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#### Abstract

**Objective:** To estimate the incidence of postpartum haemorrhage (PPH) and massive postpartum haemorrhage (MPPH) in a multiethnic population and to evaluate the risk factors associated with the massive postpartum haemorrhage.

**Methods:** Retrospective review of all deliveries in a large Middle Eastern tertiary center, over two years. All patients with gestational age of 24 weeks or greater with a postpartum blood loss of 500 ml and above were included in this study. Data collected from electronic medical records and analyzed.

**Results:** The rate of PPH was 5.1% and the incidence of MPPH was 0.69%. The MPPH rate appears 4 - 5 times higher (2,3%) among the South East Asian women than any other community in Qatar. The most common preexisting risk factors were previous LSCS and previous miscarriage with the rates of 39% and 34% respectively. Most significant findings among the index pregnancy risk factors was the presence placenta praevia or accreta and it was strongly associated to traumatic PPH and blood loss. The most common intrapartum risk factors were emergency LSCS (41.5%), followed by epidural (37.4%).

**Conclusion:** This study has revealed that like other developed countries the incidence of postpartum haemorrhage in Qatar represents a significant problem. PPH and MPPH are key performance indicators to assess the obstetric outcome and service. Understanding various risk factors and its association with underlying causes of MPPH will help to be proactive in the management and prevention of MPPH.

Keywords: Massive Postpartum Haemorrhage; Incidence; Etiology; Risk Factors; Multiethnic Population

#### Introduction

Postpartum hemorrhage (PPH) is associated with significant maternal morbidity, long term disability and mortality. According to the WHO(World Health Organization), although the overall incidence of maternal mortality due to PPH shows a downward trend especially in developed world, it is still of major concern in both high income and low income countries accounting for a quarter of maternal deaths worldwide. In a systematic analysis performed by the WHO; postpartum haemorrhage is a leading direct cause of maternal death [1].

Over the years various quality improvement tools have been established globally to prevent PPH. In keeping with this, standardized protocols to manage PPH in a timely and efficient manner have been developed. Consequently these proactive interventions instituted by WHO, UNICEF (United Nations International Emergency Fund) and various obstetric societies, have resulted in a significant reduction in the overall incidence of maternal death due to PPH [1,2].

However, maternal mortality due PPH is still a leading cause of death in low income countries accounting for about 60% of maternal deaths [3]. Though the ranking of PPH as a cause of maternal death is decreasing gradually in industrialized countries, for reasons which are unclear, the incidence of PPH shows an increasing trend in Australia, Canada and United States [4-6].

According to MBRRACE- UK PPH has become the eighth leading cause of maternal death in the United Kingdom, while in the United States it is the fourth leading cause [7,8]. These national data and the reviews from industrialized countries shows an increasing trend in PPH in high income countries. This implies that along with low income countries, high income countries should continue their efforts to reduce the incidence of PPH further as maternal survival is a crucial determinant of infant survival and wellbeing and indeed, for the wellbeing of society.

The risk factors for PPH vary from region to region. Further reduction in the incidence of PPH irrespective of demographic and economic disparity is imperative. Therefore it is quintessential that all regions should have a clear understanding of the major demographic and clinical determinants leading to PPH in their communities. Quality improvement steps should be taken based on these determinants in order to bring down the maternal morbidity and mortality caused by PPH in targeted populations.

Specifically, though there is much literature regarding the incidence and risk factors of MPPH from all over the world, there is a paucity of data with specific relevance to the Middle East. A Middle Eastern perspective on patients with MPPH will increase the understanding of its determinants and its magnitude among the diverse Middle Eastern multiethnic population and thus will facilitate the preventive aspects and management of MPPH in this population.

#### Definitions

According to local guideline CG10056; Prevention, early detection and management of postpartum hemorrhage, the following definitions were adopted:

- PPH: Abnormal bleeding after delivery that makes the patient symptomatic and/or results in signs of hypovolemia OR a total blood loss ≥ 500 ml after vaginal delivery (≥ 1000 ml blood loss after C-section).
- Primary PPH: Occurs within the first 24 hours after vaginal delivery or C-section.
- Minor obstetric hemorrhage: 500 ml 1000 ml blood loss, with no evidence of clinical shock.
- Major obstetric hemorrhage: More than 1000 ml blood loss OR with evidence of clinical shock.
- Massive obstetric hemorrhage: Hemorrhage of more than 1500 ml estimation OR acute loss requiring transfusion of > 4 units of PRBC OR suspicion/evidence of DIC due to hemorrhage.

#### Methods

A retrospective review was undertaken of all deliveries in a large Middle Eastern tertiary center, The Women's Hospital, Doha, State of Qatar over two years from November 2015 to October 2017. This study was conducted as a part of the quality improvement initiative to review the management of PPH in this institution. As a part of ongoing performance assessment all PPH of more than 500ml is recorded through the internal incident reporting system (Occurrence Variance Accidents). All patients with gestational age of 24 weeks or greater with a postpartum blood loss of 1500 ml and above were included in this study. According to the local hospital guideline any blood loss of 1500ml or more is considered as MPPH [15].

During the study period there were 1640 cases of PPH recorded among 32572 deliveries in our unit. Each case was reviewed and data entered by the investigators into a standard data collection Excel sheet and data was analyzed using SPSS version 20. This database was then interrogated to identify determinants of PPH.

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No external funding bodies were involved in this study.

Institutional authority was given to perform the study.

#### Results

There were 1640 cases of PPH (blood loss greater than 500 ml) recorded among 32572 deliveries (5.1%). Of these, there were 224 cases of MPPH where the blood loss was 1500 ml and greater (0.69% of the total deliveries and 13.6% of the cases of PPH). The most common underlying cause for massive postpartum haemorrhage is tissue trauma (41.1%) which was followed by combined (35.7%), atony (21.4%) and retained placenta(1.8%).

<b>Cause</b> s	N (%)		
Atony	48 (21.4%)		
Tissue Trauma	92 (41.1%)		
Combined	80 (35.7%)		
Retained placenta	4 (1.8%)		
Bleeding disorders	Nil		

There were no patients who had a PPH due to an inherent or acquired bleeding disorder (Table 1).

#### Table 1: Causes of massive postpartum haemorrhage.

Among the patients who had a MPPH 77% had hospital based antenatal care and 19% had antenatal care in the primary health centre or private health centre. Only 4% of patients did not book in any of the health care facility for the antenatal care. Majority of our patients are spontaneously conceived (95.1%) while 4.9% patient had conceived by assisted reproductive techniques.

The incidence of MPPH and its rates among different ethnic population has been formulated in table 2. Sixty six percent of our patients who had massive PPH was from MENA (Middle Eastern and North African) region out of those 30% were from the indigenous Qatari population. It was noted that the MPPH rate was high among the South East Asian women especially among women from Philippines than any other community in Qatar.

Ethnicity	Massive PPH N (%)	Total number of deliveries	Massive PPH rate
MENA region	149 (68%)	23387	0.64%
South Asian	31 (13.8%)	5931	0.52%
South East Asian	36 (16%)	1537	2.3%
Others	8 (3.5%)	1717	0.46%
Total	224	32572	0.68%

#### Table 2: Demographic risk factors.

The mean age was 32.0 years (SD 5.5, range 17 - 45 years). The mean gestational age was 37.6 weeks (SD3.0, range, 27 - 43 weeks). The median parity was 2.7 (SD 1.94, range, 0 - 14). The mean BMI was 32.1 (SD 5.2, range, 21 - 49).

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According to the WHO classification of obesity 69% of patients were obese and out of that 8.5% were morbidly obese. Table 3 denotes the number (%) of patients with BMI  $\ge$  25, Age  $\ge$  35 years and parity  $\ge$  3.

Variables	%	Correlation with Blood Loss	P value	Correlation with 4Ts (Which one)	P value
Previous miscarriage	34,3%	No	0,6	No	0,9
Previous uterine surgery	0.9%	No	0,8	No	0,7
Previous PPH	3,1%	No	1	Tissue PPH (0,35)	0,011
Previous LSCS	38,6%	0,3	< 0,001	Atony (-0,17)	0,01
				Trauma (0,24)	< 0,001
Fibroid uterus	1,3%	No	0,8	None	0,8
Bleeding disorders	1,8%	No	0,5	None	0,5
Diabetes Mellitus	3,6%	No	0,5	Traumatic (0,13)	0,047
Hypertension	4,9%	No	0,3	No	0,2

#### Table 3: Preexisting risk factors

The 4 Ts are; trauma, uterine tone, placental tissue, thrombin or coagulation.

The risk factors for MPPH other than demographic risk factors are classified into preexisting risk factors, risk factors in index pregnancy and intrapartum risk factors. Each variable is correlated to blood loss and the underlying cause for MPPH. The findings of each group are summarized in tables 4-6.

The most common preexisting risk factors were a previous lower segment caesarean section (39%) (LSCS), and a previous history of miscarriage (34%). Patients with history of a previous LSCS demonstrated a significant association with both atonic and traumatic PPH (Table 3). A previous history of PPH was significantly correlated with retained placental tissue as the cause for PPH with (p = 0.01). There were no cases with previous history of manual removal of placenta as a predisposing factor and only 7(3.1%) cases with a previous history of PPH. Preexisting Diabetes mellitus was significantly associated with traumatic PPH (p = 0.047). Table 3 details the correlation between preexisting risk factors and blood loss.

Overall 85 cases of patients with PPH had a previous LSCS as a risk factor. The number of previous caesarean section ranges from 1 previous one to 8 previous LSCS. There were 60 cases of placenta praevia out of 224 cases of MPPH (27%). Notably 80% of cases with placenta praevia had a previous LSCS as a risk factor.

With regards to the index pregnancy risk factors, there were 210 singleton pregnancies with 12 sets of twin pregnancy and 2 sets of triplets. Gestational diabetes and hypertensive disorders in pregnancy noted as a predisposing factor in 23.2% and 10% respectively. IVF (*in vitro* fertilization) was noted in 4.9% of cases and was significantly associated with both traumatic and combined PPH. Pre-delivery anemia was noted in 10% of cases. There were a total of 37% cases of antepartum hemorrhage with placenta praevia or accreta in 27% of cases and abruptio placentae in 9.8% of cases.

The most significant finding in this group was the presence placenta praevia or accreta, associated with traumatic PPH and blood loss with p value of <0.001 for both correlations. Abruptio placentae is significantly correlated with both atonic and traumatic postpartum haemorrhage but a stronger association noted with an atonic uterus (p < 0.001). A preexisting intrauterine fetal demise was noted in 3.1% of cases and it was correlated with retained placental tissue as the cause of PPH (p = 0.01). The index pregnancy risk factors and its correlation to blood loss and cause of PPH is summarized in table 4.

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Variables           IVF pregnancy		N (%)	Correlation with Blood Loss	P value	Correlation with 4Ts (Which one)	<b>P value</b> 0,048
		11 (4,9%)	No	0,2	Combined (0,13)	
				Traumatic (-0,1,5)	0,027	
Number of	Single	210 (93,7%)	No	0,5	No	0,2
conception	Twins	12 (5,4%)	No	0,5	No	0,2
conception	Triplets	2 (0,9%)	No	0,6	No	0,7
Ana	emia	23 (10.3%)	No	0,4	No	0,3
Medications Aspirin Or enoxaoparin		3 (1,3%)	No	0,8	No	0,5
Preecla-mpsia	Non severe PET	11 (4,9%)	No	0,7	No	0,5
	Severe PET	9 (4%)	No	0,9	No	0,3
Gestationa	al Diabetes	52 (23,2%)	No	0,8	No	0,5
Polyhyd	Polyhydramnios 8		No	0,4	Tissue (0,16)	0,02
	Placenta			Atony (-0,2)	0,003	
Antepartum	Praevia/ Accreta	61 (27,2%)	0,33	< 0,001	Traumatic (0,3)	< 0,001
Heamorrhage				Atony (0,27)	< 0,001	
	Abruption	22 (9,8%)	No	0,2	Traumatic (-0,22)	0,001
PPF	ROM	3 (1,3%)	No	0,6	No	0,8
Intrauterine	fetal demise	7 (3,1%)	No	0,7	Tissue (0,17)	0,01

 Table 4: Index pregnancy obstetric risk factors.

Table 5 outlines the most common intrapartum risk factors. The most important are emergency LSCS (41.5%), followed by an epidural anaesthetic (37.4%). Other intrapartum risk factors included labour induction with either vaginal prostagalndins or artificial rupture of membrane with or without oxytocin (30.6%) and episiotomy (24%), Elective LSCS (18.3%) instrumental delivery (13.4%) and prolonged second stage (11.2%). Spontaneous rupture of membrane more than 24 hours was noted in 1.8% of cases and it was significantly correlated to retained placental tissue as the cause for PPH (p < 0.001).

Variables		%	Correlation with Blood Loss	P value	Correlation with 4Ts (Which one)	P value
Labour	Prostaglandin	14.7%	-0,15	0,03	No	0,9
induction	Oxytocin	15.9%	-0,14	0,04	No	0,4
S	SRM >24 hrs	1.8% No		0,4	Tissue (0,24)	< 0,001
Cho	orioamnionitis	1.8%	No	0,6	No	0,9
Prol	onged 2 <sup>nd</sup> stage	11.2%	No	0,09	No	0,4
			-0,24	< 0,001	Combined (0,15)	0,03
Epidural		37.4%		Traumatic (-0,14)	0,03	
Episiotomy			0,18	0,008	Combined (0,3)	< 0,001
		2.4%		Traumatic (-0,26)	< 0,001	
	OASIS	1.3%	No	0,3	No	0,5
	< 1,5 kg	4.9%	No	0,6	No	0,7
	1,5 - 3.9 Kg	81.7%	-0,2	0,004	Combine (0,15)	0,04
Birth weight					Traumatic (-0,24)	<0,001
	> 3,9 - 4,5 Kg	12.1%	No	0,6	No	0,2
	> 4,5 Kg	1.3%	No	0,6	No	0,7
Shoulder dystocia		0.4%	No	0,4	No	0,6

Table 5: Intrapartum risk factors.

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An epidural in labour was noted to have statistically significant association with blood loss (p < 0.001) and to both combined and traumatic PPH (p = 0.03). A prolonged second stage was noted in 11.2% of cases, chorioamnionitis in 1.8% of cases and Obstetric Anal Sphincter Injury Syndrome (OASIS) in 1.3% of cases. None of these factors showed a positive correlation to either blood loss or any of the underlying 4T's. An episiotomy was an intrapartum risk factor for MPPH which was positively correlated to both blood loss (p = 0.008) and traumatic PPH (p < 0.01).

In regards to mode of delivery (Table 6) an emergency LSCS was the commonest mode of delivery in those patients who had MPPH. Among the emergency LSCS there were 14 cases of second stage LSCS (6.25%). Both elective LSCS (18.2%) and emergency LSCS (42.2%) were positively correlated to the combined cause for MPPH.

Variables		%	Correlation with Blood Loss	P value	Correlation with 4Ts (Which one)	P value
	Normal delivery	23,2%	-0,17	0,01	Combined (0,22)	< 0,001
					Tissue (0,22)	< 0,001
					Traumatic (-0,32)	< 0,001
Mode of delivery	VBAC	3,6%	No	0,7	Tissue (0,4)	< 0,001
	Instrumental	13,4%	No	0,07	Combined (0,15)	0,03
	Elective LSCS	18,2%	No	0,11	Combined (-0,13)	0,049
	Emergency LSCS	42,2%	0,15	0,025	Combined (-0,2)	0,003
	Second stage LSCS	4%	No	0,5	Combined (-0,15)	0,02
					Traumatic (0,15)	0,02

#### Table 6: Intrapartum risk factors: mode of delivery.

23.2% of cases with MPPH had a vaginal delivery and it was positively correlated to tissue, trauma and combined causes of PPH (p < 0.001). A vaginal delivery was also found to be strongly associated to the blood loss with (p = 0.01) when compared to other modes of delivery.

Instrumental delivery was associated to combined PPH as the underlying reason for MPPH (p = 0.03). Vaginal birth after caesarean section was noted in 3.6% cases and it is statistically significant to retained placental tissue as the cause (p < 0.001).

#### Discussion

There are very few studies in the literature which have reviewed MPPH of 1500 ml or more. The criteria to define MPPH are not consistent across various continents which makes the comparison of incidence of MPPH across the globe a difficult task. The definition of MPPH of 1500 ml or more blood loss derives from the local PPH guideline on the prevention and management of PPH [15].

A case control study performed in Norway defined 1500 ml or more blood loss as severe PPH and a local guideline in the United Kingdom has taken 1500 ml blood loss or more as Major postpartum haemorrhage [16,17]. This review details only the MPPH cases when women lose more than 1500 ml (25 to 35% of blood volume) rapidly after delivery, it is associated with significant morbidity and mortality as this will cause major cardiovascular and haematological changes leading to hypovolemic shock and coagulopathies. The determination of the risk factors for MPPH in the local population will help proactive measures to prevent MPPH and ensure timely intervention by multidisciplinary team members.

The incidence of PPH varies from country to country and marked variations are seen between the low income and high income countries [1]. In high income countries e.g. United States and France the incidence of severe PPH) is 3% and 6.4 % respectively while in low income countries e.g. Uganda and Nigeria the incidence is 9% and 4.5% respectively [9-12]. In this study the rate of PH was 5.1% which was in keeping with other high income countries.

The MPPH rate was 0.69% (6.9 per 1000 deliveries) which is similar to a retrospective study done in United Kingdom (0.5%) when a similar blood loss of 1500 ml was taken as the criterion to define MPPH [13].

According to WHO study in 2004 it was noted that during the period of 1972 to 2002 the incidence of PPH in Qatar was 0.55% [14]. The host institution represents the whole country as more than 80% of births in Qatar occur in the institution. When compared to the WHO data published in 2004 there is a significant increase in the rates of PPH (from 0.55% to 5.1%) has noted over these 15 years (2002 - 2015). There may be better case ascertainment over the period of time. This significant rise may also be attributed to the sharp rise in the country's expatriate population, increasing number of primary caesarean sections and thereby sharp rise in repeat caesarean section which is associated with complications like abnormal placentation, adhesions etc. Also contributed by the developing problem of obesity, multiparity and high incidence of women conceiving in latter period of their reproductive life. This significant rise in PPH is considered as major findings in our study which will help us to analyze our present quality improvement measures in place in prevention of postpartum haemorrhage. This increase in PPH was also observed in other high income countries like Australia, Canada, France [4,5,9].

According to the literature the most common cause of PPH is qn atonic uterus [10] which is contradictory to our findings where the most common underlying cause for MPPH in this study was tissue trauma. This can be attributed to the fact that majority of deliveries were operative deliveries which includes emergency LSCS (42.2%), Elective LSCS (18.2%) and instrumental delivery (13.4%). This also can be related to the high numbers of placenta praevia and accreta cases who had massive obstetric haemorrhage. The comparatively low incidence of an atonic uterus in our population can be attributed to the adoption of active management of third stage of labour for all patients and also due to the strict adherence to the local guideline on prevention and treatment of PPH. In addition to the above measures the unit continually publishes and uses quality matrixes to inform the staff and positively influence improvement in care delivery.

Previous studies have shown that the maternal ethnicity is an independent risk factor for PPH [18-20]. Different ethnic groups have their own ethnic specific health problems which expose them to the risk of adverse obstetric complications like PPH.

Studies performed decades ago pointed out that the Asian and Hispanic women were at higher risk for PPH [21,22]. As the years have passed a systematic review and metanalysis done in 2012 to assess the regional variation in the prevalence of PPH showed that Asian countries has the lowest prevalence of postpartum haemorrhage (1.9%) followed by Latin America, and Europe (3%). In the same review the prevalence of severe PPH in North America was (4.3%) while Africa had the highest prevalence of severe PPH at 5.1% [23]. According to a three year cohort study done in United States concluded that racial and ethnic disparities exist for multiple adverse obstetric outcomes but cannot be explained by differences in patient characteristics [24]. Case ascertainment and primary medical facilities and medico-legal issues may contribute to the different rates found in different countries.

This regional changing variations in the prevalence of MPPH can be due to increased prevalence of modifiable risk factors like obesity, smoking, advanced maternal age which are seen more in industrialised countries than the non industrialised countries and also due to the disparity in the health care facilities or access to the medical care in certain regions like Africa. Non-modifiable genetic, environmental and cultural variations also play a role in the causal of MPPH.

In this study it was found that the South East Asian women are at higher risk for PPH when compared to both Arab and non-Arab communities. The rate of MPPH among the South East Asian community was 2.3% while the rate of MPPH in other communities are between 0.4 to 0.6% which is a significant finding in our study. Among the south East Asian women 98% of patients are from Philippines.

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A population based study from Norway has also highlighted the fact that south east Asian women (2.1%) are at more risk of severe obstetric haemorrhage than European (1.1%), middle eastern (0.7%) or any other community (1.1%) [20]. There are no other literature available to support that the South East Asian women are at higher risk for PPH.

According to a WHO multi country survey on PPH and its risk factors, older mothers are associated with higher tares of PPH [26]. Alternatively, a retrospective cohort multivariate study indicated that aging was actually associated with decreased PPH, the risk decreasing progressively from those aged 25 - 29 years to those aged  $\geq$  40 years compared with the 20 - 24 years group [27]. Similar results were found in population based comparative study between Canada and France where women in the younger age group tend to have increased risk of PPH [28]. In this study the mean age of patients with a MPPH was 32 years and 36.6% of patients were above 35 years of age.

A retrospective cohort study of 24,634 women in childbirth has found that the impact of obesity as an independent risk factor for MPPH is minimal but it is a powerful potentiating factor in maternal outcome [29]. In this study 87% of patient had a BMI > 25 kg/m<sup>2</sup> but no significant correlation between BMI and MPPH was found. A large population based cohort study clearly points out that risk of atonic PPH increased rapidly with increasing BMI [30]. This negative correlation between BMI and massive PPH may be attributed to the proactive measures taken to prevent PPH especially in high risk cases.

According to a retrospective cohort study from Australia, an IVF pregnancy is associated with increased risk of postpartum haemorrhage (11.1 versus 7.9%) when compared to general population [32]. In this study an IVF pregnancy was significantly correlated to both combined and traumatic PPH. This may be due to other contributing factors such as advanced maternal age, associated co morbidities, multiple fetuses, use of enoxaparin and aspirin which are frequently associated with IVF pregnancies.

A meta- analysis of association of placenta praevia with history of caesarean delivery and abortion concluded that the risk of placenta praevia increases with number of prior caesarean deliveries and miscarriages [31]. In our study it was noted that placenta praevia is strongly associated with traumatic PPH which is thought provoking whether increasing uteroteonics as first line treatment in cases of placenta praevia with bleeding will be a valuable initial measure or do we need to adopt early effective strategies to treat traumatic PPH in patients with placenta praevia.

In this study, there was a statistically significant association between both atonic and traumatic PPH (and not a coagulopathy) with abruptio placentae. An epidural in labour is positively correlated to combined and traumatic PPH and that may be associated with prolonged labour and instrumental delivery.

The strength of this study is the large number of cases with MPPH that lends validity to the findings, The limitations are that this is a retrospective study and not a case control study therefore there are limitations to depict absolute or relative risk of PPH associated with each risk factor.

#### Conclusion

The incidence of MPPH in a multiethnic population was comparable to other developed countries. The South Asian population had an incidence of MPPH of 4 - 5 times the prevalence of other communities. This study has revealed that like other developed countries the incidence of PPH in Qatar is also showing an upward trend. In view of this change in the trend and our quest to reduce the maternal near miss mortality associated with MPPH, PPH is taken as a key performance indicator to assess obstetric outcome and service. Understanding various risk factors and its association with underlying causes of MPPH will help in the management and prevention of MPPH. Qatar is continuing the initiatives taken by the WHO to prevent PPH.

#### **Conflict of Interest**

Authors state no conflict of interest

#### **Details of Ethics Approval**

As this is a study based on an audit done as a part of quality improvement project, ethical approval from the research committee is not applicable for this study.

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