

Yours Sincerely,

……

Dr. S. Gqola,