

ORIGINAL ARTICLE

PREVALENCE OF MATERNAL NEAR-MISS AND MATERNAL MORTALITY, THEIR DISTRIBUTION BY GESTATION AND GRAVIDITY AND CAUSES IN WOMEN WITH LIVE BIRTHS IN DISTRICT PESHAWAR, PAKISTAN

Sonia Rafiq¹, Sumaira Yasmin¹,  Nazia Liaqat¹, Ghazala Shams²

Departments of Obstetrics & Gynaecology, ¹Lady Reading Hospital & ²Khyber Girls Medical College, Peshawar, Pakistan

ABSTRACT

Background: Maternal near-miss (MNM) and maternal mortality (MM) are indicators for quality of health care system. The objectives of our study were to determine prevalence of MNM and MM and their distribution by gestation and gravidity and their causes in women with live births population of District Peshawar, Pakistan.

Material & Methods: This cross-sectional study was conducted at Department of Obstetrics and Gynaecology, Lady Reading Hospital, Peshawar, Pakistan from January 2017 to June 2017. From assumed population of 185,676 pregnant women in District Peshawar, 10% prevalence of MNM, 1.0448% margin of error and 95%CL, sample size was calculated 3,115. All women with live birth were eligible. Presence of MNM and MM, causes of MNM and MM, gestational age and gravidity were six variables. Being nominal, all were analysed by count and ratio or percentage with 80%CI. MNM Ratio was calculated per 1,000 live births and MM Ratio per 100,000 live births.

Results: Out of 3,115 women with live births, MNM cases were 494 with MNMR 158.59/1,000 (80%CI 150.19-166.97) and MM cases were 16 with MMR 513.64/100,000 population (95%CI 349.50-677.78). There were 232 MNM cases in ≤ 28 weeks and 262 in > 28 weeks gestational age with similar MNMR between these groups. There were 244 MNM cases in primigravida and 250 in multigravida with similar MNMR between these groups. There were five MM cases in ≤ 28 weeks and 11 in > 28 weeks gestational age with similar MMR between these groups. There were five MM cases in primigravida and 11 in multigravida with similar MMR between these groups as their CIs are overlapping. Haemorrhage was most common cause for MNM in 365 (11.7175%) cases and for MM in 8 (0.2568%) cases.

Conclusion: The maternal near-miss ratio (MNMR) and maternal mortality ratio (MMR) are relatively higher in population of District, Peshawar, Pakistan. MNMR and MMR both have similar prevalence in ≤ 28 weeks and in > 28 weeks gestational age groups and also similar in primigravida and in multigravida groups. Haemorrhage (antepartum and postpartum) was most common cause both for maternal near-miss (MNM) and maternal mortality (MM).

KEY WORDS: Maternal Near-miss; Maternal Mortality; Maternal Deaths; Eclampsia; Haemorrhage; Sepsis.

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Corresponding Author:

Dr. Sumaira Yasmin
Assistant Professor
Department of Obstetrics and Gynaecology
Lady Reading Hospital, Peshawar, Pakistan
E-mail: drsumairayasmin@gmail.com

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1. INTRODUCTION

1.1 Background: As per WHO statement, amidst the objectives for health determinants for the millennium, the maternal mortality rate (MMR) is an indicator of paramount importance in maternal health.¹ Globally maternal death ratio for 2017 was estimated at 211 deaths per 100,000 live births.² Reduction in maternal mortality ratio indicates improvement in health care system.

There are patients who are termed near-miss patients who in spite of development of deadly obstetric complications during pregnancy and postpartum period of up to 42 days, survived that complication.³ Thus patients presenting with severe obstetric complications are of paramount importance as they may end up as near-miss or even in maternal mortality. These obstetric determinants need to be highlighted and prevented in order to achieve the goals of improved maternal health

In 2010, WHO and UNICEF adjusted the various maternal mortality statistics and proclaimed the death of almost 358,000 women around the world from maternal causes, including 87% in Africa and Asia.⁴

In 2015 in Pakistan, MMR was 276/100,000 live births.⁵ In order to improve provision of healthcare system to the people, near-miss events and the near-miss statistics must be included in national health indicators. According to 2009 WHO consensus, timely and ample treatment for obstetric complications can be given on maternal near-miss definition and set criteria for case identification by defining the criteria.^{6,7}

For Pakistan, the great challenging Millennium Development Goal (MDG) is to decrease maternal mortality. An inclusive access is required as it is interconnected with several more social factors. An influential tool for policy makers could be important for analyzing and evaluating near-miss with health care system.

1.2 Research Objectives (RO): To determine the;

RO 1-2: prevalence of maternal near-miss and maternal mortality in women with live births population of District Peshawar, Pakistan.

RO 3-6: distribution of maternal near-miss and maternal mortality by gestational age and gravidity in women with live births population of District Peshawar, Pakistan.

RO 7-8: causes of maternal near-miss and maternal mortality in women with live births population of District Peshawar, Pakistan.

1.3 Operational Definitions

Table 1.3 shows operational definitions used in this study.

Table 1.3: Operational definitions in a study for prevalence of maternal near-miss and maternal mortality

Maternal death (Mortality) (MM)	“Maternal death is defined as death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and the site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes”. ⁸
Maternal near-miss (MNM)	“A MNM case is defined as a woman who nearly died but survived a complication that occurred during pregnancy, childbirth or within 42 days of termination of pregnancy”. ^{6,9}
Severe maternal outcomes	“SMO refers to a life-threatening condition (i.e. organ dysfunction), including all maternal deaths and maternal near-miss cases”. ¹⁰
Live birth	“LB refers to the birth of an offspring which breathes or shows evidence of life”. ¹⁰
MNM ratio (MNMR)	“MNMR refers to the number of maternal near-miss cases per 1000 live births (MNMR=MNM/LB)”. ¹⁰
Severe postpartum haemorrhage	“Genital bleeding after delivery, with at least one of the following: perceived abnormal bleeding (1000 ml or more) or any bleeding with hypotension or blood transfusion”. ¹⁰
Severe pre-eclampsia	“Persistent systolic blood pressure of 160 mmHg or more or a diastolic blood pressure of 110 mmHg; proteinuria of 5 g or more in 24 hours; oliguria of <400 ml in 24 hours; and HELLP syndrome or pulmonary oedema. Excludes Eclampsia”. ¹⁰
Eclampsia	“Generalized fits in a patient without previous history of epilepsy. Includes coma in pre-eclampsia”. ¹⁰
Severe systemic infection or sepsis	“Presence of fever (body temperature >38°C), a confirmed or suspected infection (e.g. chorioamnionitis, septic abortion, endometritis, pneumonia), and at least one of the following: heart rate >90, respiratory rate >20, leukopenia (white blood cells <4000), leukocytosis (white blood cells >12 000)”. ¹⁰
Uterine rupture	“Rupture of uterus during labour confirmed by laparotomy”. ¹⁰

2. MATERIALS AND METHODS

2.1 Design, Setting & Duration: This cross-sectional study was conducted at the Department of Obstetrics and Gynaecology, Lady Reading Hospital, Peshawar, Pakistan from January 2017 to June 2017. The Ethical Review Board of the institution accorded approval to the study. Formal consent of patients/ attendants was sought for inclusion in the study.

2.2 Population & Sampling: The population of District Peshawar was assumed to be 4.2 million in first half of 2017. It included 2,032,800 ($48.4 \times 4,200,000/100 = 2,032,800$) women, which further included 928,380 ($45.67 \times 2,032,800/100 = 928,379.76$) women in child bearing age (15-49 years). Assuming 20% pregnancy in this age group, we will have 185,676 ($928,380 \times 20/100$) pregnant women; our population at risk for maternal near-miss and maternal mortality. With this much population, assumed prevalence of maternal near-miss as 10% in this population, 1.0448% margin of error and 95%CL, sample size¹¹ came to be 3,115, using consecutive method. All women with live birth were eligible for inclusion.

2.3 Conduct of Procedure: All these pregnant women were admitted for deliveries. History was taken and general physical and obstetrical examinations were done. Routine investigations, including urine R/E, blood complete with ESR, ABO/Rh grouping and pelvic USG were conducted. Routine management for delivery was offered. In case of complications, standard protocols were employed, including relevant investigations and relevant treatment, including but not limited to IV line, IV fluids and blood transfusion etc.

2.4 Data Collection Plan: Presence of maternal near-miss (yes & no), presence of maternal mortality (yes & no), causes of MNM and causes of MM were four research variables (attributes), while gestational age (≤ 28 weeks & > 28 weeks) and gravidity (primigravida & multigravida) were two grouping variables/factors (attributes). The measurement scale for all

these variables was nominal.

2.5 Data Analysis Plan: The data for the sample was analysed by count and ratio (MNMR & MMR), while it was inferred on to the population as confidence interval for MNMR & MMR at 80% confidence level, using Wilson score interval method.¹²

For causes of MNM and MM, counts and percentages were calculated with CI at 80%CL, using Wilson score interval method.¹² The comparison of prevalence among the sub-samples was based upon their confidence intervals (CIs) i.e. estimated parameters for proportion for population, not their counts for the sub-samples. The prevalence was considered as similar when there was overlapping of CIs, otherwise dissimilar. MMR was evaluated per 100,000 live births, whereas MNMR was evaluated using 1,000 live births as the denominator.

3. RESULTS

3.1 Prevalence of MNM and MM: Out of 3,115 women with live births, there were 494 MNM cases with maternal near-miss ratio (MNMR) of 158.59/1,000 ($494 \times 1,000/3,115 = 158.59$) population (95%CI 150.19-166.97).

There were 16 MM cases with maternal mortality ratio (MMR) of 513.64/100,000 ($16 \times 100,000/3,115 = 513.64$) population (95%CI 349.50-677.78).

3.2 Distribution of MNM by gestational age and gravidity: There were 232 MNM cases with MNMR of 74.48/1,000 (80%CI 68.67-80.73) in ≤ 28 weeks and 262 MNM cases with MNMR of 84.11/1,000 (80%CI 77.95-90.70) in > 28 weeks gestational age. The MNMR was similar between these groups, as their CIs are overlapping. (Table 3.2)

There were 244 MNM cases with MNMR of 78.33/1,000 (80%CI 72.38-84.72) in primigravida and 250 MNM cases with MNMR of 80.26/1,000 (CI 74.23-86.71) in multigravida. The MNMR was similar between the primigravida and multigravida groups as their CIs are overlapping. (Table 3.2)

Table 3.2: Distribution of maternal near-miss (MNM) by gestational age and gravidity in women with live births population of District Peshawar (n=3,115)

Variable	Attributes	Sample analysis for MNM		Estimated MNM Ratio/1,000 live births in population at 80%CL	
		Count	MNM Ratio/1,000 live births	Lower	Upper
Gestational age	≤ 28 weeks	232	$232 \times 1,000/3,115 = 74.48$	68.67	80.73
	> 28 weeks	262	$262 \times 1,000/3,115 = 84.11$	77.95	90.70
Gravidity	Primigravida	244	$244 \times 1,000/3,115 = 78.33$	72.38	84.72
	Multigravida	250	$250 \times 1,000/3,115 = 80.26$	74.23	86.71
Cases with MNM		494	$494 \times 1,000/3,115 = 158.59$	150.38	167.15
Cases with no MNM		2,621	$2,621 \times 1,000/3,115 = 841.41$	823.84	849.62
Total		3,115	3,115	Population parameters	

3.3 Distribution of maternal mortality (MM) by gestational age and gravidity: There were 05 MM cases with MMR of 160.51/100,000 (80%CI 192.20-282.35) in ≤ 28 weeks and 11 MM cases with MMR of 353.13/100,000 (80%CI 240.62-517.95) in > 28 weeks gestational age. The MMR was similar between these groups, as their CIs are overlapping. (Table 3.3)

There were 05 MM cases with MMR of 160.51/100,000 (80%CI 192.20-282.35) in primigravida and 11 MM cases with MMR of 353.13/100,000 (80%CI 240.62-517.95) in multigravida. The MMR was similar be-

tween the primigravida and multigravida groups as their CIs are overlapping. (Table 3.3)

3.4 Causes of MNM: Haemorrhage (including antepartum and postpartum) was the most common cause for MNM in 365 (11.7175%) cases, while sepsis was the least common cause in four (0.1284) cases. (Table 3.4)

3.5 Causes of MM: Haemorrhage (including antepartum and postpartum) was the most common cause for MM in 8 (0.2568%) cases, while all other causes were in two (0.0642%) cases each. (Table 3.5)

Table 3.3: Distribution of MM by gestational age and gravidity in women with live births population of District Peshawar (n=3,115)

Variable	Attributes	Sample analysis for MM		Estimated MM Ratio/100,000 live births in population at 80%CL	
		Count	MM Ratio/100,000 live births	Lower	Upper
Gestational age	≤ 28 weeks	05	$05 \times 100,000 / 3,115 = 160.51$	91.20	282.35
	> 28 weeks	11	$11 \times 100,000 / 3,115 = 353.13$	240.62	517.95
Gravidity	Primigravida	05	$05 \times 100,000 / 3,115 = 160.51$	91.20	282.35
	Multigravida	11	$11 \times 100,000 / 3,115 = 353.13$	240.62	517.95
Cases with MM		16	$16 \times 100,000 / 3,115 = 513.64$	373.56	705.87
Cases with no MM		3,099	$3,099 \times 100,000 / 3,115 = 99486.36$	99294.12	99626.44
Total		3,115	3,115	Population parameters	

Table 3.4: Causes of MNM in women with live births population of District Peshawar (n=3,115)

Attributes	Sample statistics for causes for MNM		80%CI for proportion	
	Count	Percentage	Lower	Upper
Haemorrhage (APH/PPH)	365	$365 \times 100 / 3,115 = 11.7175$	10.9991	12.4763
Hypertensive disorders (Eclampsia, Pre-eclampsia, HELLP syndrome)	120	$120 \times 100 / 3,115 = 03.8523$	3.4341	4.3191
Sepsis	04	$04 \times 100 / 3,115 = 0.1284$	0.0683	0.2409
Indirect causes	05	$05 \times 100 / 3,115 = 0.1605$	0.0912	0.2823
Cases with MNM	494	$494 \times 100 / 3,115 = 15.8587$	15.0380	16.7155
Cases with no MNM	2,621	$2,621 \times 100 / 3,115 = 84.1413$	83.2845	84.9620
Total	3,115	3,115 (100%)	Population parameters	

Table 3.5: Causes of MM in women with live births population of District Peshawar (n=3,115)

Attributes	Sample statistics for causes for MM		80%CI for proportion	
	Count	Percentage	Lower	Upper
Haemorrhage (APH/PPH)	08	$08 \times 100 / 3,115 = 0.2568$	0.1639	0.4021
Hypertensive disorders (Eclampsia, Pre-eclampsia, HELLP syndrome)	02	$02 \times 100 / 3,115 = 0.0642$	0.0266	0.1543
Sepsis	02	$02 \times 100 / 3,115 = 0.0642$	0.0266	0.1543
Indirect causes	02	$02 \times 100 / 3,115 = 0.0642$	0.0266	0.1543
Anaesthesia complications	02	$02 \times 100 / 3,115 = 0.0642$	0.0266	0.1543
Cases with MM	16	$16 \times 100 / 3,115 = 0.5136$	0.3735	0.7058
Cases with no MM	3,099	$3,099 \times 100 / 3,115 = 99.4864$	99.2941	99.6264
Total	3,115	3,115 (100%)	Population parameters	

4. DISCUSSION

4.1 Prevalence of MNM/ MNM Ratio and MM/ MM Ratio:

In our study, out of 3,115 women with live births, there were 494 maternal near-miss (MNM) cases with maternal near-miss ratio (MNMR) of 158.59/1,000 population (95%CI 150.19-166.97).

There were 16 maternal mortality (MM) cases with maternal mortality ratio (MMR) of 513.64/100,000 population (95%CI 349.50-677.78).

Table 4.1 shows MNM cases & MNM Ratio from 17 studies and MM cases & MM Ratio from 18 different studies/ populations. Comparisons for MNMR and MMR are based on their confidence intervals of ratios for population, not on their ratios for the sample.

Here MNM Ratios of all these 17 populations/ studies are lower than our study.

MM Ratio is reported similar to our study by Ansari, et al.¹⁴ It is reported higher than our study by Mustafa, et al.¹⁷, Sultana, et al.¹⁸, Amita, et al.²¹, Alemu, et al.²⁴,

Oladapo, et al.²⁶, and Akpan, et al.²⁷

MM Ratio is reported lower than our study by Shaheen, et al.¹³, Shahid, et al.¹⁵, Aziz, et al.¹⁶, Roopa, et al.¹⁹, Singh, et al.²⁰, Kansara, et al.²², Dhingra, et al.²³, Heemelaar, et al.²⁵, Chikadaya, et al.²⁸, David, et al.²⁹ and Lotufo, et al.³⁰

The caliber of maternal health care is illustrated by obstetric death. In our part of the world the near-misses are not usually used as a measure of the obstetric quality care as is also not used in many regions having increased MMR.

In our project, we have sorted out the maternal near-miss cases. In our study/ population, the MNMR was 158.59/1,000 live birth, which is quite high. It could be due to the fact that we used the morbidity and organ system based criteria for the diagnosis of MNM patients. We have not used intensive care admission criteria for near-miss. Due to overburdened ICU in our setup, most of the mothers with severe morbidity are dealt with in our obstetric units in close liaison

Table 4.1: MNM & MNM Ratio and MM & MM Ratio for different populations

S. No.	Author	City	Country	Duration	Live births	MNM cases	MNM Ratio/1000	MM cases	MM Ratio/ 100,000
	Our study	Peshawar	Pakistan	2017	3115	494	158.59	16	513.64
1	Shaheen, et al. ¹³	Rawalpindi	Pakistan	2012-13	15757	198	12.56	49	310.97
2	Ansari, et al. ¹⁴	Kharian	Pakistan	2013	1035	76	73.43	7	676.32
3	Shahid, et al. ¹⁵	Lahore	Pakistan	2014	2371	124	52.29	7	295.23
4	Aziz, et al. ¹⁶	District Thatta	Pakistan	2010-18	87172			278	318.90
5	Mustafa, et al. ¹⁷	Karachi	Pakistan	2006	822	44	53.52	6	729.92
6	Sultana, et al. ¹⁸	Karachi	Pakistan	2018	1811	57	31.47	15	828.27
7	Roopa, et al. ¹⁹	Manipal	India	2011-12	7330	131	17.87	23	313.77
8	Singh, et al. ²⁰	Jamshed-pur	India	2016-19	14636	153	10.45	38	259.63
9	Amita, et al. ²¹	Lucknow	India	2011-12	5273	633	120.04	247	4684.24
10	Kansara, et al. ²²	Ahmed-abad	India	2019	3200	16	5	6	187.50
11	Dhingra, et al. ²³	Delhi	India	2012-14	18631	161	8.64	35	187.85
12	Alemu, et al. ²⁴	Juba	South Sudan	2016	994	94	94.57	10	1006.03
13	Heemelaar, et al. ²⁵	Windhoek	Namibia	2018	5772	194	33.61	9	155.92
14	Oladapo, et al. ²⁶	Nationwide	Nigeria	2012-13	91724	1451	15.81	998	1088.04
15	Akpan, et al. ²⁷	Calabar	Nigeria	2012-16	10111	691	68.34	99	979.13
16	Chikadaya, et al. ²⁸	Harare	Zimbabwe	2016	11871	110	9.26	13	109.51
17	David, et al. ²⁹	Maputo	Mozambique	2008	27916	564	20.20	71	254.33
18	Lotufo, et al. ³⁰	Limeria	Brazil	2004-07	9683	43	4.44	5	51.63

with ICU staff. They are not fortunate enough to get admission in ICU, yet quite fortunate to escape mortality. This has led to a higher enrollment of women in near-miss cases.

In our setup MMR was 513.64/100,000 live births which is quite high. The reasons could be that we usually receive critically serious patients coming from far off areas who have delays in referrals from primary care facilities as well as in their transportation. Moreover, most of these patients are attended by untrained traditional birth attendants, who are unaware of the warning signs and they try to handle the patient till the very end. As a result, the patients with postpartum hemorrhage and ruptured uterus are usually received in irreversible shocks. These patients lose their golden hour of resuscitation either at their primary place or on the way to hospital.

4.2 Distribution of MNM by gestational age and gravidity: Our study showed 494 MNM cases, including 232 cases in ≤ 28 weeks and 262 in >28 weeks gestational age. The MNMR was similar between these groups, as their CIs are overlapping. (Table 3.2)

Opposing to our study, Singh, et al.²⁰ reported 153 MNM cases out of 14,636 live births. Here MNM was more common in >28 weeks gestational age as 115 (75.1%) than ≤ 28 weeks as 38 (24.9%) cases. Most of the complications are observed in late pregnancy after 28 weeks of gestation. Consequently MNM and MM are more frequently seen in gestational age of more than 28 weeks as compared with lesser gestational ages. More vigilant monitoring of patients with any obstetric complications in late trimester of pregnancy is thus needed.

Our study showed 244 MNM cases in primigravida and 250 in multigravida. The MNMR was similar between the primigravida and multigravida groups as their CIs are overlapping. (Table 3.2)

Opposing to our study, Singh, et al.²⁰ reported 153 MNM cases out of 14,636 live births. Here MNM was more common in multigravida 96 (62.7%) than primigravida 57 (37.3%).

4.3 Distribution of MM by gestational age and gravidity: Our study showed 494 MM cases, including 05 cases in ≤ 28 weeks and 11 in >28 weeks gestational age. The MMR was similar between these groups, as their CIs are overlapping. (Table 3.3)

Opposing to our study, Singh, et al.²⁰ reported 38 MM cases out of 14,636 live births. Here MM was more common in >28 weeks gestational age as 36 (94.7%) than ≤ 28 weeks as two (5.3%) cases.

Our study showed 05 MM cases in primigravida and 11 in multigravida. The MMR was similar between the primigravida and multigravida groups as their CIs are overlapping. (Table 3.3)

Opposing to our study, Singh, et al.²⁰ reported 38 MM cases out of 14,636 live births. Here MM was more

common in multigravida 28 (73.7%) than primigravida 10 (26.3%).

Our study showed maternal near-miss to maternal mortality ratio of 1:31, which means for every 31 life threatening obstetric complications who survived, there was one maternal death. Better health care is revealed by large ratios. Many studies have showed lower maternal mortality to near-miss ratio of 1:4 by Shaheen, et al.¹³, from Rawalpindi, Pakistan, 1:10.85 by Ansari, et al.¹⁴ from Kharian, Pakistan, 1:7 by Mustafa, et al.¹⁷ from Karachi, Pakistan, 1:4 by Singh, et al.²⁰ from Jamshedpur, India, 1:2.56 by Pandey, et al.²¹ from Lucknow, India, and 1:8.5 by Chikadaya, et al.²⁸ from Harare, Zimbabwe. This ratio is indicative of the standard of obstetrical care. In case this ratio rises over a period of time, it reflects the advancement attained in obstetric health care. So instead of a single estimation, yearly estimation may help us in improving the care provided.

4.4 Causes of MNM and MM: Our study showed haemorrhage (including antepartum and postpartum) as the most common cause for MNM in 365 (11.7175%) cases, while sepsis was the least common cause in four (0.1284) cases. (Table 3.4)

Our study showed haemorrhage (including antepartum and postpartum) as the most common cause for MM in 08 (0.2568%) cases, while all other causes were in two (0.0642%) cases each. (Table 3.5)

Among the causes of near-miss events, hemorrhage (31.8%) was the leading cause, followed by hypertensive disorders (28.2%) as depicted by Chikadaya, et al.²⁸ from Harare, Zimbabwe.

Ours Lady Reading Hospital is a teaching hospital, providing services to population of district Peshawar and surrounding areas. Here most cases are received in already serious condition; therefore mortality index for sepsis and indirect causes is high. The delays in referrals and in transportation are considered as major causes for increased morbidity and mortality.

Haemorrhage, hypertensive disorders and puerperal sepsis were the leading causes of near-miss cases. Maternal near-miss have its own implications on mother as well as the new born baby, including many psycho-social effects in addition to the physical distress to the mother. MNM is increasingly used as an indicator for quality of obstetric care and clinical practice.

As near-miss analysis indicates quality of health care, it is important to be notified in the national health care indices in order to reduce the high maternal mortality. The high risk groups of patients are to be identified and special care to be given to these targeted populations. Similarly, more high risk groups are to be identified in a large scale studies as the limitation of the study is that it is a single center audit data, setting collection spanning over six months period.

4.5 Marwat Logical Trajectory of Research Process:

We have employed this 8-steps hierarchical research model in our project, developed by Dr. Muhammad Marwat.³¹⁻³³

CONCLUSION

The maternal near-miss ratio (MNMR) and maternal mortality ratio (MMR) are relatively higher in population of District, Peshawar, Pakistan. MNMR and MMR both have similar prevalence in ≤ 28 weeks and in > 28 weeks gestational age groups and also similar in primigravida and in multigravida groups. Haemorrhage (antepartum and postpartum) was most common cause both for maternal near-miss (MNM) and maternal mortality (MM).

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CONFLICT OF INTEREST
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design: SR, SY, NL
Acquisition, Analysis or Interpretation of Data: SR, SY, NL, GS
Manuscript Writing & Approval: SR, SY, NL, GS

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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