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Wilhelm Herbst[1], Shastra Bhoora[2,3], Halvani Moodley[4], Ashesh Ranchod[5,6], Tracy Westgarth-Taylor[7] and Jarrod Zamparini[8]

Abstract

Background: Pulmonary embolism (PE) is a common cause of maternal death during pregnancy and the puerperium yet data on its prevalence in middle-income countries is lacking.

Methods: We examined the medical records and CTPA (computed tomography pulmonary angiography) images of 67 women in an obstetric high care unit during pregnancy and the puerperium. We aimed to determine the prevalence of PE in a high-risk obstetric population undergoing CTPA, assess associated clinical features in this cohort, and determine the prevalence of alternative CT findings.

Results: CTPA detected PE in 11 women (16.42%) and alternative CT findings in 46 (68.6%). Women with PE had a lower systolic blood pressure than those without PE ($P = 0.001$). Multiple gestation, preterm rupture of membranes, and gestational diabetes were linked to higher PE prevalence.

Conclusions: This study, set in an upper middle-income country, demonstrated a higher CTPA yield for PE and alternative diagnoses than in international literature, emphasising context-specific assessments.

Keywords

Pregnancy, postpartum, pulmonary embolism, CTPA

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Background

Venous thromboembolism (VTE), including pulmonary embolism (PE), is the most common cause of maternal death during pregnancy and the puerperium in developed countries.[1] The risk for VTE is significantly increased during pregnancy and the postpartum period, as these patients are in a physiological state of hypercoagulability, are prone to venous stasis and may have superimposed endothelial damage.[2]

Women have a 5-fold increased risk of developing VTE during pregnancy, as compared to their non-pregnant counterparts.[3] Globally, the incidence of PE in pregnant or postpartum women ranges from 1 to 2 per 1000 to 3 per 10,000 deliveries,[2,4] and one death in every 100,000 deliveries.[5] In South Africa, PE accounted for 40 maternal deaths in 2022, with a maternal mortality rate of 4.1 per 100,000 live births.[6]

More than half of VTE cases in pregnancy occur before 20 weeks' gestation,[4] and 80% of VTE cases in the postpartum period occur within the first 3 weeks following delivery.[7]

Despite the increased risk of VTE in pregnancy, there is a lower incidence of PE diagnosed by CTPA (computed tomography pulmonary angiography) in pregnant than non-pregnant women, likely due to an increase in testing due to the presence of non-specific symptoms. A 2015 study found that 2% of pregnant women had a positive CTPA compared to 16% of non-pregnant women.[8] A 17-year retrospective study conducted at a single centre in Switzerland, published in 2020, observed that CTPA rarely indicated PE in pregnancy, with an alternative diagnosis found in 30% of pregnant women investigated.[9] Similarly, a 2023 study including 86 pregnant and 354 non-pregnant women investigated for PE by either CTPA or V/Q scan, noted positive scan rates of 3.5% and 8.8% in pregnant and non-pregnant women, respectively.[10]

[1]Department of Internal Medicine, Faculty of Health Sciences, Charlotte Maxeke Johannesburg Academic Hospital, University of the Witwatersrand, Johannesburg, South Africa
[2]Department of Obstetrics and Gynaecology, Charlotte Maxeke Johannesburg Academic Hospital, University of the Witwatersrand, Johannesburg, South Africa
[3]Department of Obstetrics and Gynaecology, Baylor College of Medicine, Houston, TX, USA
[4]Department of Radiology, Charlotte Maxeke Johannesburg Academic Hospital, University of the Witwatersrand, Johannesburg, South Africa
[5]Department of Radiology, School of Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa
[6]National Radiology Services Incorporated (NRS Inc.), Johannesburg, South Africa
[7]Department of Radiology, Netcare Park Lane Hospital, Johannesburg, South Africa
[8]Obstetric Internal Medicine Unit, Charlotte Maxeke Johannesburg Academic Hospital, University of the Witwatersrand, Johannesburg, South Africa

Corresponding author:
Wilhelm Herbst, Department of Internal Medicine, Faculty of Health Sciences, Charlotte Maxeke Johannesburg Academic Hospital, University of the Witwatersrand, 7 York Road, Parktown, Johannesburg, 2193, South Africa.
Email: wherbst.herbst@gmail.com

Low molecular weight heparin is the preferred pharmacologic agent for thromboprophylaxis during pregnancy in South Africa and is recommended based on risk stratification during pregnancy and for up to 6 weeks' postpartum.[11]

In non-pregnant women, PE can be safely excluded in the presence of a normal D-dimer in addition to a low pre-test probability.[12] The American Thoracic Society (ATS),[13] the Society of Obstetricians and Gynaecologists of Canada (SOGC),[14] and the Royal College of Obstetricians and Gynaecologists (RCOG)[15] recommends that a D-dimer should not be used in pregnancy to exclude PE as most studies investigating the use of D-dimer in diagnosing PE, have not included pregnant women.[16]

van der Pol et al. found that the pregnancy-adapted YEARS algorithm safely excluded PE in pregnant women with suspected PE, allowing CTPA to be avoided in 32%–65% of women.[17] A South African study found that the pregnancy-adapted YEARS algorithm successfully risk-stratified women in a single institution and would have reduced the number of CTPAs by 25.7% without missing any PE.[18]

Accepted standards outlined by the Royal College of Radiologists state that CTPA should detect PE in 15.4%–37.4% and alternative diagnoses in up to 56% in the general population.[19]

Most studies have disregarded pregnant women when investigating the diagnosis of PE.[12] Increased circulatory volume and altered cardiac output in pregnancy, may lead to lower pulmonary artery opacification influencing the quality of CTPA.[20] Insufficient opacification of the pulmonary vasculature during CTPA is described twice as often among pregnant women compared to those who are not pregnant.[21] Normal CTPA imaging in pregnancy, has a high negative predictive value.[22]

In this study, we investigated the use of CTPA to diagnose PE in pregnant and postpartum women admitted to a high care setting in South Africa. We aimed to evaluate the prevalence of PE and alternative diagnoses as well as compare the clinical features of women with and without PE.

Methods

We performed a cross-sectional retrospective analysis at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), an academic centre in Johannesburg, South Africa. Pregnant and postpartum women admitted to the obstetric high care unit (OHCU) between 1 January and 31 December 2019, who underwent CTPA for the suspicion of PE were consecutively enrolled in this study. We excluded women who had a PE diagnosed by a method other than CTPA, such as V/Q scan, due to limited availability in our setting. Women with imaging performed elsewhere, women with known PE diagnosed prior to admission, and women who were not pregnant or beyond 6 weeks' post-delivery were also excluded.

The names and hospital numbers of all women admitted to the OHCU for the study period were collected from the ward admission register and cross-referenced with the hospital picture archiving and communicating system to determine which women underwent CTPA. The included participant details were anonymised and allocated a unique study number. The CTPA images were reported on by two consultant radiologists (AR and TW-T) who were blinded from each other's findings. The discrepant readings were reviewed by a third consultant radiologist (HM), also blinded from the findings of the other readers.

A final diagnosis was considered as agreement by two or more readers. Those studies with inconclusive findings or failing to achieve consensus among at least two readers, were interpreted as not having PE for the purposes of the study. The hospital files for the relevant participants were collected from hospital archives and clinical data was extracted. Data was captured in Microsoft Excel 16.78 (Microsoft Corporation, Redmond, WA, USA) and statistical analysis was performed using Prism 10 (GraphPad Software Inc., La Jolla, CA, USA). Given the non-parametric nature of the data, the Mann–Whitney U test was employed for continuous variables, while the Fisher's exact test was utilised for categorical variables to determine significance.

Results

A total of 732 women were admitted during the period under review, CTPAs were performed on 71 women, of which 3 were not pregnant nor in the postpartum period and 1 had missing images, excluding them from the study, leaving a total of 67 women in the final analysis (Figure 1). There were six scans with inconclusive findings which were interpreted as not having PE for the purposes of the study. We did not assess the direct indication for CTPA in our cohort; however, women admitted to the CMJAH OHCU usually undergo CTPA due to the presence of either an unexplained tachycardia, respiratory symptoms and/or cardiac symptoms (with a normal echocardiogram).

The PE and non-PE groups were of similar age and race. The majority of the cohort were postpartum (82% in the PE group and 87.5% in the no PE group), and caesarean section was the most common mode of delivery in keeping with local trends. The high caesarean section rate at our centre has been described previously by Guidozzi et al.[23]; however, in our cohort we believe that the low rate of normal vaginal delivery may be as a result of only including women in a high care setting, placing them in a higher risk category. Additionally, the high rate of preterm delivery in both groups may also be explained by the prevalence of obstetric complications leading to iatrogenic preterm deliveries. Table 1 provides demographic and pregnancy-related data of the cohort.

Eleven women (16.4%) had a confirmed PE; 2 (18%) were pregnant and 9 (82%) postpartum and the majority ($n = 10$, 90.9%) had peripheral PEs. Two women (18.2%) had a single embolism and 9 (81.8%) had multiple emboli. The gestational age at delivery (in postpartum women) or time of scan (in pregnant women) was not significantly different ($P = 0.259$) in the non-PE group (median 34.5 weeks, interquartile range [IQR] 30–38), compared to those with PE (median 30 weeks, IQR 26–38). Women with PE were more likely to have multiple gestation (27%) than without PE (4%) ($P = 0.028$). There was a larger proportion of women with alternative CT findings among those in the group with PE ($n = 9$, 81.8%) compared to those without PE ($n = 37$, 66.1%), yet the difference was not significant ($P = 0.481$) (Table 2).

The difference in the technical adequacy of the CTPAs between the two groups overall was not significant ($P = 0.556$), nor was it significant when comparing the two groups in pregnant women ($P = 0.861$) and postpartum women ($P = 0.661$) (Table 2). This was assessed by measuring the opacification of the pulmonary artery (Hounsfield units), between the two groups (median 237 HU, IQR 216–277 versus median 247 HU, IQR 209–285 in the PE and non-PE groups, respectively). There was a 17% ($n = 12$) rate of inadequate scans, determined by a minimum of 210 HU required to be considered acceptable for a diagnostic CTPA in the general population.[24] There was no difference in rate of motion artefact between the two groups ($P = 0.492$). Compression ultrasonography and Doppler of the lower limbs were done on 4 women in the non-PE group and one in the PE group; however, none had a confirmed deep vein thrombosis (DVT).

As shown in Table 2, our cohort had a high prevalence of alternative diagnoses, such as pleural effusion, ground glass opacification and atelectasis, on CTPA in both groups (Figure 2). In addition, pregnancy complications including obstetric haemorrhage, hypertension and anaemia were prevalent, as shown in Table 3.

There was a significant difference in systolic blood pressure (sBP) between the two groups ($P = 0.001$) with lower sBP in the PE group (median 119 mmHg, IQR 110–124) than in the non-PE group (median 134 mmHg, IQR 120.3–146). There were no differences in other clinical features including the body mass index or mid upper arm circumference

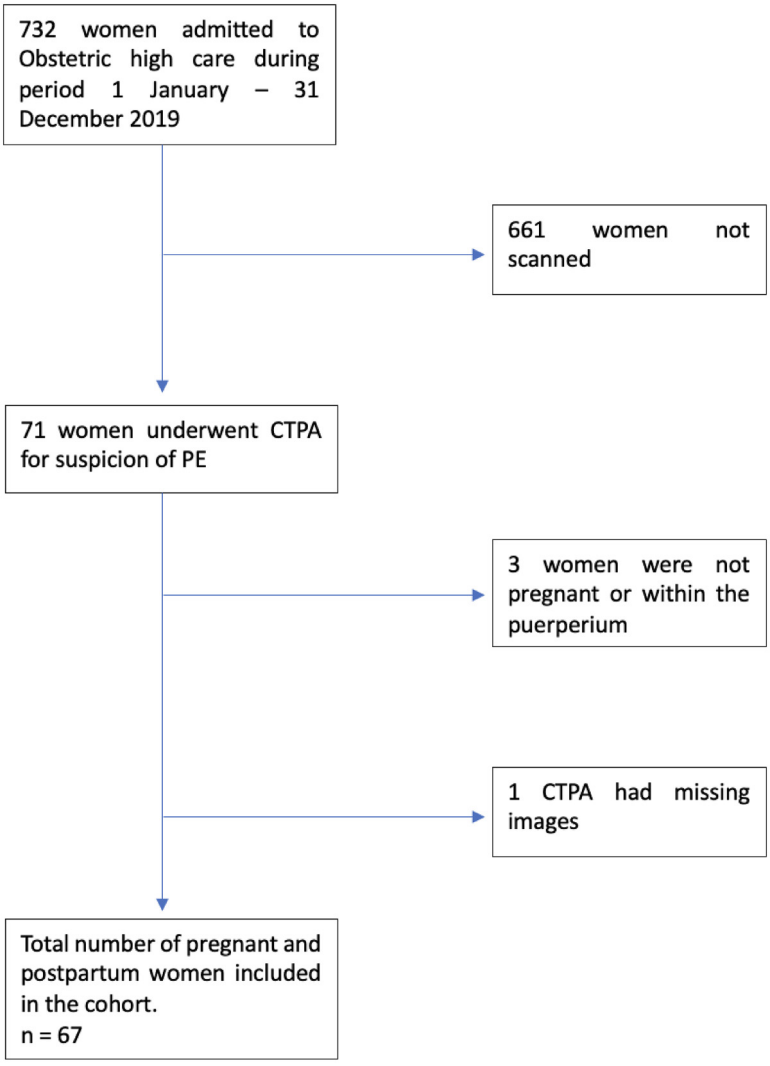


Figure 1. Study population.

between the two groups. Despite most women being tachycardic, there were no differences in electrocardiogram (ECG) findings between the two groups. It is not our standard protocol to analyse D-dimer routinely for the suspicion of PE in pregnancy, therefore only 27 women (40%) had D-dimers available. There was, however, no difference in D-dimers between the two groups ($P = 0.219$).

Biochemical inflammatory markers were available in a similar proportion of women, showing no difference between the groups, reflected by a median C-reactive protein of 112 mg/L in the PE group (10/11) and 100 mg/L in the non-PE group (51/56) and a median procalcitonin of 0.37 µg/L in the PE group (8/11) and 0.31 µg/L in the non-PE group. A diagnosis of puerperal sepsis was made in 36.4% in the PE group compared to 62.5% in the non-PE group; however, the difference was not significant ($P = 0.18$). There were no other differences demonstrated in biochemistry between the two groups.

No women died in the non-PE group, while one woman died in the PE group (9%); however, it is unclear if the death was directly caused by PE. Most women had a pregnancy-related complication, with the exception of two women (3.6%) in the non-PE group.

There were two women with HIV (18.2%) in the PE group, one of whom had a CD4 (CD4 = 464 cells/mm^3) and HIV viral load (VL = 764 copies/ml) available, whilst there were 17 women with HIV in the non-PE group (30.4%) where 15 had a CD4 result (median 344.5 cells/mm^3, IQR 269–457.75) and all had a VL ($n = 17$, median 217 copies/ml, IQR 0–2472.25).

Premature rupture of membranes (PROM) was significantly more prevalent ($P = 0.025$) among those with PE ($n = 2$, 18.2%) compared to those without PE ($n = 0$, 0%). There were no other complications or comorbidities with a significant difference between the groups (Table 3).

The Wells' score showed no correlation to PE, as all 67 (100%) women had a Wells' score of at least 4.5 (high risk for PE). When analysing the utility of the YEARS score,[25] seven women in the PE group and 20 women in the non-PE group had a D-dimer result available allowing the YEARS Score to be calculated. All seven (100%) women in the PE group had a positive YEARS score, while 17 (85%) women in the non-PE group had a positive YEARS score. The difference was not significant ($P = 0.545$) (Figure 3).

We performed a Bonferroni correction to account for multiple comparisons among the variables that were significantly different in univariate analysis (sBP, multiple gestation and PROM). After correction, sBP (corrected $P = 0.003$) was the only variable that remained statistically significant (correct $\alpha = 0.0167$). However, due to the small sample size, these findings should be interpreted with caution.

Table 1. Demographics and pregnancy details.

Demographics	PE ($n=11$), *n* (%)	No PE ($n=56$), *n* (%)	*P*-value
Age (years), median (IQR)	29 (26–35)	30 (26–33.75)	0.977
18–25	2 (18.18%)	12 (21.43%)	0.992
26–30	4 (36.36%)	18 (32.14%)	
31–35	3 (27.27%)	16 (28.57%)	
>35	2 (18.18%)	10 (17.86%)	
Race	PE, *n* (%)	No PE, *n* (%)	*P*-value
Black African	11 (100%)	55 (98%)	>0.999
White	0 (0%)	1 (2%)	
Pregnancy details	PE, *n* (%)	No PE, *n* (%)	*P*-value
Postpartum	9 (82%)	49 (87.5%)	0.635
Pregnant	2 (18%)	7 (12.5%)	
Multiple gestation	3 (27%)	2 (4%)	0.028
Booked for antenatal care	8 (73%)	45 (80%)	0.686
Not booked for antenatal care	3 (27%)	11 (20%)	
Gestational age at time of scan (weeks), median (IQR)	22.5 (18.8–26.3)	24 (21–28.5)	>0.999
Days post-partum at time of scan, median (IQR)	2 (2–6)	5 (2–9)	0.177
Caesarean section	9 (82%)	41 (73.2%)	0.334
Normal vaginal delivery	0 (0%)	8 (14.3%)	
Gravidity (number of pregnancies), median (IQR)	3 (1–3)	2 (1–3)	0.971
Parity (number of live births), median (IQR)	2 (1 −3)	2 (1–3)	0.714
Previous miscarriages (number), median (IQR)	0 (0–0)	0 (0–0)	0.841
Clinical features	PE ($n=11$)	No PE ($n=56$)	*P*-value
Systolic BP in pregnant group (mmHg), median (IQR)	123 (122.5–123.5)	137 (134–146)	0.222
Systolic BP in postpartum group (mmHg), median (IQR)	119 (110–124)	132 (120–145)	0.019
Diastolic BP in pregnant group (mmHg), median (IQR)	84 (83.5–84.5)	85 (77–86)	0.972
Diastolic BP in postpartum group (mmHg), median (IQR)	76 (66–78)	85 (72–92)	0.051
Heart rate in pregnant group, median (IQR)	119.5 (118.3–120.8)	110 (105.5–120)	0.472
Heart rate in postpartum group, median (IQR)	110 (109–117)	112 (107–116)	0.529

Table 2. Alternative CT findings.

CT findings	PE ($n=11$), *n* (%)	No PE ($n=56$), *n* (%)	*P*-value
Pleural effusion	4 (36.4%)	14 (25%)	0.469
Ground glass opacification	6 (54.5%)	16 (28.6%)	0.157
Consolidation	3 (27.3%)	11 (19.6%)	0.686
Cavitation	0 (0%)	1 (1.8%)	>0.999
Bronchiectasis	0 (0%)	2 (3.6%)	>0.999
Atelectasis	8 (72.7%)	24 (42.9%)	0.101
Nodules	0 (0%)	5 (8.9%)	0.582
Opacification of pulmonary artery (HU), median (IQR) in pregnant group	233 (231–235)	234 (210.5–286)	0.861
Opacification of pulmonary artery (HU), median (IQR) in post-partum group	237 (216–277)	248 (214–285)	0.661

Discussion

In our study CTPA detected PE in 16.42% and alternative CT findings in 68.6% of our cohort, which is higher than reported in international literature. A large meta-analysis and systematic review of 17 studies, including 25,339 women, found a 12.4% positivity rate for VTE in nonpregnant women, compared with 4.1% in pregnant women.[26] The high positivity rate of PE as well as alternative CT findings in our study may be attributed to only including women admitted to a high care unit, having underlying associated co-morbidities assigning them to a higher risk category than other pregnant and postpartum women.

We also note the high prevalence of alternative diagnoses (Table 2) and pregnancy complications (Table 3) in our cohort. This may be because the women included in the study were drawn from a high-risk population given the study was performed in a high care unit in an academic (i.e., referral only) centre. Additionally, as the study only included women who underwent CTPA, and not V/Q, this may have increased the sensitivity for detecting alternative pathologies, especially given the hospital's protocol for investigating PE, where CTPA is warranted if the chest X-ray is abnormal. A V/Q scan is preferred if the chest X-ray is normal.

No clinical or biochemical biomarkers predicted PE in our cohort, similar to an Australian study evaluating the use of CTPA and V/Q in pregnancy and the puerperium.[27] The use of algorithms such as the modified YEARS and Wells' scores were limited in our cohort and would have been of no utility in reducing the number of CT scans done, especially considering the low specificity of the YEARS algorithm in the immediate postpartum period.[28] The Wells' criteria, which factors in tachycardia and lower limb oedema, is not particularly useful in pregnancy, given that these manifestations are frequently seen.[29] However, given our limited sample size, future studies are needed to further assess their utility in our

Table 3. Pregnancy complications and comorbidities.

Pregnancy complications	PE ($n=11$), n (%)	No PE ($n=56$), n (%)	P-value
No complications	0 (0%)	2 (3.6%)	>0.999
Obstetric haemorrhage	5 (45.5%)	19 (33.9%)	0.505
Ante-partum haemorrhage	2 (18.2%)	6 (10.7%)	0.609
Post-partum haemorrhage	3 (27.3%)	13 (23.2%)	0.7159
Hypertensive disorders	7 (63.6%)	42 (75%)	0.469
Pregnancy-induced hypertension	1 (9.1%)	12 (21.4%)	0.677
Pre-eclampsia	3 (27.3%)	18 (32.1%)	>0.999
Eclampsia	1 (9.1%)	9 (16.1%)	>0.999
HELLP	2 (18.2%)	3 (5.4%)	0.186
Obstetric complications	4 (36.36%)	6 (10.71%)	0.051
Placenta praevia	1 (9.1%)	2 (3.6%)	0.421
Preterm labour	0 (0%)	2 (3.6%)	>0.999
Other	10 (90.1%)	42 (75%)	0.4329
Post-partum cardiomyopathy	2 (18.2%)	13 (23.2%)	>0.999
Anaemia	8 (72.7%)	29 (51.8%)	0.321
Gestational diabetes	1 (9.1%)	2 (3.6%)	0.421
Relook laparotomy	3 (27.2%)	8 (14.3%)	0.371
ICU	5 (45.5%)	14 (25%)	0.27
Comorbidities	**PE ($n=11$), n (%)**	**No PE ($n=56$), n (%)**	**P-value**
Autoimmune disease	1 (9.1%)	3 (5.4%)	0.521
Anti-phospholipid syndrome	0 (0%)	2 (3.6%)	>0.999
Chronic kidney disease	0 (0%)	4 (7.1%)	>0.999
Pre-existing diabetes mellitus	1 (9.1%)	1 (1.8%)	0.304
Heart failure	0 (0%)	8 (14.3%)	0.335
Hypertension	2 (18.2%)	9 (16.1%)	>0.999
Previous tuberculosis	0 (0%)	2 (3.6%)	>0.999
Valvular heart disease	0 (0%)	5 (8.9%)	0.582
Previous VTE	0 (0%)	4 (7.1%)	>0.999
HIV	2 (18.2%)	17 (30.4%)	0.722

setting. This is in keeping with recommendations outlined by SOGC[14] and RCOG,[15] which advise against clinical predictors to assess VTE in pregnant women.

Despite international guidelines considering maternal age over 35 years a risk factor for PE, there was no significant difference in the age of the PE and the non-PE groups in our cohort.[30] There is evidence from the UK[31] and USA[32] that Black, Asian and minority ethnicities have a much higher maternal mortality rate, with the highest among Black women. There is evidence that PE is more prevalent in black ethnicities,[33] with a higher disease severity compared to other ethnicities.[34] The majority of our cohort were of Black ethnicity, making it difficult to compare outcomes related to ethnicity and to assess whether disparities exist. This emphasises the importance of the high risk in this group, and the need for further research in a South African context.

Caesarean delivery rate in the South African private sector was 73.2% in 2015,[35] and increased from 15.1% in 2006[36] to 31.1% in 2022[6] in the public sector. Caesarean delivery is not done on maternal request in the South African public sector.[35] South African data shows that pregnant women who die from PE are more likely to have had a caesarean delivery.[37] In our cohort all women in the PE group were delivered by caesarean section, although this was for obstetric indications and not due to PE. While Caesarean delivery is a known risk factor for the development of PE,[38] this was not demonstrated in our cohort and mode of delivery was not a risk factor for PE.

The most significant obstetric complication in our cohort was PROM with a higher prevalence in those with PE ($P=2$, 18.2%) compared to those without PE ($n=0$, 0%) ($P=0.025$). Our small sample size limits the interpretation of this and there were a number of confounding factors: both women with PROM in the PE group were HIV positive, developed puerperal sepsis and had undergone caesarean delivery by gestational age of 28 and 35 weeks, respectively. Only one of these women had a CD4 (CD4 = 464 cells/mm^3) and HIV (VL = 764 copies/ml) available, and neither had a history of previous tuberculosis. PE was diagnosed after delivery in both women. The development of PE in these women was likely multifactorial; however, prolonged bed rest prescribed for the treatment of PROM was associated with an increased risk for PE in a study by Kovacevich et al. (16.5 cases per 1000 compared to 0.8 per 1000 among pregnant women for whom this therapy was not prescribed).[39]

Systolic BP was significantly lower ($P=0.001$) in the PE group, as was seen in the DiPEP study; however, there were no differences in diastolic BP and heart rate (Table 1). Out of keeping with the lower systolic BP in the PE group is that majority of these were peripheral PEs; however, 81.8% of the women with PE had multiple emboli. The high prevalence of obstetric haemorrhage ($n=5$, 45.5%), puerperal sepsis ($n=4$, 36.4%) and postpartum cardiomyopathy ($n=2$, 18.2%) may have contributed to the lower systolic BP in women with a PE. Hypotension associated with PE is attributed to acute right ventricular dilatation compromising left ventricular filling and reducing cardiac output. Right ventricular dysfunction seen on echocardiography has been shown to correlate with pulmonary arterial obstruction of >30%, which is expected to occur with a large central PE.[40] Echocardiography was not available to assess for right ventricular strain; however, there were no ECG features to suggest this.

Pregnancy is known to be a hypercoagulable state,[41] in addition to the postpartum period is also known to carry an increased risk of VTE.[42] Despite multiple gestation,[15] HIV,[43] antiphospholipid syndrome,[44] and

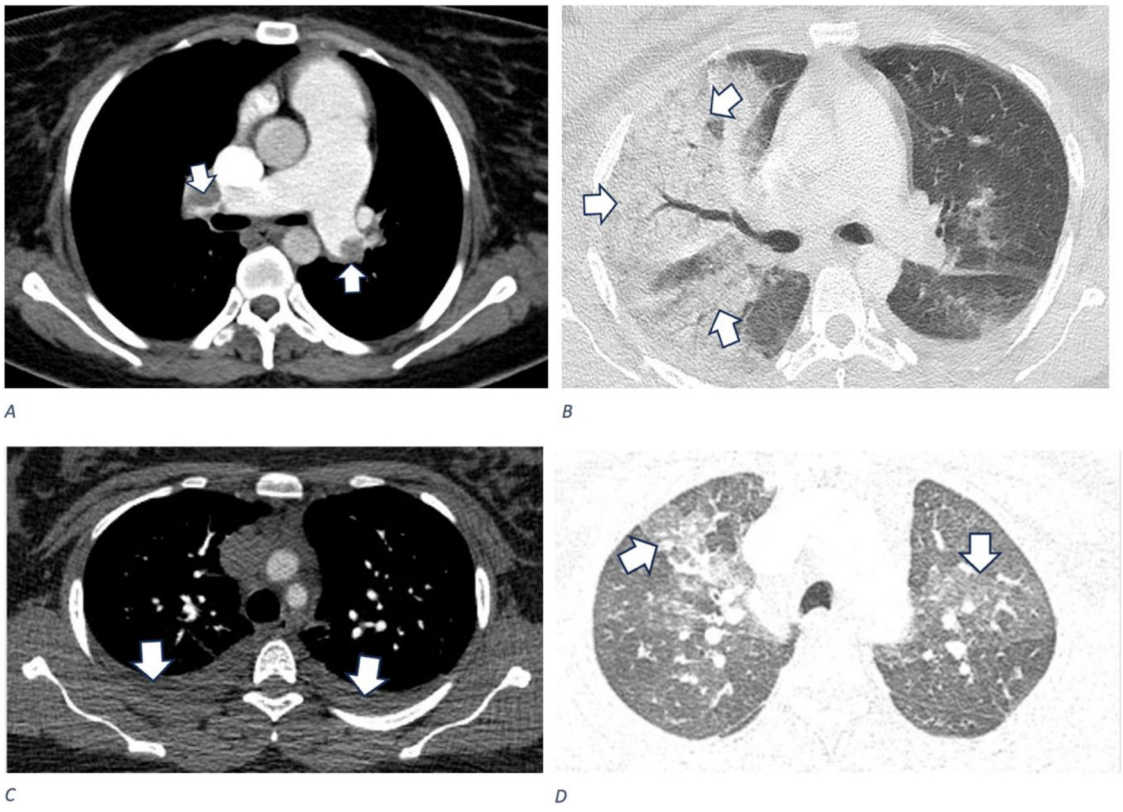


Figure 2. CTPA analysis of four different women demonstrating (A) bilateral proximal pulmonary embolism in main pulmonary arteries, (B) consolidation, (C) bilateral pleural effusions, and (D) ground glass opacities.

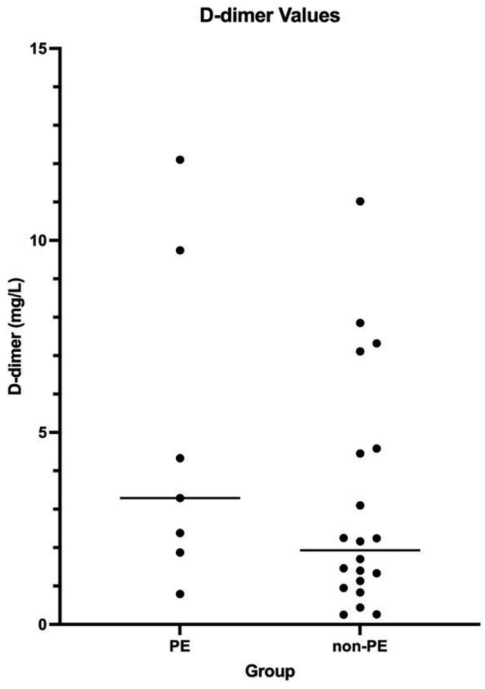


Figure 3. D-dimer values.

obesity[45] known to be associated with increased risk for PE, none were significant risk factors in our cohort (Table 3).

The strengths of this analysis are driven from the racial representation in our cohort, largely consisting of Black African women, an underrepresented group in other studies, which underpins the need and potential for further research. Additionally, the data investigated were largely complete, all the CTPAs in our cohort contained adequate quality images, and were reviewed by specialist radiologists. Yet, the findings of this analysis must be interpreted in the context of some limitations. The first being, the small sample size. Considering our study was performed at a single centre including only women admitted to a high care setting, this in itself might be a major contributory factor to the high PE burden in our population, as these women were all in a higher risk category by nature of their condition. While some of the alternative diagnoses identified, such as pleural effusion and consolidation, could potentially be detected using chest X-ray, X-rays were not reviewed as part of our protocol due to the limited availability of these images. CTPA provides a more comprehensive evaluation, particularly for subtle findings and vascular pathologies. However, the question remains whether CTPA could have been avoided in many of the women in our study, given that alternative findings could have been derived from X-ray alone. This is a potential topic for future research.

Conclusion

PE remains a significant contributor to morbidity during pregnancy and the puerperium. While clinical and laboratory features were not reliable to exclude PE in our study, considering the higher detection rate of PE as well as alternative CT diagnoses compared to international literature, it is justifiable to consider CTPA when suspecting PE in this population.

CTPA has a good yield for diagnosing PE and unmasking alternative diagnoses in a middle-income country setting, especially in women with multiple morbidities during pregnancy and the postpartum period. Our findings highlight the high prevalence of alternative diagnoses in a high-risk obstetric population undergoing CTPA in an African setting, where such data is often underreported. Larger studies are needed to evaluate the significance of variables that were not part of our initial hypothesis (e.g. low sBP, multiple gestation and PROM) to predict the risk for PE in our setting. Future research should focus on prospective studies in South African, African and low- and middle-income settings. There is a need to develop more targeted imaging protocols for high-risk obstetric patients and to evaluate the role of D-dimer and scoring systems to predict PE in our population.

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Declaration of conflicting interests

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Ethical approval

Ethical approval was obtained from the Wits Human Research Ethics Committee (Medical), Clearance Certificate No. M220255.

Informed consent

Informed consent was not sought for the present study because of its retrospective design.

Guarantor

WH.

Contributorship

WH and JZ conceived the study. SB assisted with data identification and retrieval. WH gained ethics approval, conducted the literature review, designed the data collection tool, collected raw data and wrote the first draft of the manuscript. HM, TW-T and AR reviewed and reported all CT images. All authors contributed to the final manuscript.

ORCID iDs

Wilhelm Herbst https://orcid.org/0000-0001-9480-3290
Ashesh Ranchod https://orcid.org/0000-0002-8229-9979
Jarrod Zamparini https://orcid.org/0000-0002-1365-5650

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