Risk factors for composite adverse outcomes of postpartum haemorrhage in a low-resource setting: a single-centre cross-sectional study in Mpilo Central Hospital, Bulawayo, Zimbabwe [version 1; peer review: 2 approved with reservations, 1 not approved]

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Abstract

Background: Primary postpartum haemorrhage continues to cause considerable global maternal morbidity and mortality. The aim of this study was to determine the risk factors for composite adverse outcomes in postpartum haemorrhage using multivariable logistic regression. The findings could potentially be used to anticipate and prevent composite adverse outcomes in postpartum haemorrhage.

Methods: This was a retrospective cross-sectional study carried out at Mpilo Central Hospital, a government tertiary referral centre, covering the period 1 July 2016 to 30 November 2019. Participants were included in the study if they had a diagnosis of postpartum haemorrhage. Those variables that had a p<0.2 from the univariate logistic regression analyses were considered for multivariable logistic regression. The association between independent variables and the dependent variable was assessed using odds ratio with 95% confidence intervals, to identify independent risk factors for composite adverse outcomes in PPH.

Results: The independent risk factors for composite adverse outcomes in postpartum haemorrhage were place of dwelling (AOR 4.57, 95% CI 1.87-11.12, p=0.01), prior history of a Caesarean section (AOR 2.57, 95% CI 1.10-6.00, p=0.03), APH (AOR 5.45, 95% CI 2.23-13.27, p<0.0001), antenatal haemoglobin level (AOR 19.64, 95% CI 1.44-268.50, p=0.03), and delivery by Caesarean section (AOR 10.21, 95% CI 4.39-23.74, p<0.0001). Blood loss was also an independent risk factor for composite adverse outcomes in postpartum haemorrhage with the following blood loss; 1001-1500 ml (AOR 9.94, 95% CI 3.68-
26.88, \( p<0.0001 \), 500-1000 ml (AOR 41.27, 95% CI 11.32-150.54, \( p <0.0001 \)), and 2001 ml (AOR 164.77, 95% CI 31.06-874.25, \( p<0.0001 \)).

**Conclusions:** This study found that the independent predictors for composite adverse outcomes in PPH were rural dwelling, prior history of a Caesarean section, antenatal haemoglobin level, delivery by Caesarean section, and blood. In low- and middle-income countries, such information should help in increasing clinical vigilance and preventing maternal deaths.

**Keywords**
Postpartum haemorrhage, risk factors, composite adverse outcomes, low-resource settings
Introduction
Primary postpartum haemorrhage (PPH) is defined as a cumulative blood loss from the genital tract of ≥500 mL or more following a normal vaginal delivery or ≥1,000 mL or more following a caesarean section within 24 hours of delivery evidenced by a rise in the pulse rate, and falling blood pressure\textsuperscript{1-3}.

In 2017, approximately 810 women died from causes related to pregnancy and childbirth, and 94% of all maternal deaths occurred in low and lower middle-income countries\textsuperscript{4}. In a systematic analysis, Say \textit{et al.} found that low- and middle-income countries accounted for 480,000 maternal deaths (32%) compared with 1200 (8%) in the developed regions\textsuperscript{5}. PPH is the leading cause of maternal deaths in SSA\textsuperscript{6}.

The multi-country Survey on Maternal and Newborn Health reported the prevalence of PPH as 1.2%, with higher rates in developing countries than developed ones\textsuperscript{6}. Other studies in Sub-Saharan Africa (SSA) reported rates of 1.6% in Zimbabwe, 16.6% in Southern Ethiopia, 9% in Uganda and 23.6% in Cameroon\textsuperscript{1,3,6}, respectively. Ford \textit{et al.} reported increasing PPH rates from 6.1% in 2003 to 8.3% in 2011 (\textit{p}<0.0001) in Australia\textsuperscript{7}.

Two-thirds of women with PPH having no identifiable risk factors\textsuperscript{8}. Recognized risk factors for PPH include previous PPH, twin gestation, large baby, induction of labour, prolonged labour, operative delivery, preeclampsia, caesarean delivery, grand multiparity, maternal age 35 or above, and postdates\textsuperscript{9-11}.

Tort \textit{et al.} used a multivariable logistic mixed model to identify factors that were significantly associated with PPH maternal death\textsuperscript{12}. However, in this study PPH maternal death or serious morbidity were used as composite adverse outcomes.

The aim of this research was to documents risk factors for poor composite adverse outcome in PPH. This could help clinicians identify which women with PPH are at risk of composite adverse outcomes and increase further the clinical vigilance associated with the management of PPH thereby preventing deaths.

Methods
Study type, setting and participants
This was a retrospective cross-sectional study carried out at Mpilo Central Hospital, a government tertiary referral centre, covering the period 1 July 2016 to 30 November 2019. Mpilo Central Hospital is situated in the township of Mzilikazi in Bulawayo. Bulawayo is the second largest city in Zimbabwe after the capital city Harare, with a population of 653,337 as of the 2012 census\textsuperscript{13}. Participants were included in the study if they had a diagnosis of postpartum haemorrhage within 24 hours of delivery at Mpilo Central Hospital. Women that delivered outside the hospital were excluded from the study.

Independent variables
The independent variables included socio-demographic factors, mode of delivery, fetal characteristics, blood loss, laboratory tests, causes of PPH and the management of PPH.

Main outcome measure
The main outcome of interest for the study was the composite adverse outcome which included maternal death or serious morbidity (either of hypovolaemic shock or haemoglobin <4 g/dL or massive blood transfusion >4 units or hysterectomy or admission to ICU or coagulopathy or major organ dysfunction), similar to the Delphi consensus study on PPH\textsuperscript{14}.

Sample size calculation
The Cochran sample size formula was used to calculate the sample size as follows; $n_0 = z^2 pq/e^2$

where $n_0 =$sample size
$z =$ is the selected critical value of desired confidence level
$p =$ is the estimated proportion of an attribute that is present in the population
$q =$ is 1-$p$ and $e =$ is the desired level of precision

Assuming the maximum variability, which is equal to 50% ($p = 0.5$) and taking 95% confidence level with ±5% precision, the calculation for the required sample size was as follows;

$p = 0.5$ and hence $q = 1-0.5 = 0.5$, $e = 0.05$; $z = 1.96$

So, $n_0 = (1.96)^2(0.5)(0.5)/(0.05)^2$

$= 384.16$

=385

Data collection
Data collection was done using a paper data collection tool (see Extended data)\textsuperscript{15} that was used to collect secondary data from the labour ward delivery registers, and mortality registers. Hospital case notes were retrieved the clinical data were extracted.

Data analysis
Data were cleaned, coded and entered into a Microsoft Excel spreadsheet, then exported to SPSS Version 20 (IBM, Armonk, NY, USA) for analysis. Descriptive statistical analyses were performed and presented as frequencies and percentages for categorical variables. Bivariate correlations of association between main independent variables and the outcome measures were performed using Pearson 2-tailed chi-square test. A $p$ value of <0.05 was considered to be statistically significant, and these were considered for the univariate logistic regression. Those variables that had a $p<$0.2 from the univariate logistic regression analyses were considered for multivariable logistic regression. The association between independent variables and the dependent variable was assessed using odds ratio with 95%
confidence intervals, to identify independent risk factors for composite adverse outcomes in PPH, holding other variables constant and adjusting for co-variates. The Hosmer-Lemeshow goodness-of-fit was used to check if the model fitted well. A p<0.05 was taken as statistically significant.

**Ethical approval**

The Ethics Committee at Mpilo Central Hospital made a ruling for all retrospective studies to go ahead in the institution from 2016 onwards as long as the data remained anonymous; the committee waived the requirement for patient consent. No ethical issues will arise during the study as all the data will remain anonymous with no identifying personal data. Minutes of the Committee’s inaugural meeting held on the 13th October 2016 set out the requirements of all the studies at the institution.

**Results**

**Socio-demographic characteristics of participants**

A total of 386 cases of PPH were recorded during the period 1 July 2016 to 30 October 2019. The summary of maternal and fetal characteristics are shown in the Supplementary Tables in the Extended data15. Deidentified results are available for each patient as Underlying data15.

**Risk factors for composite adverse outcomes**

Table 1 and Table 2 show the results of the multivariable logistic regression. Rural women were 4.6 times more likely to be statistically significantly associated with composite adverse outcomes compared to women from urban areas (AOR 4.57, 95% CI 1.87-11.12, p=0.01).

**History of Caesarean section**

Women with a prior history of a Caesarean section were statistically significantly associated with composite adverse outcomes in PPH. Such women were 2.6 times more likely to be statistically significantly associated with composite adverse outcomes in PPH, compared to women without such history (AOR 2.57, 95% CI 1.10-6.00, p=0.03).

**APH**

APH was statistically significantly associated with composite adverse outcomes in PPH. Women who presented with APH were 5.5 times more likely to be statistically significantly associated with composite adverse outcomes in PPH compared to women who had no APH (AOR 5.45, 95% CI 2.23-13.27, p<0.0001).

**Antenatal haemoglobin count**

Antenatal haemoglobin count was also statistically significantly associated with composite adverse outcomes in PPH. Women with haemoglobin counts of 0–5.99 g/dL were 19.6 times more likely to be statistically significantly associated with composite adverse outcomes in PPH compared with women with haemoglobin counts of 11 g/dL and above (AOR 19.64, 95% CI 1.44-268.50, p=0.03).

**Delivery by Caesarean section**

Delivery by Caesarean section was statistically significantly associated with composite adverse outcomes in PPH. Women who had a Caesarean section were 10.2 times more likely to be statistically significantly associated with composite adverse outcomes in PPH compared to women who delivered vaginally (AOR 10.21, 95% CI 4.39-23.74, p<0.0001).

**Blood loss**

Blood loss was statistically significantly associated with composite adverse outcomes in PPH. The odds rose significantly higher as the amount of blood loss increased. Women who lost 1001–1500 ml of blood were 9.9 times more likely to be statistically significantly associated with composite adverse outcomes, compared to women that lost 500–1000 ml (AOR 9.94, 95% CI 3.68-26.88, p<0.0001). The odds rose to 41.3 times more likely to be associated with composite adverse outcomes in those women who lost 1501–2000ml compared to those women who lost 500–1000 ml (AOR 41.27, 95% CI 11.32-150.54, p<0.0001). Whereas women who lost 2001 ml and above were 164.8 times more likely to be statistically significantly associated with composite adverse outcomes in PPH compared to women who lost 500–1000 ml (AOR 164.77, 95% CI 31.06-874.25, p<0.0001).

**Discussion**

PPH rates have been reported to be rising in both low-income and high-income countries11,19. This means that PPH will remain an important global subject. The strength of this research is that it involves a large homogenous group of patients with PPH, in SSA where PPH continues to contribute significantly to global mortality and morbidity.

Rural women were 4.6 times most likely to be statistically significantly associated with composite adverse outcomes compared to women from urban areas (AOR 4.57, 95% CI 1.87-11.12, p=0.01). National governments need to made healthcare accessible to rural women so that the Sustainable Development Goals on Maternal Mortality to reduce global maternal mortality ratio to less than 70 per 100,000 live births by 203014 could be achievable.

Women with a prior history of a Caesarean section were statistically significantly associated with composite adverse outcomes in PPH. These women are not only at risk of developing a PPH (OR 3.15, 95% CI 1.02-10.3)19, but the women were 2.6 times most likely to be statistically significantly associated with composite adverse outcomes in PPH, compared to women without such history (AOR 2.57, 95% CI 1.10-6.00, p=0.03). The means that women with a prior history of a Caesarean section should receive extra clinical vigilance.

APH was statistically significantly associated with composite adverse outcomes in PPH. Women who presented with APH were 5.5 times more likely to be statistically significantly
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*Vacuum, forceps not enough data for regression analysis
associated with composite adverse outcomes in PPH compared to women who had no APH (AOR 5.45, 95% CI 2.23-13.27, \( p<0.0001 \)).

Women with haemoglobin levels of 0–5.99 g/dL were 19.6 times more likely to be statistically significantly associated with composite adverse outcomes in PPH compared to women with haemoglobin levels of 11 g/dL and above (AOR 19.64, 95% CI 1.44-268.50, \( p=0.03 \)). Anaemia should be screened for antenatally and women should receive treatment so that they enter labour with normal haemoglobin counts.

Women who had a Caesarean section were 10.2 times more likely to be statistically significantly associated with composite adverse outcomes in PPH compared to women who delivered vaginally (AOR 10.21, 95% CI 4.39-23.74, \( p<0.0001 \)). Women would have had Caesarean sections should be closely monitored post-operatively.

Women who lost 2001 ml of blood and above were 164.8 times more likely to be statistically significantly associated with composite adverse outcomes in PPH compared to women who lost 500–1000ml (AOR 164.77, 95% CI 31.06-874.25, \( p<0.0001 \)). The amount of blood loss was found to be related to adverse maternal outcomes\(^9\). Prompt, effective management of PPH\(^9\), should be the aim to reduce the amount of blood loss and prevent the development of composite adverse outcomes.

**Limitations**
The major limitation of this study is that it was a retrospective, single-centre study that used secondary data. This could limit the generalizability of its findings to other centres of low-resourced settings.

**Conclusions**
The independent predictors for composite adverse outcomes in PPH were rural dwelling, prior history of a Caesarean section, antenatal haemoglobin level, and delivery by Caesarean section. Blood loss was also an independent predictor for composite adverse outcomes in PPH. Crucially, this new information should help in increasing clinical vigilance and preventing maternal deaths especially in low- and middle-income countries where PPH mortality is of high prevalence. Regular on-site training of staff can focus on drilling on these important issues and can improve outcomes\(^9\).

**Data availability**

**Underlying data**
Mendeley Data: Composite adverse outcomes in primary PPH.
https://doi.org/10.17632/wjtm8mgcc.3\(^{18}\).

This project contains the following underlying data:
- PPH-Data-Share (XLSX). The raw de-identified data gathered from each patient examined in this study.
- de-identified individual-level data for all patients.

**Extended data**
Mendeley Data: Composite adverse outcomes in primary PPH.
https://doi.org/10.17632/wjtm8mgcc.3\(^{19}\).

This project contains the following extended data:
- Data Collection Sheet-PPH (DOCX).
- Supplementary tables - PPH mortality (DOCX).
  - Table 1: Maternal and fetal characteristics.
  - Table B: Socio-demographic characteristics of study patients.
  - Table C: Present risk factors for PPH
  - Table D: Fetal birth weight, blood loss and causes of PPH
  - Table E: Management and outcomes in PPH
  - Table F: Bivariate correlations between independent variables and composite adverse outcome.

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

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**References**


Open Peer Review

Current Peer Review Status: ?  ✗  ?

Version 1

Reviewer Report 18 September 2020

https://doi.org/10.5256/f1000research.25139.r69904

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Eba Abdisa

Department of Psychiatry, School of Nursing and Midwifery, Institute of Health Sciences, Wollega University, Nekemte, Ethiopia

Title: Risk factors for composite adverse outcomes of postpartum hemorrhage in a low-resource setting: a single-center cross-sectional study in Mpilo Central Hospital, Bulawayo, Zimbabwe

- The title seems interesting, particularly it tried to address the problem of the low-income countries, but it should be arranged as "Risk factors for Composite adverse outcome of postpartum hemorrhage in Mpilo central hospital, Bulawayo, Zimbabwe: Cross sectional study" - this is because this country is known to be in low resource by default; no need to say "in a low resource setting".

Abstract:

Background: "Primary postpartum hemorrhage continues to cause considerable global maternal morbidity and mortality."

- Rewrite the above statement as "Globally, primary postpartum hemorrhage continues to cause considerable maternal morbidity and mortality".

Conclusion: how is such information useful for preventing death? What are possible methods? Who will use this information? You must state some of them in the background section. From all independent factors, which one is difficult to prevent? Be specific when you conclude your findings.

Introduction:

- Your citation in paragraph one: you didn't take the information from the primary results, rather you cited the secondary result(paper). Please try to address the first research finding and cite it correctly

- Instead of ‘say et al, ford et al, Tort et al’, use ‘researcher(s), report(s), finding(s)...

- Are the 810 women's death related to PPH? You must be specific.
What makes the increment of PPH from 6.1%-8.3% in Australia? Please present some evidence findings for the reason that the researchers stated.

In paragraph 5, you said, ‘Tort et al used multivariable mixed mode’, please state only what the study assessed and what it got, and avoid the methodology the researchers used.

Poor composite adverse outcome (para. 5): you must clearly define it.

Significance of the study: the last paragraph stated the importance of this study. But do you think that your findings might help only clinicians? What about your study population? What about the policy makers?

Your introduction section seems shallow.

APH: write the full version.

**Methods:**

Why did you only use a single study setting? Please justify.

What if the women delivered outside by developed PPH? Why did you exclude such a risk group? Giving birth out of healthcare setting will even be expected to the complication. Please say something.

Detailed description is expected regarding your study area: number of deliveries per year/month, number of skilled birth attendants (midwifery, physicians & others).

Data collection: this seems shallow. It was not clear how you selected your study group (sample size). How did you collect data of 385? Did you start from a specific year? Example random vs nonrandom?

Data analysis: software package that you used to enter data(excel). In this case, it seems difficult to manage missed data and mistakes. Why don't you use Epidata, epi-info...?

Why did the committee waive the requirement for patient consent?

Discussion: It seems well organized.

But consider to compare your findings with others' past international/national findings and put your opinion when you get the difference.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: women health, mental health, clinical condition, child health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 26 August 2020

https://doi.org/10.5256/f1000research.25139.r64325

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Michael Johnson Mahande
Department of Epidemiology & Biostatistics, Institute of Public Health, Kilimanjaro Christian Medical University College, Moshi, Tanzania

Risk factors for composite adverse postpartum haemorrhage in a low resources setting: a single-centre cross sectional study in Mpilo Central Hospital Bulawayo, Zimbabwe.

Section
Comment, question, suggestion.

Abstract
1. The abstract background should consist a few statements that explain the meaning and aim of the study not the model used. The model used (multivariable logistic regression) can be explained in the methods section.

Introduction
Background
1. No comment.

Methodology
1. Why did authors calculate sample size while the study utilized data that were retrospective
collected? I expected the study could use all available data and power could be calculated instead of the sample size.

Results
1. It could be more important if the tables for social demographic characteristics and clinical characteristics were included in the manuscript.

2. In presenting numbers in the table is better to have the standard decimal points to be presented especially when presenting p-values.

3. Consider combining single and divorced in marital status as divorced have few participants for regression analysis.

Discussion
1. NONE.

Strengths and limitations
1. Despite being a study involving a single center, what is the strength of this study?

Conclusion
1. No comment.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Reproductive Health, Maternal Newborn & Sexual Adolescent Health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.
Jaffu O. Chilongola
Kilimanjaro Christian Medical Centre, Kilimanjaro Clinical Research Institute, Moshi, Tanzania

1. It is surprising that this manuscript has only one author. This means the lone author did everything from conceiving the ideas, data collection, analysis, writing the manuscript. It has to be confirmed that NO one else has participated in this work.

2. Age ranges in table 1 variables are too narrow to provide useful information on the outcome variable.

3. The analyses are weak perhaps because the design was also weak. When A low post delivery Hb level is considered as a risk for PPH it brings the confusion what would otherwise be expected. Similary, when Ruptured uterus is tested for its association with PPH. Many of the predictors are obviously inherently related to the outcome variable. It is unclear what information this manuscript attempting to bring forth.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
No

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Infectious diseases, Immunology, Molecular Biology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.
Author Response 11 Oct 2020

Solwayo Ngwenya, Mpilo Central Hospital, Bulawayo, Zimbabwe

Reviewer 1

1. It is surprising that this manuscript has only one author. This means the lone author did everything from conceiving the ideas, data collection, analysis, writing the manuscript. It has to be confirmed that NO one else has participated in this work. I can confirm that I am the sole author. Response: I have done many studies of this magnitude before as a sole author.

2. Age ranges in table 1 variables are too narrow to provide useful information on the outcome variable. Response: I have decided to leave them as they are as this didn't not affect the logistic regression.

3. The analyses are weak perhaps because the design was also weak. When A low post delivery Hb level is considered as a risk for PPH it brings the confusion what would otherwise be expected. Similary, when Ruptured uterus is tested for its association with PPH. Many of the predictors are obviously inherently related to the outcome variable. It is unclear what information this manuscript attempting to bring forth. Response: Comments noted.

**Competing Interests:** None