

AN INSIGHT INTO POSTPARTUM HEMORRHAGE AND ITS ASSOCIATED RISK FACTORS

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ABSTRACT

Background: Postpartum hemorrhage is a leading cause of maternal death and pregnancy-related morbidities. It is difficult to predict, as risk factors vary among people. *Objective:* We aimed to assess whether antenatal diseases are associated with increased risk of postpartum hemorrhage. *Methods:* We did a cross-sectional study conducted in the different hospitals of the Department of Gynaecology and Obstetrics in rural areas of Southern Punjab, Pakistan, for a period of six months, from October 2020 to March 2021. The following data was collected by using a standard prepared questionnaire containing demographic information, presenting complains, physical examination records, and diagnostic laboratory reports. Descriptive statistics were used to calculate the frequencies and percentages, while inferential statistics were used to determine the significance, associated risk factors, and prevalence of postpartum hemorrhage. *Results:* Women had an average age of 29.7 ± 5.91 years. There were 79 (44.5%) women positive for PPH. A statistically significant relationship between postpartum hemorrhage positive and the age of the women was found. Similarly, when we checked the association of postpartum hemorrhage with antenatal diseases, a significant association between PPH and anaemia and urinary tract infections was distinguished. *Conclusion:* The study report shows that postpartum hemorrhage may be associated with increased maternal age and the incidence of anaemia and urinary tract infections.

Key words: Postpartum Hemorrhage; Maternal Mortality; PPH; Anemia; Postpartum complications

1. Introduction

Excessive vaginal bleeding following childbirth, known as postpartum hemorrhage (PPH), is a predominant cause of maternal mortality and morbidity worldwide (Owen, Cassidy, and Weeks 2021). In 1995, the World Health Organization (WHO) estimated that about 0.5 million women died worldwide in developing countries due to complicated pregnancies (World Health Organization, 2012). Postpartum hemorrhage is defined as blood loss from the vaginal tract of more than 500 mL in vaginal delivery, with severe postpartum hemorrhage (SPPH). It is categorized as a loss of 1000 mL or more, followed by caesarean section and very severe postpartum hemorrhage (VSPH), definite as a loss of 2500 mL or more (Bateman et al. 2010; Bienstock, Eke, and Hueppchen 2021). An estimate of 125,000 maternal deaths each year reported due to PPH accounts for approximately a quarter of all maternal mortality globally. Because developing countries have roughly 125 million births each year, the risk of maternal death from PPH is about 1 in 1000 deliveries (Borovac-Pinheiro et al. 2018; Organization 2018; Prata, Bell, and Weidert 2013). In the maternal deaths in the United Kingdom and Australia, postpartum hemorrhages were the prominent cause of maternal deaths (Friedman and Ananth 2020). Meanwhile, postpartum hemorrhage occurs in 4-6% of vaginal deliveries (Chung et al. 2017; Gadappa et al. 2018).

Postpartum hemorrhage is caused by the failure of the uterus to contract appropriately after birth (atonic PPH) (Suarez et al. 2020), which accounts for 90% of PPH in most countries; genital tract trauma accounts for about 7% of PPH (Shields, Goffman, and Caughey 2017), bleeding due to placental tissue retention and coagulation system failure currently accounts for the remaining 3% (Sentilhes, Kayem, and Mattuizzi 2021; Zhao et al. 2021). There are many risk factors proposed for postpartum hemorrhage, such as multiple pregnancies leading to anaemia, higher gravida, advanced maternal age, pregnancy-induced hypertension, and the induction of labour have been the leading causes of higher incidence of postpartum hemorrhage (Attali and Yogev 2021; Thompson et al. 2015). The purpose of the current study was to investigate risk factors associated for postpartum hemorrhage in rural areas of Southern Punjab.

2. Methodology

This was a cross-sectional study in which the study population was the pregnant women of rural areas of Southern Punjab who suffered from postpartum hemorrhage during and after delivery. Our study population was all mothers who delivered at basic health units and rural health clinics in Southern Punjab from October 2020 to March 2021. The current study was designed to sample size of 176 pregnant women (100% response rate) with different complications. Moreover, a clause of an ethics statement is also included about informed consent to make sure the respondent that their information will be kept confidential and will be used only for research purposes. The patient sample size was calculated using an online WHO sample size calculator, with a 5% margin error and a 95% confidence interval. The sample was calculated by Sharma *et al.*, sample collection method (Sharma et al. 2020). Meanwhile, in the current study, a convenient questionnaire based on observations was used to approach the patients at Different BHUs (Basic Health Units), RHCs (Rural Health Clinics) hospitals of the gynaecology department of South Punjab. Pregnant women of the reproductive age group of 15-45 years, present at the time of delivery or before (confirmed through UPT and LMP). Blood pressure was measured by sphygmomanometer while patients having symptoms of anaemia were confirmed through a

hemoglobinometer (or Hb meter), which was a rapid confirmatory test for anaemia to detect the concentration of Hb in the blood. After a complete medical history, In order to identify bacteria in urine samples collected from individuals exhibiting signs of urinary tract infections, urine dipstick analysis and culture were performed. Antimicrobial susceptibility testing on the isolates using the disc diffusion method was done in addition to calculating the validity of the dipstick test in the screening of UTIs. The disc diffusion method was used to assess the antibiotic susceptibility of isolates on Mueller-Hinton agar. Ciprofloxacin (5g), Gentamycin (20g), tetracycline (30g), Ceftriaxone (30g), kanamycin (30g), cefotaxime (30g), and ampicillin (10g) were among the antibiotics used. The plates with the disc were incubated overnight at 37 oC in an inverted configuration. Zones of inhibition were estimated using a ruler to the precise millimetre, and standards suggested by CLSI M100-S12 were compared. (Wayne 2006).

For confirmation of Hepatitis B and C, the rapid kit test was performed if the patient suspected hepatitis they were further confirmed with immune-chromatographic test which was performed by rapid immunochromatography (ICT) kit (Australia and Abbot, USA) which is commonly used for the screening of the seropositivity (antigen-detection) in the blood sample of the infected patient. The collected blood samples were centrifuged at 6000 rpm for 15 minutes before processing to obtain serum. An approximately 9-10 μ L serum was collected through a sterile plastic dropper and immediately transferred to the ICT tubes. Three drops of serum were put into the ICT screening device well under careful circumstances and reacting color appeared due to coated antigens. After 15 minutes, results were noted as, if the line appears on the R-line it gives a positive result and if no line appears on T-line it gives a negative result. For further confirmation, patients were suggested for the ELISA (Enzymes-linked immunosorbent assay) or Polymerase chain reaction (PCR). While gestational diabetes was confirmed through a glucometer. The patients were excluded who refused informed give consent and the required information. The women's history of bleeding disorders was also excluded from the study.

The collected data were entered into an excel sheet, and then it was cleaved and decoded using SPSS sky server Version 2020. The quantitative variable in this study, e.g., age, was present using mean \pm SD. And the qualitative data like PPH (present/absent) was presented as frequency and percentage. Descriptive statistics were used to calculate the frequencies and percentages, while inferential statistics were used to determine the significance associated with risk factors of developing postpartum hemorrhage. The level of significance selected for the study $p < 0.05$ level (Rani 2015).

3. Results

Our study population's mean age was 29.78 ± 5.91 years, with women's minimum and maximum ages of 15 and 45 years, respectively (Table 1). While the frequency of the age group of 15-25 years was $n = 52$ (29.5%), the frequency of the age group 26-35 years was $n = 96$ (54.5%), and the frequency of age group 36-45 years was 28 (15.9%) (Table 2).

Table 1. Age Distribution of the Women

N (number of patients)	176
Age (Mean \pm SD)	29.78 \pm 5.91
Minimum (Age)	15
Maximum (Age)	45

Table 2. Frequencies and Percentages according to age groups

Age Groups	Frequency	Valid Percentage (%)	Cumulative Percentage (%)
15 - 25 years	52	29.5	29.5
26 - 35 years	96	54.5	84.1
36 - 45 years	28	15.9	100.0
Total	176	100.0	

Several valuable results were observed, 79 (44.5%) women were positive for PPH, 21 (11.9%) patients were positive between the ages of 15 and 25, 39 (22.2%) were positive between the ages of 26 and 35, and 19 (10.8%) were positive between the ages of 36 and 45 (Table 3). The p-value for the association between PPH and age was 0.029, which is less than 0.05, which fulfilled the requirements of our null hypothesis and showed a significant association between PPH and age. As with the increase in age, the risk of PPH also increases and vice versa (Table 4).

Out of 176 recruited patients 79 (55.11%) were positive for PPH while 97 (44.89%) were negative for PPH as displayed in Figure 1.

Table 3. Descriptive statistics for PPH

Age Groups	Frequency	Valid percentage (%)	Cumulative percentage (%)
N	79	44.9	100
15-25 (Years)	21	26.6	26.6
26-35 (Years)	38	48.1	74.7
36-45 (Years)	20	25.3	100.0

Table 4: Association of PPH status with women's age

Age Groups		Positive	Negative	Total
15-25 years	Count	21	31	52
	%	11.9	17.6	29.5
26-35 years	Count	39	57	96
	%	22.2	32.4	54.6
36-45 years	Count	19	9	28
	%	10.8	5.1	15.9
Total	Count	79	97	176

	%	44.9	55.1	100
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Chi-square Test = 7.103 p-value = 0.029

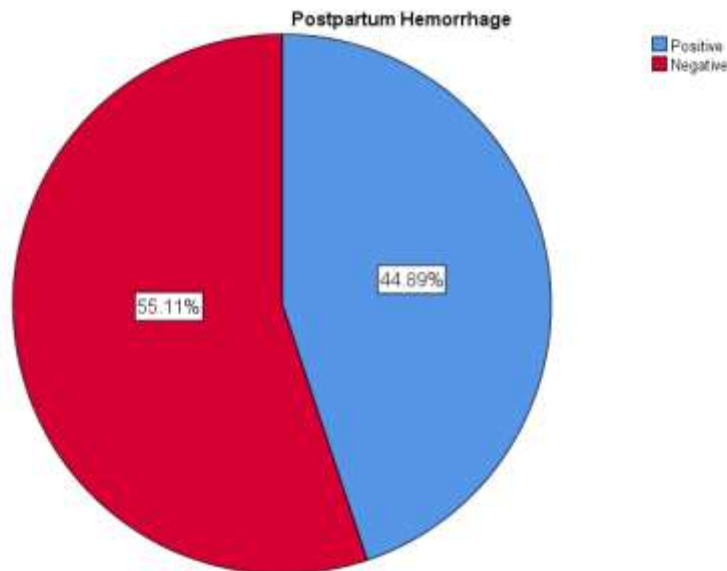


Figure 1: showing the percentage value for PPH in the study population

3.1 PPH and Antenatal Diseases

As we have found a large frequency of positive patients for postpartum hemorrhage (PPH) in our study population, we tried to find the possible risk factors that may lead to PPH. For this purpose, we checked the association of PPH with antenatal diseases. So, when we checked the association between PPH and Pregnancy-induced hypertension, 8.0% of patients were positive for PPH, and the frequency of PIH, 16.5% of patients were positive for PIH but negative for PPH. On the other hand, 36.9% of patients were positive for PPH and negative for PPH, and 38.6% of patients were negative for both. The P-Value of association for PPH and PIH was 0.062, greater than 0.05. So, we reject our null hypothesis as no significant association was found between PIH and PPH. While no patient was positive in the case of epilepsy and PPH, 0.6% of patients were positive for epilepsy and negative for PPH. The P-Value of the association between PPH and epilepsy was 0.365, also greater than 0.05. Hence, we reject our null hypothesis as there was no significant association between PPH and epilepsy. On the other hand, in the case of gestational diabetes mellitus and PPH, no patient was positive, while 0.6% of patients were positive for GDM and negative for PPH. The P-value for the association between PPH and GDM was 0.399, greater than 0.05. Thus, we reject our null hypothesis as there was no significant association between GDM and PPH. Also, when we checked the association between anaemia and PPH, we found 26.1% of patients who were positive for both anaemia and PPH. The following facts have been observed 22.7% of patients were anaemic but negative for PPH. 18.8% of patients were positive for PPH but negative for anaemia. And 32.4% of patients were negative for both PPH and anaemia. The P-value of the association between PPH and anaemia was 0.025, which was less than 0.05. Hence, it meets our null hypothesis requirements as there was a significant association between anaemia and PPH, which indicates that anaemic patients were at a higher risk of developing PPH and vice versa.

Similarly, in the case of UTI and PPH, we found 4.0% of positive patients for both UTI and PPH. 14.8% of patients were positive for UTI but had a negative history of PPH. While 40.9% of patients tested positive for PPH but did not test positive for UTI, 40.3% of patients were negative for both PPH and UTI. The P-value for the association of PPH and UTI was 0.002, which was less than 0.05. Thus, it was also accomplishing the requirements of our null hypothesis. There was a significant association between UTI and PPH, which indicates that UTI patients had a higher risk of developing PPH and vice versa.

Likewise, in the case of Hepatitis B along with PPH, no patient was positive, while 1.7% of patients were positive for Hepatitis B and negative for PPH. The P-value of the association between PPH and hepatitis B was 0.115, greater than 0.05. So, we reject our null hypothesis as there was no significant association between hepatitis B and PPH. And in the case of hepatitis C and PPH, 4.5% of patients were positive for both, and 4.5% of patients were positive for Hepatitis C and negative for PPH. On the other hand, 40.3% of patients were positive for PPH and negative for hepatitis C, while 50.6% were negative for both hepatitis C and PPH. The P-value of association for PPH and hepatitis C was 0.666, greater than 0.05. So, it also rejects our null hypothesis as there was also no significant association between hepatitis C and PPH (Table 5).

Table 5. Association of PPH with antenatal diseases

Diseases			Postpartum hemorrhage		Pearson Chi-square
			Positive	Negative	P value
PIH	Positive	Count	14	29	0.062
		%	8.0%	16.5%	
	Negative	Count	65	68	
		%	36.9%	38.6%	
Epilepsy	Positive	Count	0	1	0.365
		%	0.0%	0.6%	
	Negative	Count	79	96	
		%	44.9%	54.5%	
GDM	Positive	Count	0	1	0.399
		%	0.0%	0.6%	
	Negative	Count	79	96	
		%	44.9%	54.5%	
Anaemia	Positive	Count	46	40	0.025
		%	26.1%	22.7%	
	Negative	Count	33	57	
		%	18.8%	32.4%	
UTI	Positive	Count	7	26	0.002
		%	4.0%	14.8%	

	Negative	Count	72	71	
		%	40.9%	40.3%	
Hepatitis B	Positive	Count	0	3	0.115
		%	0.0%	1.7%	
	Negative	Count	79	94	
		%	44.9%	53.4%	
Hepatitis C	Positive	Count	8	8	0.666
		%	4.5%	4.5%	
	Negative	Count	71	89	
		%	40.3%	50.6%	

The results indicate the age ratio of patients in our study population. According to the mother's age, 1 patient was the extreme minimum age of 15 years, and two patients were the extreme maximum age of 45 years in our study population. The population pyramid provides details about the number of patients positive for PPH according to age group. The left side of the graph shows the frequency of positive patients (in blue color), while the right side shows the frequency of negative patients (red color) in our study population. Total of 21 patients were positive for PPH within the age group of 15–25 years, 39 patients were positive from the age group of 26–36 years, and 19 patients with PPH were from the age group of 36–45 years. On the other hand, 31 patients were negative for PPH in the age group of 15–25 years, 57 patients were negative in the age group of 26–35 years, and 9 patients were negative in the age group of 36–45 years (figure 2).

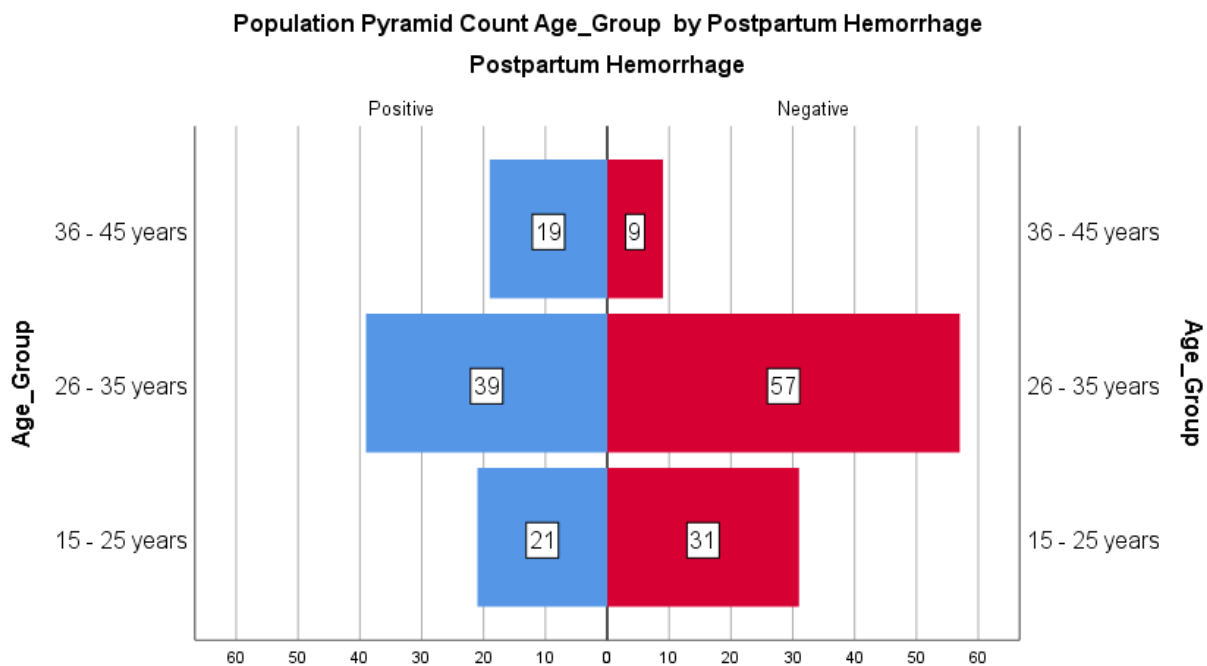


Figure 2: showing the population pyramid for PPH according to age groups

4. Discussion

Even though postpartum haemorrhage occurs more frequently in some places and among some ethnic groups than others, it is still the only factor in maternal mortality and morbidity. (Cohen 2018). Primary postpartum haemorrhage is defined as an estimated blood loss of more than 500 mL following vaginal delivery and more than 1000 mL following caesarean delivery. (Bateman et al. 2010; Cavazos-Rehg et al. 2015). The risk factors for PPH were anaemic, older age, multiple gravida, and higher urinary tract infections.

The postpartum hemorrhage rate in the present study (44.5%) is higher than the global incidence of 6% of PPH, which is reported by Clavert *et al.* (Clavert et al. 2012) and higher than the previous reported by Mazhar *et al.* 1.6% in Pakistan (Mazhar, Batool, and Batool 2018). This higher incidence of postpartum hemorrhage in the current study may have been varied as it was the first study of its type in this area and may have been inclined by the characteristics of the study population. These were the higher frequency of rural women reported for postpartum hemorrhage.

In contrast to the higher incidence of postpartum hemorrhage in this study, we tried to determine the associated risk factors of PPH with age and other antenatal diseases. However, the current study found that the immense majority of women with an older age group had a higher incidence of PPH. The women aged 26-35 years old had a higher incidence of PPH with 22.2% versus women aged 15-25 years old 11.9%. The following raises concern about the higher incidence of older-age pregnancy. However, this study reveals that with the increase in maternal age, the risk for developing PPH also increases, which correlates with previously reported studies by Cavazos-Rehg *et al.* and Aoyama *et al.* that pregnant women of greater age had greater odds for developing postpartum hemorrhage (Aoyama et al. 2019; Cavazos-Rehg et al. 2015).

Likewise, this study also found a significant association between anaemia and PPH, similar to other studies. Parks *et al.* (2019) also found a significant association between anaemia and PPH in a prospective cohort study in Pakistan and India (Parks et al. 2019). In another retrospective cohort study done in India, Nair *et al.* (2016) reported that anaemic patients had a nine times higher risk of developing PPH, and both had a strong association. (Nair et al. 2016).

On the other hand, this study also found a significant association between urinary tract infections (UTI) and PPH due to a higher incidence of urinary tract infections during and after delivery. The possible cause of developing higher rates of UTI may be associated with the study reported by Jabba *et al.*, which found negative maternal and fetal outcomes and revealed that developing UTI leads to anaemia (Jabba 2006). Another study found that severe anaemia can lead to infections, particularly during pregnancy (Jayaweera, Reyes, and Joseph 2019; Kabyemela et al. 2008) and that anaemia is also associated with postpartum hemorrhage (Frass 2015; Omotayo et al. 2021). This study has the following limitations: Firstly, the study was conducted in lower health facilities where services like surgery (caesarean section) and blood transfusion are not offered. Secondly, due to inadequate laboratory findings for incidence of PPH, blood was measured by the visual estimation that has been known to undervalue blood loss. However, these were 79 patients (44.9%), and it is dubious that they have significantly affected the estimate of postpartum hemorrhage risk. Thirdly, there was a small study duration and lesser antenatal visits due to the

COVID-19 Pandemic that did not have adequate power to identify risk factors for severe postpartum hemorrhage.

5. Conclusion

In conclusion, the rate of postpartum hemorrhage in rural areas of southern Punjab was 44.5%. The robust risk factors in the current study were older maternal age, anaemia, and urinary tract infections. Extra observance during the antenatal and peripartum periods is needed to identify possible risk factors and early interference to prevent women from postpartum hemorrhage. However, it may be possible for all women giving birth to have a chance of developing PPH, as some develop PPH due to any unknown risk factors.

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CONFLICT OF INTEREST: Authors declare no conflict of interest.

ETHICAL APPROVAL: The study protocol was approved by the Biosafety and Bioethics Clearance committee, University of Management and Technology Pakistan (Approval Date: 18.02.2022 and Ref. #: DLSBBC-2022-03).

INFORMED CONSENT: All participants permitted the informed consent form.

AUTHOR CONTRIBUTIONS: Asma Irshad conceived the idea of the study, supervised the project and intensively edited the language of the manuscript. Maria Oubaid worked on the research methodology and helped in drafting the manuscript. Mubbasher Munir worked on the results and analysis, and interpretation of model results. Tasneem Qureshi and Sana Khalid proofread the manuscript. All authors have read and agreed to the published version of the manuscript.

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