

Clinical Risk Factors affecting the Pregnancy Outcome using Pakistan Maternal Mortality Survey (PMMS) 2019

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ABSTRACT

Background: South Asia is the world's most populous region, and it also has the highest rate of pregnancy loss. It is necessary to understand the risk factors for pregnancy loss in South Asian countries like Pakistan for reducing the global burden of pregnancy loss.

Aim: To determine the potential clinical factors affecting pregnancy outcomes of Pakistani women aged 15-49 years during 2016-2019.

Study design: This study was conducted using Pakistan Maternal Mortality Survey (PMMS 2019) during 2020-2021. All eligible ever-married women (n=7096) aged 15-49 were selected for this study. In this study, the clinical risk factors considered are fever, unconsciousness, high blood pressure, diabetes, vaginal bleeding, problems associated with the placenta, problems associated with the position of the baby, and preeclampsia. The response variable was pregnancy outcome comprising four categories that are live-birth, stillbirth, miscarriage, and abortion. A multinomial logistic regression model was applied to test the relationship between the dependent variable and each of the eight risk factors.

Results: Multinomial logistic regression model identified that fever (OR=0.723), vaginal bleeding (OR=1.614), high blood pressure (OR=1.473), and problems associated with the position of the baby (OR=0.396) are significantly associated with a stillbirth at a 10% level of significance. Additionally, unconsciousness (OR=1.019) appears as a potential risk factor for abortion. Practical implication: Understanding the most significant risk factors that contribute to negative pregnancy outcomes, it can prioritize resources to improve maternal health. Also, assistance to healthcare providers and policymakers in making informed decisions regarding maternal health in Pakistan can be provided.

Conclusion: Fever, vaginal bleeding, high blood pressure, problems associated with the position of the baby are significant risk factors of stillbirth. However, unconsciousness identified a risk factor of abortion. It is concluded that in Pakistan pregnancy loss can be reduced by controlling the prevalence of diseases during pregnancy.

Keywords: Abortion, Clinical risk factors, Miscarriage, Multinomial logistic model, Pregnancy loss, Stillbirth

INTRODUCTION

Pregnancy outcome includes live birth, stillbirth, spontaneous abortion, and therapeutic abortion¹⁶. According to World Health Organization (WHO), "a live birth is the complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of pregnancy, which, after such separation, breathes or shows any other evidence of life, such as the beating of the heart, pulsation of the umbilical cord, or any definite movement of voluntary muscles, whether or not the umbilical cord has been cut or the placenta is attached". Pregnancy loss includes miscarriage, stillbirth, and abortion, which causes physical and psychological trauma to mothers, is a barrier to achieving the Sustainable Development Goals (SDG). Low- and middle-income nations bear the brunt of the global pregnancy loss burden¹⁷. Pregnancy loss is a devastating reality faced by many mothers worldwide e.g., up to 20% of pregnancies terminate in miscarriage. In 2010–2014, 35 induced abortions per 1000 women aged 15–44 years happened annually, and an estimated 2.6 million stillbirths occurred in 2015¹¹. South Asia is the world's most populous region, and it also has the highest rate of pregnancy loss. United Nations rated Pakistan fourth in terms of annual births and first in terms of stillbirths. In India, Pakistan, and Bangladesh combined, 178 million (255%) of the 698 million babies born worldwide were born between 2010 and 2015, yet 917 800 (350%) of the 2,620,000 stillbirths occurred in these countries. As a result, understanding the risk factors for pregnancy loss in South Asia is critical for developing effective therapies and for reducing the global burden of pregnancy loss.

WHO describes miscarriage as the expulsion or extraction from its mother of an embryo or fetus weighing 500 g or less⁵. It refers to the loss of a pregnancy within the first 24 weeks of pregnancy⁷. Miscarriage is one of the most prevalent but understudied complications of pregnancy. Pakistan is a developing

nation with inadequate healthcare resources. In Pakistan, the yearly predicted miscarriage rate has risen to 29 per thousand women aged 15 to 49. Incomplete and missed miscarriages occur in approximately 15% of clinically diagnosed pregnancies and 890,000 women every year, with 15% experiencing problems linked to unsafe miscarriage¹⁵.

Furthermore, ethnic origin, the mother's psychological condition, a very low or very high pre-pregnancy BMI, stress, the use of non-steroidal anti-inflammatory medicines, smoking, and alcohol intake are all linked to considerably greater rates of miscarriage. Pain, bleeding, and the possibility of hemorrhage are all possible symptoms in the most serious cases⁷. Furthermore, it is noted that women who had a miscarriage in their first pregnancy have a higher chance of miscarriage in their second pregnancy than women who had a live preceding birth. Infections are responsible for 15% of early miscarriages and 66% of late miscarriages⁷. The other risk factors of miscarriage are caffeine, tobacco, alcohol, drugs, previous miscarriage, previous induced abortion, previous deliveries, maternal age, chromosomal aberrations, uterine anatomic defects, menstrual disorders, endocrine disorders luteal, anti-phospholipid antibodies, other autoantibodies, Aloimmune factors, cytokines, sexual activity, maternal injuries, inter-pregnancy interval, ovulation induction drugs cytokines, contraceptives, maternal infection like lysteriosis, syphilis parvovirus B19, HIV⁵. Medical conditions such as induced abortion count, diabetes, and hypertension all contribute to poor reproductive health outcomes¹⁹.

Abortion is defined by the National Center for Health Statistics, the Centers for Disease Control and Prevention (CDC), and WHO as the "termination of a pregnancy before 20 weeks of gestation or the birth of a fetus weighing less than 500 g. Despite this, definitions vary greatly depending on state law". Induced abortion is defined as the intentional termination of a pregnancy before 28 weeks of gestation or with a fetal weight of less than 1000 g. It may be considered safe or unsafe in certain practical situations⁹. The WHO estimated that approximately 5.5 million African women have unsafe abortions each year. Infection, cervical

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and uterine trauma, and hemorrhage are all acute complications of induced abortion. In Pakistan, over half of all pregnancies (46%) are unplanned, with more than half resulting in induced abortion³. According to a National Post Abortion Care Survey, 2.2 million abortions occurred in Pakistan in 2012, resulting in an annual abortion rate of 50 per 1000 women. Almost 700,000 women sought medical treatment for post-abortion problems at health care facilities in the same year³.

WHO describes stillbirth as “when a baby dies after 28 weeks of pregnancy but before or during birth, the child is born without any signs of life, such as breath, voluntary muscle movement, or heartbeat.” Stillbirths are mainly caused by hypertension, eclampsia, abruption placenta, birth asphyxia, preterm labor, inadequate antenatal care, and suboptimal intrapartum care¹⁸. One of the most common negative pregnancy outcomes is stillbirth. It is frequently associated with severe maternal morbidity and long-term psychological distress in mothers and their families. According to global health statistics, approximately 2.6 million stillbirths occur each year, with 75% occurring in low- and middle-income countries. In 2015, Pakistan had the highest stillbirth rate (43.1 stillbirths per 1000 total births, compared to a global estimate of 18.4). The WHO Every Newborn Action Plan (ENAP) aims to minimize stillbirths globally by 2030, with a target of no more than 12 stillbirths per 1000 total births in each country. Despite the ENAP’s approval and an increase in the number of stillbirth studies, most nations have yet to set a stillbirth reduction target in their national health plans¹³. Despite the importance of stillbirths, they are largely unacknowledged in many countries, including Pakistan¹⁸. The main contributing conditions of stillbirths are maternal diseases, unexplained immaturity, congenital anomalies, unexplained antepartum stillbirths, obstetric complications, placental conditions, and multiple births¹³.

The objective of the study is to identify the clinical risk factors affecting the pregnancy, which can help improve maternal health by identifying areas where interventions can be targeted. The findings of this study can be used to develop targeted interventions to reduce the risks associated with pregnancy, leading to improved maternal health and reducing maternal mortality rates. As one of the most populous countries in the world, Pakistan’s maternal mortality rate has a significant impact on global maternal health outcomes. Therefore, the findings of this study have global implications for maternal health policies and interventions.

METHODOLOGY

Data source: The Pakistan Maternal Mortality Survey (PMMS 2019) marked the first time that a dedicated maternal mortality survey was conducted in Pakistan. The primary aim of the PMMS 2019 was to provide the most recent assessments of health and demographic indicators in the country. The Ministry of National Health Services was responsible for implementing this DHS program, with the National Institute of Population Studies (NIPS) leading the effort. The survey was financed by the United States Agency for International Development (USAID).

To collect data for the study, the PMMS (2019) employed six distinct types of questionnaires, namely the Short Household Questionnaire, Long Household Questionnaire, Woman’s Questionnaire, Verbal Autopsy Questionnaire, Community Questionnaire, and Fieldworker Questionnaire. Information for the current study was obtained from various sections of the Woman’s Questionnaire.

Sampling Design: PMMS 2019 employed a multistage and multiphase cluster sampling design. The selection of the survey sample involved a two-stage and two-phase stratified systematic sampling approach. The sample included both urban and rural areas in all four provinces of Pakistan, as well as Azad Jammu and Kashmir, GilgitBaltistan, Federally Administered Tribal Areas (FATA), and the Islamabad Capital Territory (ICT). The sample excluded restricted military and protected areas. In total, the

sampling universe of the four provinces contained 116,169 households. Of the occupied 110,483 households, 108,766 were successfully interviewed, resulting in a response rate of 98%. The survey successfully interviewed 11,859 of the 12,217 eligible ever-married women aged (15-49) years, resulting in a response rate of 97%.

For Azad Jammu and Kashmir, out of the occupied 16,755 households, 16,588 households were successfully interviewed, yielding a response rate of 99%. The survey successfully interviewed 1,666 of the 1,707 eligible ever-married women aged (15-49) years, resulting in a response rate of 98%. The survey conducted 150 verbal autopsy interviews in Azad Jammu and Kashmir, with a response rate of nearly 100%. For Gilgit Baltistan, out of the occupied 11,005 households, 10,872 households were successfully interviewed, resulting in a response rate of 99%. The survey successfully interviewed 1,178 of the 1,219 eligible ever-married women aged (15-49) years, resulting in a response rate of 97%. The survey conducted 88 verbal autopsy interviews in Gilgit Baltistan, with a response rate of nearly 100%.

Statistical Analysis: The present study is based on data collected from the Pakistan Maternal Mortality Survey (PMMS 2019), which was conducted by the Demographic and Health Survey (DHS) program. The study utilized the Women’s Questionnaire of PMMS 2019. The sample consisted of 7,096 eligible ever-married women aged 15-49, who were asked about their pregnancy history and maternal morbidities during pregnancy.

The response variable of interest was pregnancy outcome, which was categorized into four categories: live birth, stillbirth, miscarriage, and abortion. A random variable X_i was used to represent the response variable for the i th mother, with four possible values coded as 1, 2, 3, and 4. Specifically, if the mother had a live birth, X_i was coded as 1; if she experienced stillbirth, X_i was coded as 2; if she had a miscarriage, X_i was coded as 3; and if she underwent an abortion, X_i was coded as 4.

Relevant clinical risk factors, such as fever, unconsciousness, high blood pressure, diabetes, vaginal bleeding, problems associated with the placenta, problems associated with the position of the baby, and preeclampsia, were selected from the survey and consulted relevant literature. A Multinomial Logistic Regression Model was used to investigate the relationship between these factors and pregnancy outcome. A description of the factors used in the statistical analysis can be found in Table 1.

Table 1: Description of Risk Factors Affecting Pregnancy Outcome in PMMS (2019).

Factors	Categories & Code No.
Fever	1: Yes (37.7%) 2: No (62.2%)
Unconsciousness	1: Yes (3.1%) 2: No (92.0%)
High blood pressure	1: Yes (19.5%) 2: No (79.6%)
Diabetes	1: Yes (2.3%) 2: No (97.1%)
Vaginal bleeding	1: Yes (7.9%) 2: No (92%)
Problems associated with the placenta	1: Yes (2.8%) 2: No (95.4%)
Problems associated with the position of the baby	1: Yes (7.7%) 2: No (90.5%)
Preeclampsia	1: Yes (1.8%) 2: No (95.9%)

RESULTS AND DISCUSSION

Table-1 summarized percentages of independent variables presented in a bar diagram. Frequencies of these variables can be seen visually from Figure-1. It shows that 37.7% ($f=2669$) of women had a fever during pregnancy. Moreover, the women who had unconsciousness were 3.1% ($f=231$). It is also observed that 19.5% ($f=1326$) women had high blood pressure during pregnancy. The women who suffered from diabetes during pregnancy were 2.3% ($f=162$). Furthermore, women who had vaginal bleeding during pregnancy were 7.9% ($f=524$). Additionally, it is observed that 2.8% ($f=197$) of women had problems associated with the placenta (PAP) in pregnancy. Likewise, 7.7% ($f=511$) of the women had problems associated with the position of the baby

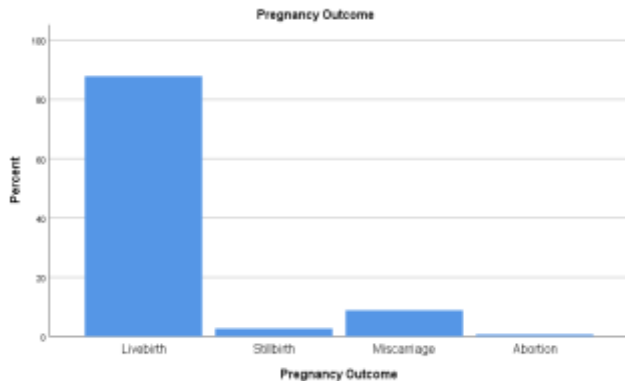
(PAB) in pregnancy. Women having preeclampsia during pregnancy were 1.8% (f=137).

Figure 1: Frequency of Factors Affecting Pregnancy Outcome (PMMS 2019).



Figure-2 shows that 88.6% (f=6288) of women deliver live births, whereas 2.5% (f=174) of the women delivered stillbirths, moreover the women whose pregnancy outcome was miscarriage were 8.4% (f=593), and 0.6% (f=40) of women are those whose pregnancy outcome was abortion. The median value along 95% CI bandwidth can be seen against each risk factor. The median value represents middle value of each risk factor.

Figure 2: Frequency of factors affecting pregnancy outcome (PMMS 2019)



The multinomial logistic regression model was applied by including all clinical risk factors to estimate their effect on pregnancy outcome. Table-2 summarizes parameter estimates and odds ratios of the multinomial logistic regression model.

Table 2: Odds ratios of multinomial logistic regression model for pregnancy outcome in Pakistan

Parameter	Stillbirth Odd Ratio	Miscarriage Odd Ratio	Abortion Odd Ratio
Intercept	---	---	---
Fever=1	0.723	0.881	0.815
Unconsciousness=1	0.420	1.019	4.080
High blood pressure=1	1.473	1.067	1.360
Diabetes=1	0.672	1.287	0.007
Vaginal bleeding=1	1.614	0.851	1.601
Problems associated with the placenta=1	0.777	1.094	0.873
Problems associated with the position of the baby=1	0.396	0.768	0.255
Preeclampsia=1	1.285	0.659	0.043

The reference category of the dependent variable was Live-birth. The reference category of all independent variables was the "No" category. It is observed from Table-1 that fever, vaginal bleeding, high blood pressure; problems associated with the position of the baby are significantly associated with a stillbirth at a 10% level of significance. While diabetes, unconsciousness, problems associated with the placenta, preeclampsia are not significantly associated with stillbirth. It is observed from Table-1 that fever, vaginal bleeding, high blood pressure, diabetes, unconsciousness, problems associated with the position of the baby, problems associated with the placenta, preeclampsia are not significantly associated with miscarriage. It is also observed that unconsciousness is significantly associated with abortion. While fever, vaginal bleeding, high blood pressure, diabetes, problems associated with the position of the baby, problems associated with the placenta, preeclampsia are not significantly associated with abortion. Table-3 describes and compares the odds ratios of all independent variables for stillbirth, miscarriage, and abortion concerning live birth.

Table 3: Comparison of stillbirth, miscarriage, and abortion with live-birth in terms of odds ratio

	Stillbirth	Miscarriage	Abortion
Fever	The woman who had a fever in pregnancy had less chance to experience a stillbirth concerning delivering a live birth than that of a woman who does not have a fever in pregnancy (OR=0.723).	The woman who had a fever in pregnancy had fewer chances to experience a miscarriage concerning delivering a live birth than that of a woman who does not have a fever in pregnancy (OR=0.881).	A woman who had a fever in pregnancy had fewer chances to experience an abortion concerning delivering a live birth than that of a woman who does not have a fever in pregnancy (OR=0.815).
Unconsciousness	A woman who had unconsciousness in pregnancy had fewer chances to experience a stillbirth concerning delivering a live birth than that of a woman who does not have unconsciousness during pregnancy (OR=0.420).	A woman who had unconsciousness in pregnancy had more chances to experience a miscarriage concerning delivering alive birth than that of a woman who does not have unconsciousness in pregnancy (OR=1.019).	A woman who had unconsciousness in pregnancy had more risk to experience an abortion concerning delivering a live birth than that of a woman who does not have unconsciousness in pregnancy (OR=4.080).
High blood pressure	A woman who had high blood pressure in pregnancy had more risk to experience a stillbirth concerning delivering a live birth than that of a woman who does not have high blood pressure in pregnancy (OR=1.473).	A woman who had high blood pressure in pregnancy had more risk to experience a miscarriage concerning delivering a live birth than that of a woman who does not have high blood pressure in pregnancy (OR=1.067).	A woman who had high blood pressure in pregnancy had more risk to experience an abortion concerning delivering alive birth than that of a woman who does not have high blood pressure in pregnancy (OR=1.360).
Diabetes	The woman who had diabetes in pregnancy had less chance to experience a stillbirth concerning delivering a live birth than that of a woman who does not have diabetes in pregnancy (OR=0.672).	The woman who had diabetes in pregnancy had more chance to experience a miscarriage concerning delivering a live birth than that of a woman who does not have diabetes in pregnancy (OR=1.287).	A woman who had diabetes in pregnancy had less chance to experience an abortion concerning delivering a live birth than that of a woman who does not have diabetes in pregnancy (OR=0.007).
Vaginal bleeding	The woman who had vaginal bleeding in pregnancy had more risk to experience a stillbirth concerning delivering a live birth than that of a woman who does not have vaginal bleeding in pregnancy (OR=1.614).	The woman who had vaginal bleeding in pregnancy had fewer chances to experience a miscarriage concerning delivering a live birth than that of a woman who does not have vaginal bleeding in pregnancy (OR=0.851).	A woman who had vaginal bleeding in pregnancy had less chance to experience an abortion concerning delivering a live birth than that of a woman who does not have vaginal bleeding in pregnancy (OR=1.601).
Problems Associated with the placenta	The woman who had problems associated with the placenta in pregnancy had less risk to experience a stillbirth concerning delivering a live birth than that of a woman who does not have problems associated with the placenta in pregnancy (OR=0.777).	A woman who had problems associated with the placenta in pregnancy had more risk to experience a miscarriage concerning delivering a live birth than that of a woman who does not have problems associated with the placenta in pregnancy (OR=1.094).	The woman who has problems associated with the placenta in pregnancy had less risk to experience an abortion concerning delivering a live birth than that of a woman who does not have problems associated with the placenta in pregnancy (OR=0.873).
Problems associated with the position of the baby	The woman who had problems associated with the position of the baby in pregnancy had less risk to experience a stillbirth concerning delivering a live birth than that of a woman who does not have problems associated with the position of the baby in pregnancy (OR=0.396).	The woman who had problems associated with the position of the baby in pregnancy had fewer risk to experience a miscarriage concerning delivering a live birth than that of a woman who does not have problems associated with the position of the baby in pregnancy (OR=0.768).	A woman who had problems associated with the position of the baby in pregnancy had less risk to experience an abortion concerning delivering live births than that of a woman who does not have problems associated with the position of the baby in pregnancy (OR=0.255).

Preeclampsia	The woman who had preeclampsia in pregnancy had more risk to experience a stillbirth concerning delivering alive birth than that of a woman who does not have preeclampsia in pregnancy (OR=1.285).	A woman who had preeclampsia in pregnancy had fewer risk to experience a miscarriage concerning delivering a live birth than that of a woman who does not have preeclampsia in pregnancy (OR=0.659).	The woman who had preeclampsia in pregnancy had less risk to experience an abortion concerning delivering a live birth than that of a woman who does not have preeclampsia in pregnancy (OR=0.043).
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Table 3 shows the Comparison of stillbirth, miscarriage, and abortion with live-birth in terms of odds ratio. From the comparison of stillbirth with live-birth, it was determined that the factors which have a significant effect on stillbirth in Pakistan are a fever, vaginal bleeding, high blood pressure, problems associated with the position of the baby. A study of stillbirths in Pakistan showed that high blood pressure during pregnancy increased the risk of stillbirth in Pakistani women¹⁸. A situational analysis on stillbirths in Pakistan showed that the major contributing clinical risk factor of stillbirth was hypertension in pregnancy¹. A systematic review of observational studies of south Asian countries revealed that the maternal hypertension was the important clinical risk factor of stillbirth in Pakistan India, Nepal and Bangladesh¹².

An analysis of reasons of stillbirth in India revealed that the major factor of stillbirths was hypertension in pregnancy¹⁴. The current study also revealed that high blood pressure is the clinical risk factor of stillbirth in Pakistani women. So, it is crucial to control high blood pressure in pregnancy to avoid stillbirths in Pakistan. A study about stillbirths in Pakistan also showed that vaginal bleeding was the risk factor of stillbirth in urban areas of Pakistan⁸. Same effect was found in current study for vaginal bleeding on stillbirths but it is not significant. A study about stillbirths in India showed that fever was the reason of stillbirth in India¹⁴. A research in urban community in Pakistan illustrated that maternal fever was minor clinical risk factor of stillbirth in Pakistan⁸. The current study also in the support of these results.

Considering the comparison of miscarriage with live birth, no risk factor appeared significantly associated with miscarriage. A study about the role of infection in miscarriage revealed that Q fever was insignificantly associated with miscarriage⁷. This study also showed that a fever variable was not significantly associated with miscarriage. A prospective study about miscarriage determined that vaginal bleeding was the leading cause of miscarriage¹⁰. Research about miscarriage showed that hypertension was the major cause of miscarriage⁴. But current study showed opposite results.

Considering the comparison of abortion concerning live birth, this comparison showed that unconsciousness was a significant cause of abortion. Research about legal abortion revealed that diabetes and hypertension were the reasons for abortion⁶. A clinical study showed that vaginal bleeding was the cause of abortion². While, the current study showed opposite results. There are many socio-demographic factors influencing pregnancy outcomes that would be included in future studies. Furthermore, it is suggested to study non-clinical risk factors like psychological disorders (depression, anxiety, chronic stress etc.). These could be as fatal as clinical factors.

Limitations of the Study: The study was based on the secondary data constrained by the framework of the previously resolved sample size and questionnaire. This study was based on only three years of survey data of Pakistan. There were many factors influencing pregnancy outcome but this study had focused on some selected factors.

CONCLUSIONS

It was observed that fever, vaginal bleeding, high blood pressure, and problems associated with the position of the baby were the potential risk factors of stillbirth. No clinical risk factor was significantly associated with abortion in Pakistan except unconsciousness. Finally, it is concluded that in Pakistan the pregnancy loss can be reduced by controlling the prevalence of diseases (fever, vaginal bleeding, high blood pressure, and

problems associated with the position of the baby, unconsciousness) during pregnancy.

Ethical Approval: This article does not contain any studies with human participants or animals performed by any of the authors.

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