Pregnancy loss in rural Bangladesh :

An analysis of burden and determinants based on a Health and Demographic Surveillance Site

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DECLARATION

I am Dr. Sahar Raza, student of the Department of Pharmacy and Public health, Independent University; present my thesis work on "Pregnancy loss in rural Bangladesh: An analysis of burden and determinants based on a Health and Demographic Surveillance Site" as requirement of completion of my master's degree. This research was performed under the supervision of Dr. Nafisa Huq, Assistant Prof. & Head of Department of Public Health, School of Pharmacy and Public Health and Dr. Ahmed Ehsanur Rahman, Associate Scientist, Maternal and Child Health Division, icddr,b.

I hereby declare that this thesis has not been submitted to any other institute and all relevant use of references have been added in the reference section.

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ABBREVIATIONS

ANC	Antenatal Care
LMIC	Low- and middle-income countries
MR	Menstrual Regulation
PL	Pregnancy Loss
SDG	Sustainable Development Goals

ABSTRACT

Aim: Pregnancy loss significantly effects the physical and mental wellbeing a woman, regardless of it being intentional or unexpected. It is important to understand the burden and risk factors of pregnancy loss to develop and implement effective preventive and management strategies.

Methods: We conducted secondary analysis of data from a Health and Demographic Surveillance Site (HDSS) of icddr,b, established in a rural sub-district of Bangladesh. We used descriptive statistics, i.e. proportions with 95% confidence intervals, to report burden of pregnancy loss. Risk factors and social determinants were explored with bivariate logistic regression models followed by a multivariate logistic regression model.

Results: A total of 21,083 pregnancy events were identified among 18,553 women between January 2018 and December 2021. Approximately 11.4% (95% CI 11, 12) of these pregnancies resulted into pregnancy loss. The proportion of early pregnancy loss (12 weeks/1st trimester) was 6.7% (95% CI 6, 7) and late pregnancy loss was 4.7% (95% CI 4, 5) among all pregnant women. The median time for pregnancy loss was 84 days (IQR-42) from the last menstrual period. 49% of the pregnancy losses were due to reasons other than medical abortions. The odds of pregnancy loss was 2.19 (p=0.02) times higher among women aged 30 years or more than those aged 20 years or less. The risks were higher among women who were pregnant for the 3rd (AOR 2.79, p=0.001) or ≥4th (AOR 6.22, p=0.001) times. The risks were also higher among pregnant women who had a previous history of pregnancy loss (AOR 1.71 p=0.0018).

Conclusion: In rural Bangladesh the burden of pregnancy loss in relatively high. The majority of them happen spontaneously and during the first trimester. Therefore, the maternal health program should take special initiatives for reaching out to pregnant women in the first trimester to effectively prevent and protect the pregnancy loss. Moreover, if there is a history of previous pregnancy loss, subsequent pregnancies should be considered high risk and rigorous monitoring should be ensured to prevent further losses.

Chapter 1
Introduction

BACKGROUND

Pregnancy loss, defined by the loss of an unborn fetus before the viable age of gestation, can bring significant physical, psychological and financial sufferings to the women. Regarding physical effects, it may result in bleeding and infection and other complications (1). If left untreated, these complications can lead to fatal consequences and impede the progress towards achieving the Sustainable Development Goal (SDG) target of reducing maternal mortality ratio to 70 per 100,000 live births or below by 2030 (2). Moreover, pregnancy loss increases in the risk of anxiety, depression, post-traumatic stress disorder, and suicide ((1). Thus, it adversely affects the mental wellbeing of women and her family members.

Each year, an estimated 23 million pregnancy loss events occur globally, which equates to more than 60 thousand pregnancy losses every day (1). According to the March of Dimes report published in 2022, 10-15% of pregnant women experience pregnancy loss. Most of the pregnancy loss burden is from low- and middle-income countries (LMICs). South-Asia has the highest rate of pregnancy loss compared to other regions (3)(4). However, these figures can be an under estimation of the true burden, since a significant proportion of women, particularly in low-resource settings, experiencing pregnancy loss may not be aware of their pregnancy status during the time of loss (5). Moreover, the variation in gestational age of viability among countries and international organizations consequently affect the estimation of overall burden. According to the World Health Organization, the age of viability is 28 weeks. However, it is 24 weeks according to the American Society of Reproductive medicine and 22 weeks according to the European Society of Human Reproduction and Embryology.

Country	Age of viability (Weeks)
Bangladesh	28
United Kingdom	24
United States of America	20
Europe	22

Table 1: Age of viability in different geographical regions

In Bangladesh, the generational age of viability is 28 weeks. It is 24 weeks in UK and 20 weeks in USA. **Table 1** shows a comparison in the age of viability across different countries. Overall, In High-income countries, the neonatal intensive care for preterm becomes more effective much earlier leading to their age of viability to be lower than developing countries (1). Pregnancy loss can occur at any time during the course of a pregnancy. An early pregnancy loss is the loss of an unborn fetus in the first 3 months of pregnancy (12 weeks/1st trimester) through

unborn fetus in the first 3 months of pregnancy (12 weeks/1st trimester) through

miscarriage/spontaneous abortion or induced abortion or menstrual regulation. On the other hand, a late pregnancy loss is the loss of an unborn fetus after 3 months of pregnancy but before the viable age of gestation through miscarriage/spontaneous abortion or induced abortion. A number of risk factors contribute to pregnancy loss. Age of the mother (5–7), education (8), and whether the woman has a previous history of pregnancy loss (1,5).

Figure 1 below summarizes different types of pregnancy loss based on gestational age. In this study the weeks of gestation is referred to the length of pregnancy from the Last Menstrual Period (LMP).

Figure 1: Outcome of interests for pregnancy loss
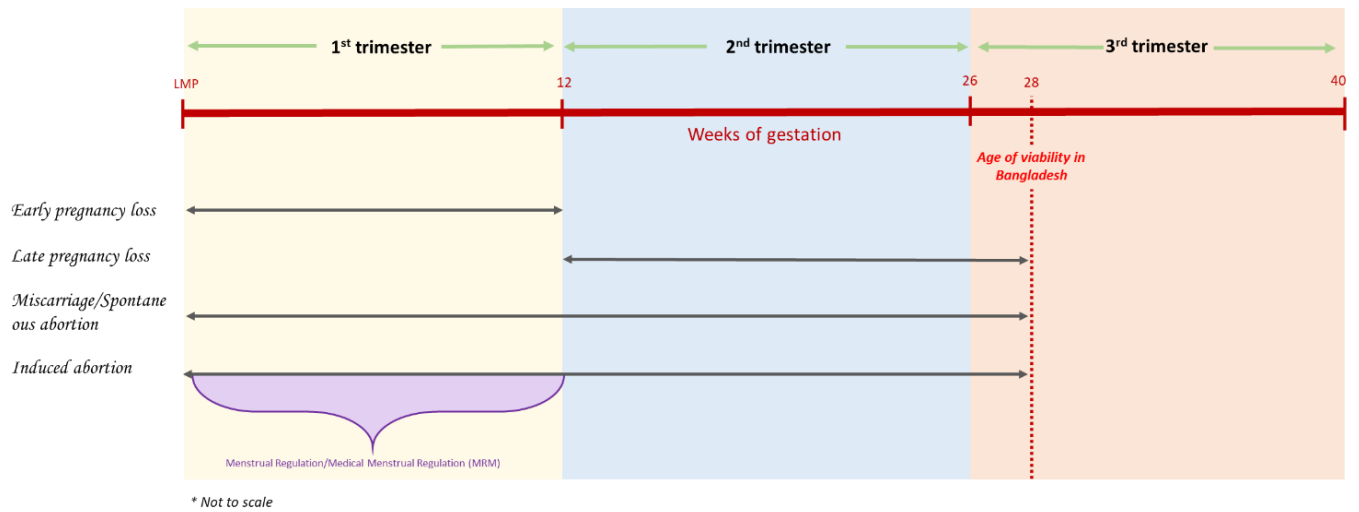
In Bangladesh, 1,194 000 induced abortions occurred in 2014 that estimated 29 abortions per 1000 women aged 15 to 49 (4) which is the most recent estimate. This estimate is also women-specific i.e. it specifies the number of abortions occurring in women but is not the estimate of pregnancy loss occurring in pregnant women. Furthermore, this estimate does not include miscarriages/spontaneous abortion, and menstrual regulation and silence about miscarriages and disregard for their impact are concerning and ought to be explored.

Abortion is illegal in Bangladesh. **Figure 2** below shows that it is only legal when it is to save the life of a women (10,11) and there is no further description as to what that constitutes. Neighboring countries such as India does have other conditions in which abortion is legal such as to preserve the mental and physical health of a women and on socioeconomic grounds. However, existing policies in Bangladesh allow a woman to go through menstrual regulation (MR), defined as the "procedure of regulating the menstrual cycle when menstruation is absent for a short duration," that was introduced in the government's family planning program in 1970s as a strategy to reduce maternal morbidity and mortality associated with unsafe abortion [10]. MR is usually conducted without a confirmatory pregnancy test, within 10 weeks of a missed menstrual period by paramedics and within 12 weeks of a missed menstrual period by medical doctors [11]. However, there is a lack of consistent gestational cut-offs across health-care providers [10], causing misunderstanding about what the cut-off point for MR is and whether it can be done or not.
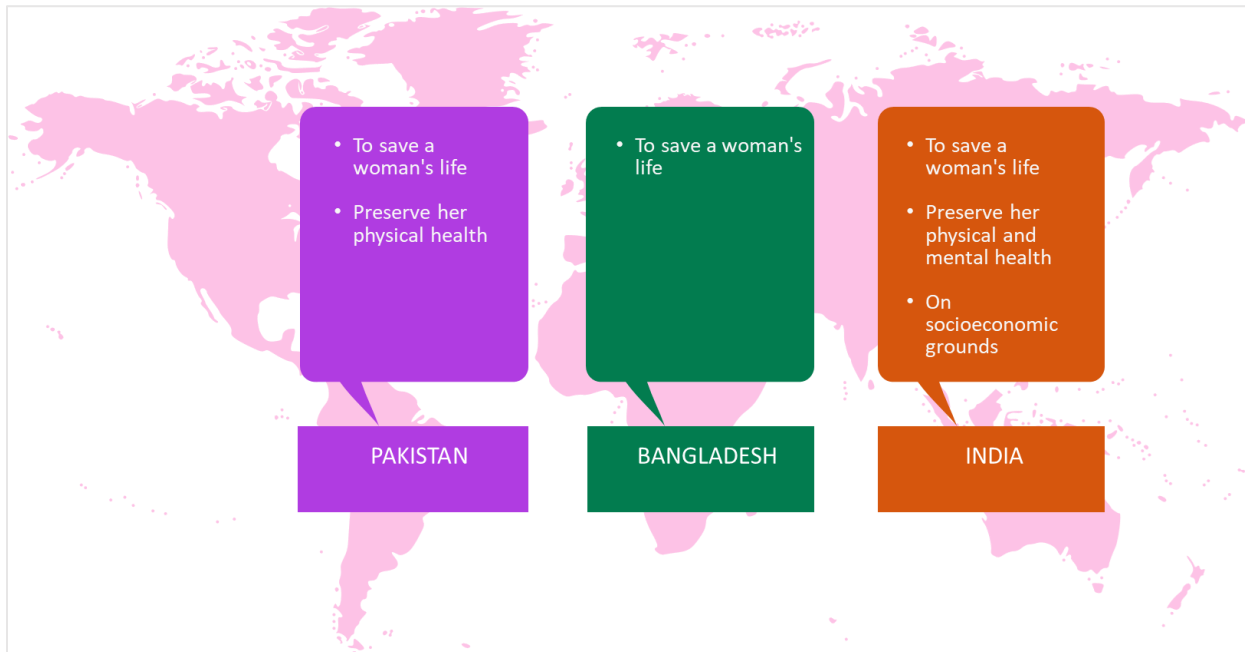
Due to the general convenience, geographic accessibility, and relative anonymity of pharmacies, many low-income women use local pharmacies as their primary source of health care services and is their first-point-of-contact (2). While the correct use of mifepristone–misoprostol for MR is a safe and effective method, even in a low-resource and legally restrictive setting like Bangladesh, in 2011, evidence from a study revealed that certain pharmacy personnel in Bangladesh were prescribing inadequate misoprostol regimens for MR (3). Furthermore, a recent study conducted in Bangladesh revealed that pharmacy personnel frequently recommended the mifepristone–misoprostol combo to people looking for a way to self-manage abortion on their own specially when it has crossed the legal limit of 10 weeks (4). Other unsafe abortion methods due to restricted laws, lack of safe abortion care services provision and sociocultural norms (13) may also be used by women who want to end their pregnancy . Complications that may arise due to this may include incomplete abortion (failure to remove or expel all of the pregnancy tissue from the uterus), hemorrhage, infection and much worse conditions such as uterine perforation and damage to the genital tract and internal organs (14). These obstetric complications including psychological factors need to be managed. Psychological effects having no physical manifestations they are difficult to recognize and the stigma and shame leads to concealment and further dismissal of symptoms. Long-term health effects in women (cardiovascular and venous to understand the risk

factors for pregnancy loss in Bangladesh and estimate the burden so that it can contribute to the planning of effective interventions and thus mitigating the burden of pregnancy loss.

OBJECTIVES

a) GENERAL OBJECTIVE
To estimate the burden of pregnancy loss among pregnant women in rural Bangladesh

b) PRIMARY OBJECTIVE
To estimate *the proportion of pregnancy loss* among pregnant women in rural Bangladesh

c) SECONDARY OBJECTIVE

a) To estimate *the proportion of different types of pregnancy loss* among pregnant women in rural Bangladesh, including *early and late pregnancy loss, miscarriage/spontaneous abortion and induced abortion*

b) To determine the *determinants of pregnancy loss* among pregnant women in rural Bangladesh

d) OPERATION DEFINITION

Early pregnancy loss	Loss of a fetus in the first 3 months of pregnancy (12 weeks/1st trimester) through miscarriage/spontaneous abortion or induced abortion, menstrual regulation and menstrual regulation with medicine (MRM)
Late pregnancy loss	Loss of a fetus in the after 3 months of pregnancy but before 28 weeks (12-24 weeks) of gestational age through miscarriage/spontaneous abortion or induced abortion.
Miscarriage/spontaneous abortion	Any pregnancy loss that has happened without the intent of termination as reported by the woman.
Induced abortion	**Induced abortion (medically-terminated pregnancy):** Any pregnancy loss that has happened with the intent of termination by allopathic medicine or medical procedures.
	Induced abortion (non-medical menstrual Regulation): Any pregnancy loss that has happened with the intent of termination by non-allopathic medicine or procedures, such as herbal, unani, local indigenous methods etc.

e) HYPOTHESIS

Not applicable

Chapter 2
Methodology

METHODOLOGY

a)   STUDY DESIGN:

I conducted secondary analysis of data from the Baliakandi Health and Demographic Surveillance Site (HDSS) of icddr,b.

b)   STUDY SITE

Baliakandi is an upazila (sub-district) of Rajbari district, situated in the central-west part of Bangladesh. It is bounded by Pangsha upazila on the north, Madhukhali upazila on the south, Rajbari sadar upazila on the east, Pangsha and Sreepur upazilas on the west. It has a land area of area 242.53 square kilometer and an estimated population of 217,973 in 2017. It has 7 unions, 151 mouzas and around 258 villages. There is one Upazila Health Complex and seven Union Health and Family Welfare Centers (UHFWC), 23 community clinics and few private clinics in Baliakandi upazila.

Figure 3: A comparison of the legal status of abortion
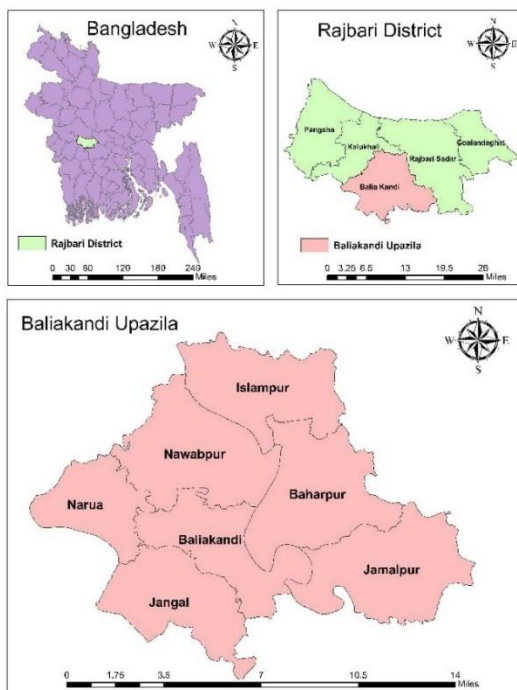
c)   HDSS DESCRIPTION

Since September 2017, icddr,b has been conducting health and demographic surveillance with GIS mapping of each household at Baliakandi upazila. The total area of the Baliakandi-HDSS is about 239 square kilometers and covered a population of around 227,540 in 2017. Through two monthly household visits, HDSS data collectors visit all households and collect information on births, deaths, marriages, divorces, and migrations. In addition to these vital events, information is also collected on various socio-demographic characteristics, such as education and socioeconomic status. Each household and individual are given a unique identifying number (unique ID) that allows all data to be linked across years against the household and individual. These records can be further linked to the Geographical Information System, which contains the geographic location of Baris, important landmarks (schools, health facilities, mosque, rural markets, etc.), road networks, and water bodies in Baliakandi.

In addition, icddr,b also has pregnancy surveillance to identify pregnancy, stillbirths, and neonatal deaths in the Baliakandi-HDSS area. Here, the data collector inquiries about the date of the last menstrual period (LMP) during the routine HDSS visit and offers a strip-test to confirm the pregnancy if a married woman under reproductive age misses a period. Once confirmed, this pregnancy is followed up to its ultimate outcome i.e., miscarriage, abortion including menstrual regulation, still birth and live birth.

d)   STUDY POPULATION

Married women under reproductive age (15-49 years) with a confirmed pregnancy were my study population.

Inclusion criteria:

- Age between 15 and 49 years
- Married
- Pregnancy confirmed by urine strip test or USG
- Permanent resident of the Baliakandi-HDSS

Exclusion criteria:

- LMP after December 2021 (so that each of the women included in the analysis have at least 36 weeks of observation from their LMPs)

e) OUTCOME VARIABLE

The primary outcome of interest is pregnancy loss. Pregnancy loss was coded as "1" when it had occurred and "0" if it had not occurred. I did not include the loss of fetus after 28th week of gestation as a pregnancy loss as it is considered as a stillbirth in Bangladesh context.

The secondary outcomes of interest are :

- Types of pregnancy loss including early pregnancy loss, late pregnancy loss, miscarriage/spontaneous abortion, induced abortion.
- Risk factors and determinants of pregnancy loss.

f) INDEPENDENT VARIABLE

The explanatory variables in this study are :

- Age of the woman and husband
- Education of the woman and husband
- Profession of the woman and husband
- Pregnancy order
- History of pregnancy loss
- Wealth quintile

g) ANALYSIS PLAN

I used the statistical software package Stata for data analysis.

The *primary outcome of interest* i.e., pregnancy loss is defined as the proportion of pregnant women experiencing miscarriage or induced abortion including menstrual regulation before completing 28 weeks of gestation.

The *secondary outcome of interest* i.e., early pregnancy loss defined as the proportion of pregnant women experiencing miscarriage or induced abortion including menstrual regulation before completing 12 weeks of gestation.

Another secondary outcome of interest i.e., late pregnancy loss defined as by proportion of pregnant women experiencing miscarriage or induced abortion after completing 12 weeks of gestation and before completing 28 weeks of gestation.

Another secondary outcome of interest i.e., spontaneous abortion defined as by proportion of pregnant women experiencing miscarriage without intending before completing 28 weeks of gestation.

Another secondary outcome of interest i.e., induced abortion **(medically-terminated pregnancy)** defined as by proportion of pregnant women experiencing abortion with intention through availing medical services before completing 28 weeks of gestation.

Another secondary outcome of interest i.e., induced abortion **(non-medically-terminated pregnancy)** defined as by proportion of pregnant women experiencing abortion with intention by non-allopathic medicine or procedures, such as herbal, unani, local indigenous methods etc. before completing 28 weeks of gestation.

Descriptive statistics were used to report the background characteristics of the study population. **Age** of the woman and her husband, **Education** level of the woman and her husband, **Profession** of the woman and her husband, **Wealth quintile**, **Family structure, History of pregnancy loss**, **Pregnancy order** of the woman were considered as background characteristics.

The woman's age was categorized into 4 categories (<20 years, 20-24 years, 25-29 years, 30 and above). The husband/partners age was categorized in 5 categories (<25 years, 25-29 years, 30-34 years, 35-39 years and >=40 years). The education for both the woman and husband/partner was categorized into No education, Primary incomplete (1-4 years of schooling), Primary complete (5 years of schooling), Secondary incomplete (6-9 years of schooling), Secondary complete or Higher (10 or more years of schooling). The pregnancy order in this study refers to the number of times a woman has been pregnant i.e. if this is her 1st pregnancy, then her pregnancy order would be 1.

I reported the outcomes of interest i.e., with proportion of pregnancy loss, early pregnancy loss and late pregnancy loss with proportions with 95% confidence intervals (CI). Then I presented the proportion disaggregated by the background characteristics (mentioned above). I also presented the proportion of pregnancy loss, early pregnancy loss and late pregnancy loss by LMP calendar months.

I explored the associations between pregnancy loss (overall pregnancy loss, early and late pregnancy loss and spontaneous abortion) and the background characteristics (as covariates) through bivariate logistic regression models. Afterwards we reported the adjusted odds ratios

through multivariable logistic regression models, where all background variables were included in the model for adjustments. We adopted this model since the global literature suggested that all these variables can potentially influence of pregnancy loss. I could not place Birth order and history of previous pregnancy loss in the same model as cell counts for some of the categories came down to less than 5 or all of them (observations) had no pregnancy loss (0) or all of them had pregnancy losses (1). Therefore, I developed a separate multivariable logistic regression model for assessing the effect of history of previous loss on subsequent pregnancy losses with a minimum set of variables. I considered an association significant at $p < 0.05$.

Figure 4: Denominators used to obtain the outcome of interest
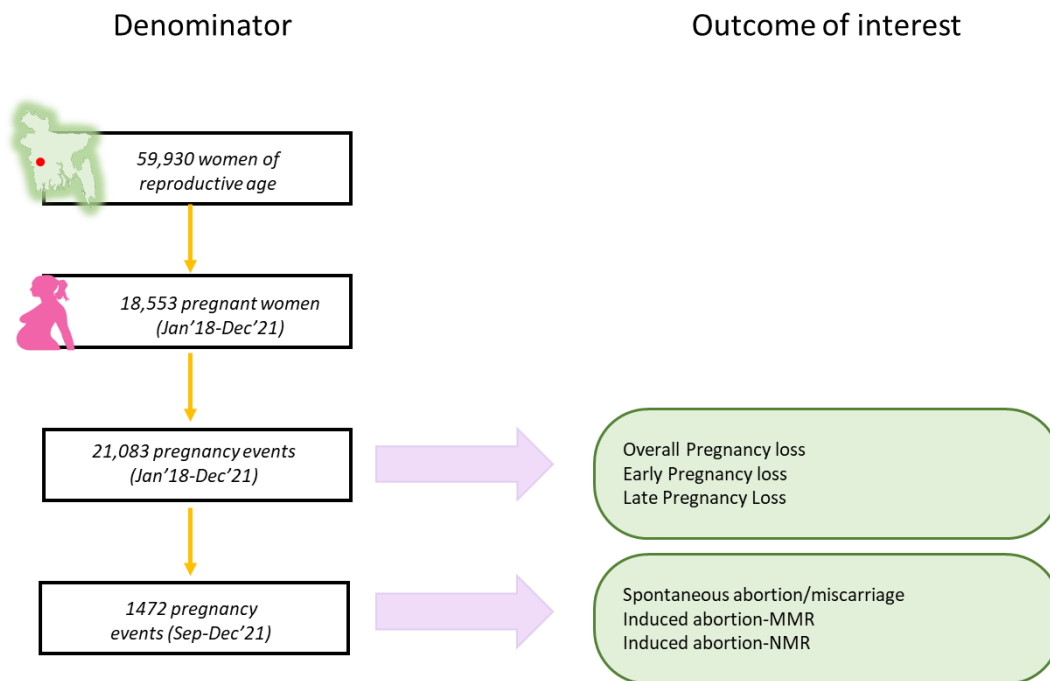
h) ETHICAL CONSIDERATION

I conducted secondary analysis of the data obtained from the Baliakandi HDSS of icddr,b. Therefore, I did not require any ethical approval. However, icddr,b obtained approval of its institutional review board which consisted of two independent committees, i.e., Research Review Committee and Ethics Review Committee for conducting the health and demographic surveillance.

Chapter 3
Results

RESULTS

The mid-year population of women of reproductive age group (15-49 years) in the Baliakandi HDSS site was 59,930 in 2018. Of these women, **18,553 women** matched the inclusion and exclusion criteria (described in the methods section) and were included in the analysis. These women had **21,083 pregnancy events** between January 2018 and December 2021.

Background characteristic of the pregnant women

Table 2 below summarizes the background characteristics of the pregnant women and their husbands/partners.

Pregnant women included in the study

Around 27% of the women were aged less than 20 years and around 20% were aged 30 years or more. Around half (5 1%) of the women had secondary incomplete level of education and approximately 29% had secondary complete level of education. Only 5% of the women were involved in some form of income generating activities. Around 37% of the women were pregnant for the first time and another 32% of women were pregnant for the second time. Approximately 12% of the women had a previous history of pregnancy loss.

Husband/partner of the women in the study

Approximately 20% of the husband/partners were below 25 years of age and around 12% were 40 years or above. Approximately 27% of the husband/partners were 30-34 years old. In terms of education, around 15% had no education and 22% had their secondary education completed or higher. Approximately 98% of the husband/partners were involved in income generating activities.

Characteristics		N	%
Age of woman (years)	<20	5,543	26.5
	20-24	6,551	31.3
	25-29	4,680	22.3
	30 and above	4,178	19.9
Education of woman	No education	762	3.6
	Primary incomplete	1732	8.2
	Primary complete	1738	8.2
	Secondary incomplete	10744	51.0
	Secondary complete or higher	6106	29.0
Profession of woman	Not involved in income generating activity	19999	94.9
	Involved in income generating activity	1084	5.1
Pregnancy order	1	7885	37.4
	2	6735	31.9
	3	3760	17.8
	>=4	2703	12.8
History of pregnancy loss	No	18,549	88.0
	Yes	2,534	12.0
Age of husband/partner (years)	<25	3818	19.7
	25-29	4539	23.4
	30-34	5199	26.8
	35-39	3593	18.5
	40 and above	2240	11.6
Education of husband/partner	No education	2949	15.2
	Primary incomplete	3950	20.4
	Primary complete	2879	14.9
	Secondary incomplete	5345	27.6
	Secondary complete or higher	4261	22.0
Profession of husband	Not involved in income generating activity	450	2.3
	Involved in income generating activity	18939	97.7
Family structure (number of family members)	≤4	6710	31.8
	≥5	14373	68.2
Wealth quintile	Lowest	3923	18.6
	Second	4138	19.6
	Middle	4405	20.9
	Fourth	4476	21.2
	Highest	4140	19.6
Total		**21,083**	

Table 2 Background characteristics of women who were pregnant between January 2018 and December 2021 (N=21,083)

Figure 5 below presents the proportions of early and late pregnancy losses in percentages. Of the 21,083 pregnancy events, 11.4% (95% CI 11, 12) resulted into pregnancy loss. The proportion of early pregnancy loss (12 weeks/1st trimester) was 6.7% (95% CI 6, 7) and late pregnancy loss was 4.7% (95% CI 4, 5).

Figure 5 Pregnancy loss, early pregnancy loss and late pregnancy loss proportions, presented in percentages with 95% confidence intervals
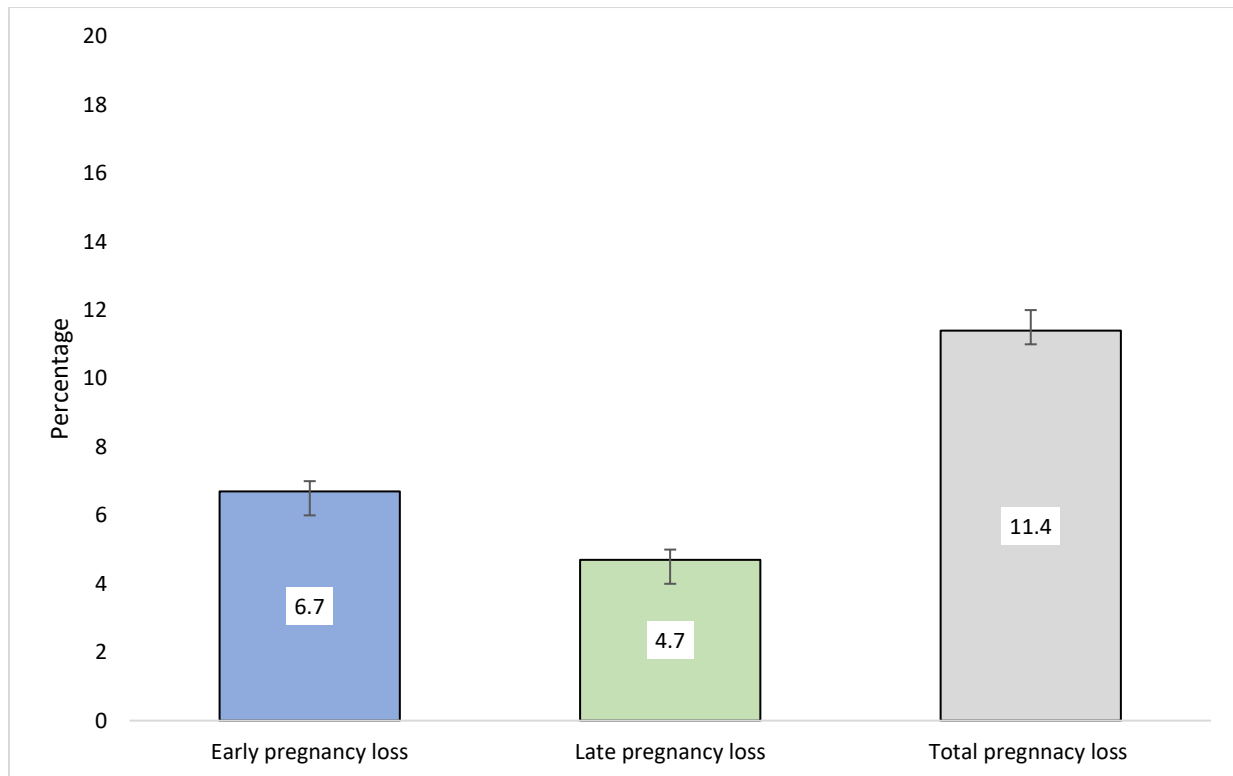
Baliakandi-HDSS started collecting data on the intention of pregnancy loss (spontaneous vs induced) from September 2021. **Figure 6** shows the pregnancy loss proportions by intention (spontaneous vs induced) among women who had LMP between September to December 2021. The proportion of spontaneous abortion (miscarriage) was 11.5% (95% CI 9,13.2) among all pregnant women. The proportion of induced abortion (medical) was 2.6% (95%CI 2.3,2.8) and induced abortion (non-medical) was 0.5% (95% CI 0.3, 0.8).

Figure 6: Types of pregnancy loss by intention among women with LMP between September and December 2021 (N=1472), presented in percentage with 95% confidence interval
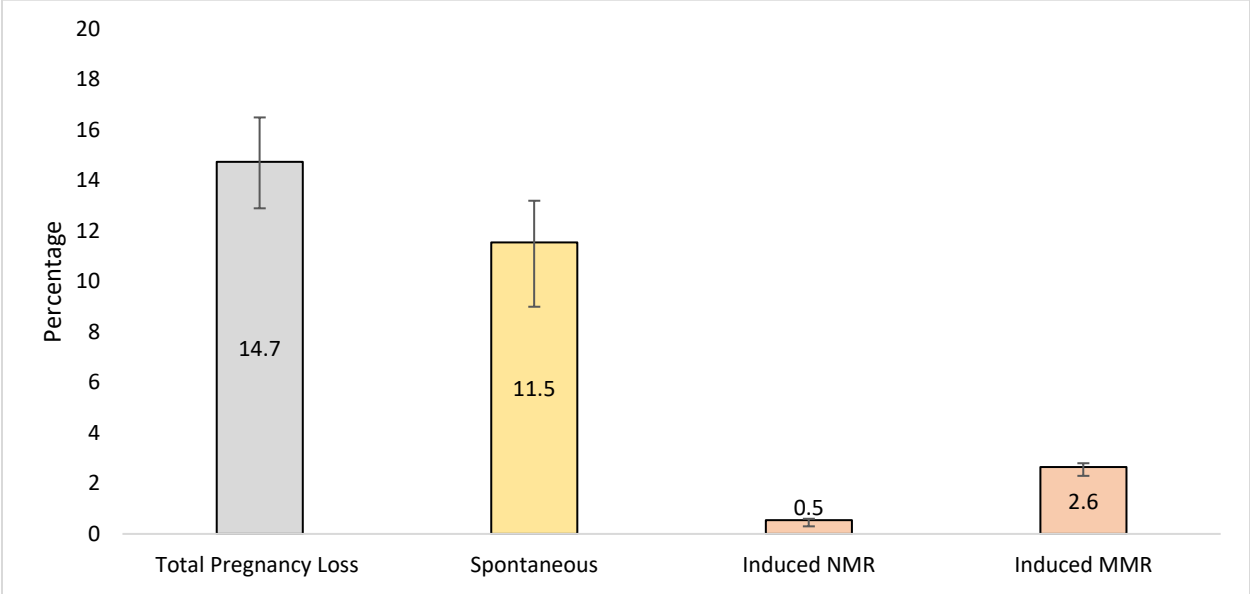
Of the 21,083 pregnancy events, there were 2,405 pregnancy losses.

Figure 7 shows the frequency distribution of pregnancy loss by gestational age. The highest number of pregnancy loss events were observed at the 12th week of gestation (n=232, 10%), followed by the 11th (n=225, 9%), the 13th (n=222, 9%), the 10th (n=216, 9%) and the 9th (n=214, 9%) weeks. Approximately 59% of the pregnancy losses happened before the 12th week of gestation i.e. early pregnancy loss and around 41% pregnancy losses happened between the 12th-28th week, i.e. late pregnancy loss. Of all the pregnancy loss events, approximately 80% happened between the 6th and the 16th week of gestation. Only around 5% of the pregnancy loss events occurred after 22nd weeks of gestation.

Figure 7: Distribution of pregnancy loss events by gestational age presented in weeks
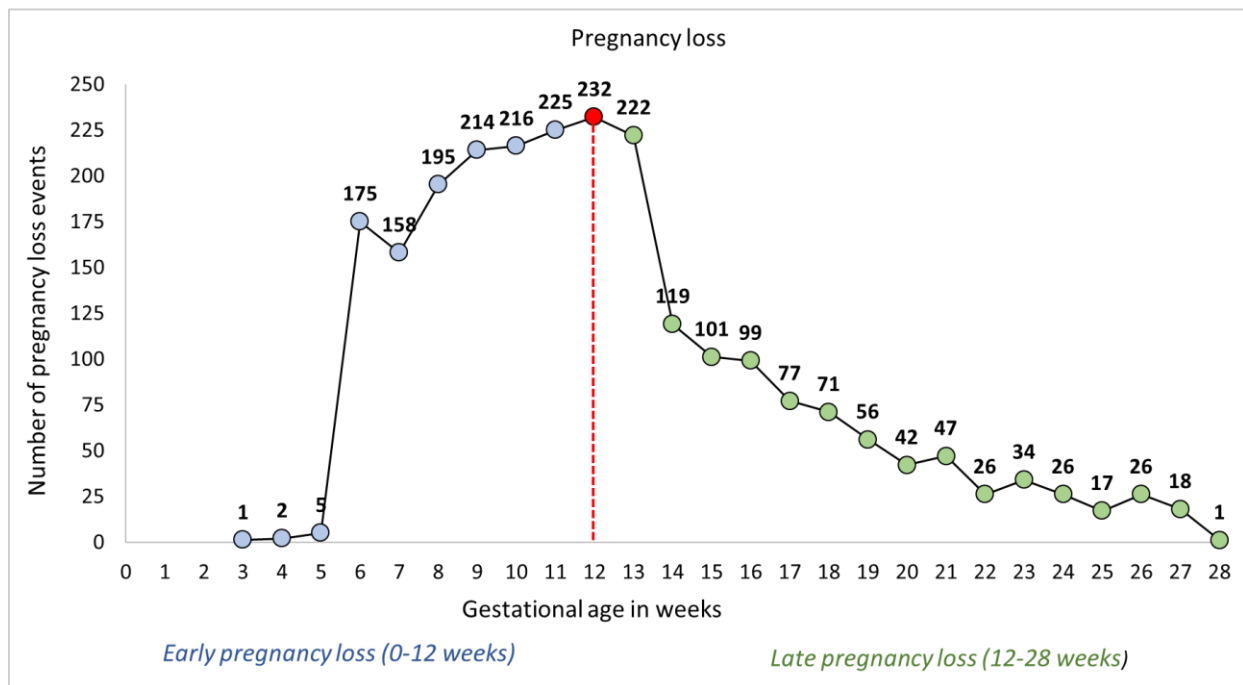
Figure 8 presents the median duration with the IQR between LMP and the pregnancy loss dates. The median duration between LMP and pregnancy loss date was 84 days (IQR 42 days). It was 68 (IQR 23) for early pregnancy loss and 115 (IQR 40) for late pregnancy loss.

Figure 8: Median duration between LMP and pregnancy loss in days
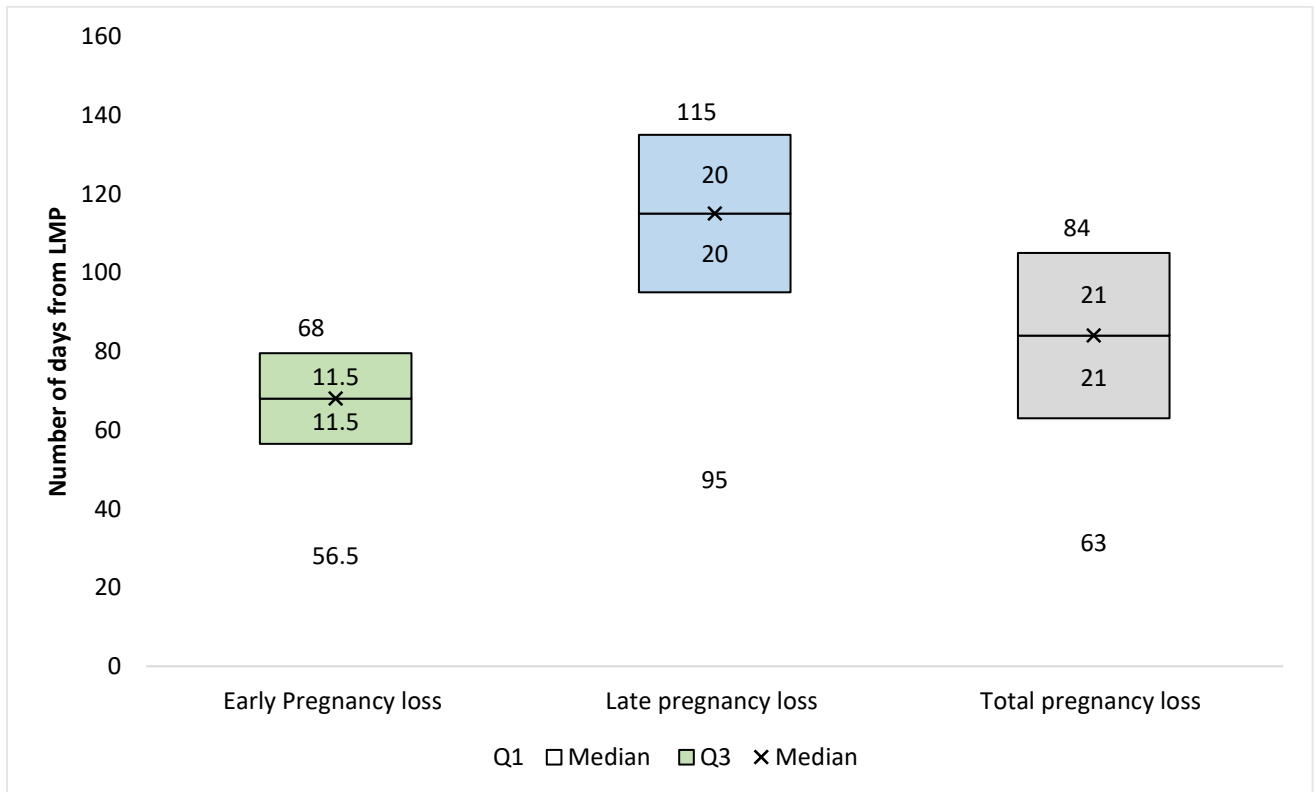
Figure 9 illustrates the proportion of pregnancy loss, early pregnancy loss and late pregnancy loss by LMP calendar years. The proportion of pregnancy loss was 11.6% (95% CI 10, 12) in 2018, 12.5 % (95% CI 11, 13) in 2019, 10.2% (95% CI 9, 11) in 2020 and 12.5% (95% CI 11, 13) in 2021. We did not observe any statistically significant difference among these proportions across the calendar years. Similarly, the proportions of early and late pregnancy loss did not differ substantially (Statistically not significant) across these years.

Figure 9: proportion of pregnancy loss by LMP calendar years, presented in percentages with 95% confidence intervals
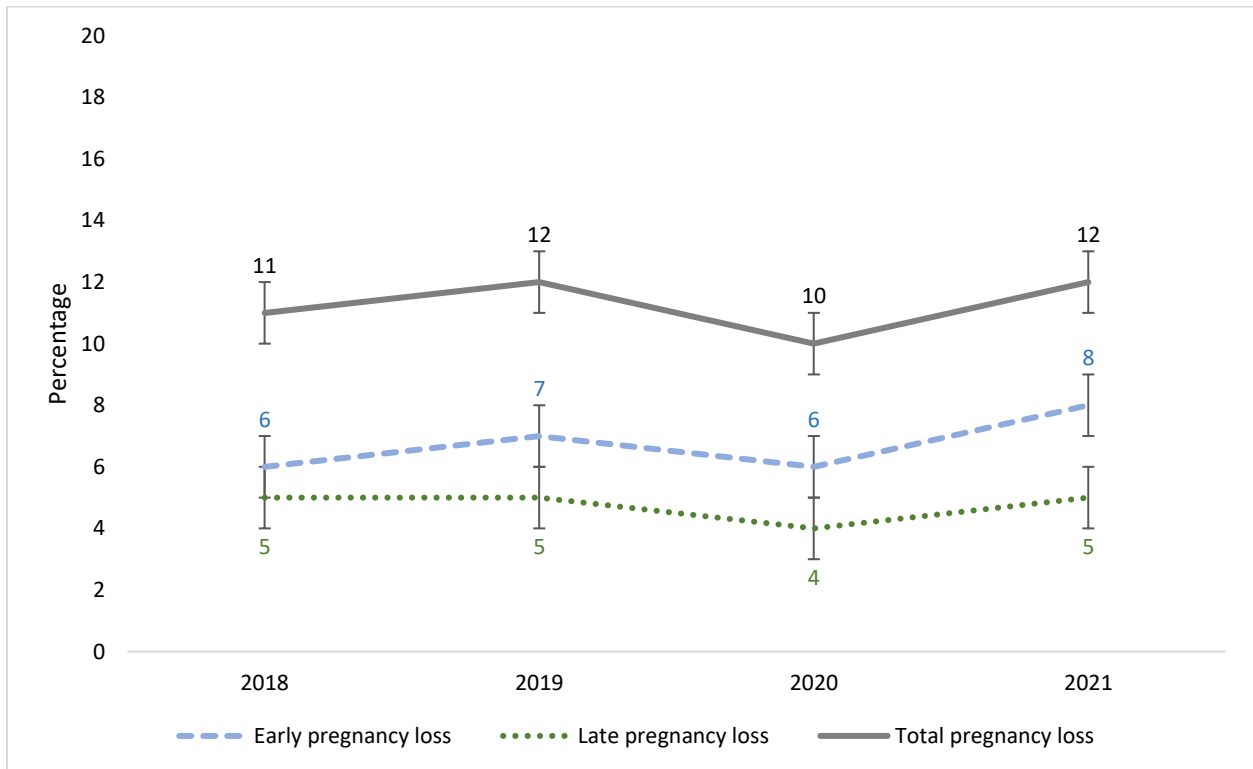
Table 3 presents the proportion of different types of pregnancy losses by background characteristics. The proportion of pregnancy loss was 11.1% (95% CI 11, 12) among women aged <20 years. However, it was 16.1% (95% CI 15,17) among pregnant women aged ≥ 30 years. The proportion of pregnancy loss was 5.2% (95% CI 5, 6) among women who were pregnant for the first time. It was 24.1% (95% CI 23, 25) among women who were pregnant for the 4th or more times. Also, the proportion of pregnancy loss was higher among women who have a history of pregnancy loss (18%) and those did not have a previous history of pregnancy loss (11%).

Characteristics		Early pregnancy loss		Late pregnancy loss		Total pregnancy loss	
		%	95% CI	%	95% CI	%	95% CI
Age of woman	<20	6.7%	6, 7	4.4%	4, 5	11.1%	11,12
	20-24	5.5%	5, 6	3.8%	3, 4	9.3%	8, 10
	25-29	6.3%	6, 7	4.5%	4, 5	10.8%	10,11
	30 and above	9.4%	8,10	6.7%	6,7	16.1%	15, 17
Education of the woman	No education	11.0%	10, 12	7.1%	6,8	18.1%	17, 19
	Primary incomplete	7.6%	7,8	5.9%	5,7	13.5%	13, 14
	Primary complete	6.6%	6, 7	5.8%	5,6	12.3%	11, 13
	Secondary incomplete	6.7%	6, 7	4.8%	4,5	11.4%	11, 12
	Secondary complete or higher	6.2%	6,7	3.5%	2,4	9.6%	8, 10
Profession of woman	Not involved in income generating activity	6.6%	6, 7	4.6%	4,5	11.2%	10, 12
	Involved in income generating activity	9.2%	8,10	5.8%	5, 7	15.0%	14, 16
Pregnancy order	1	3.2%	2, 4	2.0%	1,3	5.2%	5, 6
	2	6.6%	6, 7	4.5%	4, 5	11.1%	10, 12
	3	9.3%	8,10	6.5%	5, 7	15.8%	15, 17
	>=4	13.9%	13, 15	10.2%	9, 11	24.1%	23, 25
History of pregnancy loss	No	6.0%	5, 7	5.0%	4, 5	11.0%	11, 12
	Yes	11%	10, 12	8%	7, 8	18%	17, 18
Profession of Husband	Not involved in income generating activity	9.6%	8,10	3.6%	3,4	13.1%	12, 14
	Involved in income generating activity	6.9%	6,8	4.9%	4,6	11.7%	11, 13
	missing						
Age of Husband/Partner	<25	6.2%	5,7	4.1%	4,5	10.3%	9, 11
	25-29	6.0%	5,7	4.3%	4,5	10.3%	9,11
	30-34	6.3%	6, 7	4.6%	4,5	10.9%	10, 12
	35-39	7.4%	6,8	4.8%	4,5	12.2%	11, 13
	40 and above	10.5%	9,11	7.8%	7,8	18.3%	17, 19
Education of the husband/partner	No education	7.6%	6,8	6.3%	6,7	13.9%	13, 15
	Primary incomplete	6.6%	6, 7	4.9%	4,5	11.5%	11, 12
	Primary complete	6.5%	6, 7	4.7%	4,5	11.2%	10, 12
	Secondary incomplete	7.2%	6, 7	4.7%	4,5	12.0%	11, 13
	Secondary complete or higher	6.6%	6, 7	3.9%	4,4	10.6%	9, 11
Wealth quintile	Lowest	6.5%	6, 7	4.7%	4,5	11.1%	10, 12
	Second	7.2%	6,8	5.0%	4,5	12.1%	11, 13
	Middle	6.4%	6, 7	4.4%	4,5	10.8%	9, 12
	Fourth	6.5%	6, 7	4.9%	4,6	11.3%	10, 12
	Highest	7.3%	6,8	4.3%	4,5	11.6%	11, 12
Profession of Husband	Not involved in income generating activity	9.6%	8,10	3.6%	3,4	13.1%	12, 14
	Involved in income generating activity	6.9%	6,8	4.9%	4,6	11.7%	11, 13
	missing						
Overall		6.7%	6,7	4.7%	4,5	11.4%	11, 12

Table 3 Proportion of pregnancy loss by background characteristics, presented in percentages

Table 4 presents the relationship between background characteristics and pregnancy loss, presented in odds ratio and adjusted odds ratio with 95% confidence interval. The odds of experiencing a pregnancy loss event was 2.19 times (p=0.02) among pregnant women aged ≥30 years than the odds among pregnant women aged <20 years. The odds of experiencing a pregnancy loss event was 0.79 times (p=0.04) among pregnant women who had primary incomplete level of education than that of pregnant women with no education. The risk of pregnancy loss was higher among women who were pregnant for the 3rd (AOR 2.79, p=0.001) or the 4th or more (AOR 6.22, p=0.001) time than those who were pregnant for the first time .

Characteristics		Pregnancy loss					
		OR	p-value	CI	AOR	p-value	CI
Age of woman	<20	ref	ref	ref	ref	ref	ref
	20-24	0.81	0.06	.69,1.02	0.78	0.1	1.1
	25-29	0.97	0.67	.8,1.17	1.08	0.19	.68,.70
	30 and above	1.53	0.0003	1.33,1.76	2.19	0.02	1.16, 4.12
Age of Husband/Partner	<25	ref	ref	ref	ref	ref	ref
	25-29	1.01	0.97	.8, 1.16	0.8	0.1	.72,1.06
	30-34	1.06	0.24	.95, 1.2	0.96	0.75	.71,1.29
	35-39	1.2	0.08	.94, 1.53	1	0.99	.53,1.88
	>=40	1.94	0.0002	1.56, 2.41	1.38	0.32	.66,2.88
Education of the woman	No education	ref	ref	ref	ref	ref	ref
	Primary incomplete	0.71	0.02	.56, .91	0.79	0.04	.63, .99
	Primary complete	0.63	0.03	.43, .92	0.75	0.1	.49, 1.14
	Secondary incomplete	0.59	0.001	.47, .73	0.79	0.07	.61, 1.03
	Secondary complete or higher	0.48	0.0006	.37, .63	0.98	0.9	.7, 1.38
Education of the husband/partner	No education	ref	ref	ref	ref	ref	ref
	Primary incomplete	0.83	0.008	.74, .93	0.99	0.9	.84, 1.17
	Primary complete	0.79	0.0008	.71, .89	1	0.9	.89, 1.13
	Secondary incomplete	0.85	0.03	.73, .99	1.23	0.06	.98, 1.55
	Secondary complete or higher	0.74	0.0041	.62, .88	1.24	0.04	1, 1.54
Wealth quintile	Lowest	ref	ref	ref	ref	ref	ref
	Second	1.11	0.17	.96, 1.28	1.11	0.23	.92,1.35
	Middle	0.95	0.63	.8, 1.13	1.06	0.44	.89,1.28
	Fourth	1.01	0.81	.78, 1.30	1.14	0.22	.9,1.44
	Highest	1.02	0.62	.78, 1.34	1.2	0.1	.95,1.52
Pregnancy order	1	ref	ref	ref	ref	ref	ref
	2	2.26	0	2.02, 2.52	0.95	0.76	.63, 1.42
	3	3,38	0	2.89, 3.96	2.79	0.0013	1.79, 4.35
	>=4	5.73	0	4.79, 6.87	6.22	0.0001	3.72, 10.4
Profession of woman	Not involved in income generating activity	ref	ref	ref	ref	ref	ref
	Involved in income generating activity	1.41	0.02	1.06, 1.88	1.13	0.3	.82, 1.55
Profession of Husband	Not involved in income generating activity	ref	ref	ref	ref	ref	ref
	Involved in income generating activity	0.83	0.2	.65, 1.05	0.75	0.09	.53,1.06

Table 4: Relationship between pregnancy loss and background characteristics, presented in Odds Ratio and Adjusted Odds Ratio with 95% confidence intervals

Previous history of pregnancy loss was significantly (AOR 1.71, p=0.0018) associated with subsequent pregnancy losses after adjusting for age, education and profession of the woman as shown below in **Figure 10.**

Figure 10: Relationship between pregnancy loss and previous history of pregnancy loss, presented in Adjusted Odds Ratio with 95% confidence intervals
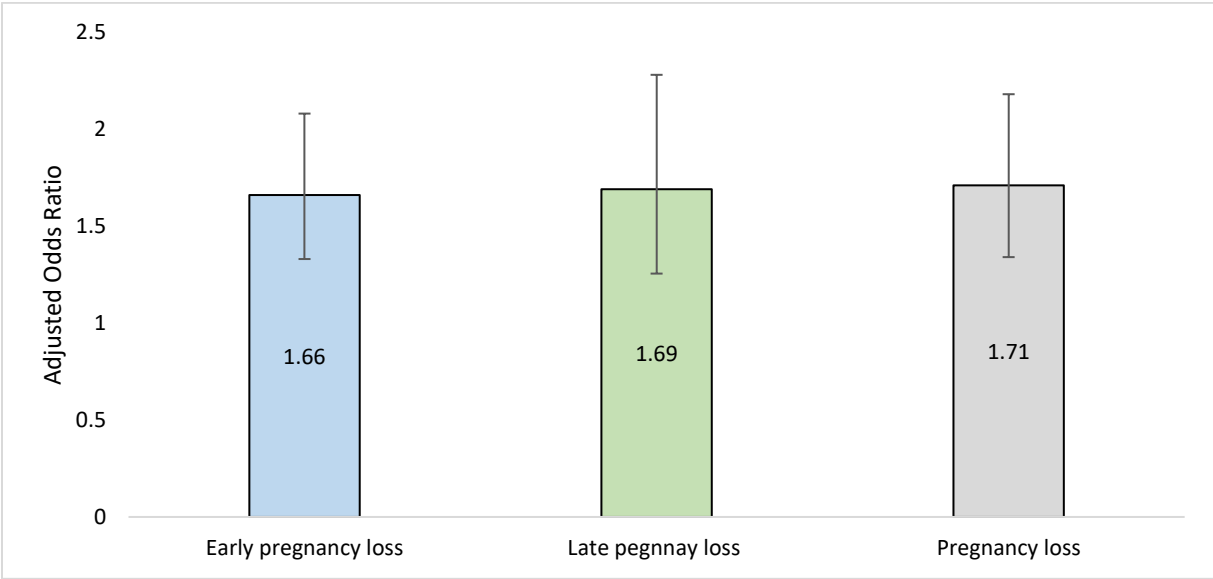
Table 5 presents the relationship between spontaneous abortion and background characteristics among women with LMP between September and December 2021 (N=1472). The risk of pregnancy loss was higher among women who were pregnant for the 4th or more (AOR 4.39, p=0.04) time than those who were pregnant for the first time .

Characteristics		N	%	95% CI		OR	p	CI	AOR	p	CI
				LL	UL						
Age of woman	<20	338	16.57	12.7	20.9	ref	ref	ref	ref	ref	ref
	20-24	394	10.15	7.3	13.5	0.57	0.07	.30, 1.09	0.45	0.11	.15, 1.32
	25-29	317	12.3	8.9	16.4	0.71	0.15	.42, 1.18	0.38	0.08	.12, 1.17
	30 and above	292	11.99	8.5	16.2	0.69	0.007	.54,.87	0.21	0.09	.03, 1.43
Education of the woman	No education	35	8.57	7	20.9	ref	ref	ref	ref	ref	ref
	Primary incomplete	107	13.08	6	18	1.61	0.5	.28,9.17	1.88	0.45	.27, 13.15
	Primary complete	126	11.11	9	14	1.33	0.7	.2, 8.88	1.38	0.7	.19, 9.85
	Secondary incomplete	789	11.66	8	15	1.41	0.6	.2,7.68	1.36	0.7	.21, 8.94
	Secondary complete or higher	415	11.33	8	18	1.36	0.6	.22,8.28	1.29	0.7	.20, 8.36
Pregnancy order	1	718	10.31	8.1	12.7	ref	ref	ref	ref	ref	ref
	2	408	13.48	10.3	17.2	1.36	0.09	.94,1.96	2.44	0.04	1.02, 5.84
	3	205	8.78	5.2	13.5	0.84	0.7	.29,2.39	1.82	0.4	.29, 11.46
	>=4	141	16.31	10.6	23.4	1.7	0.05	.99,2.90	4.39	0.04	1.06, 18.14
Profession of woman	Not involved in income generating activity	1,417	11.64	10	13.4	ref	ref	ref	ref	ref	ref
	Involved in income generating activity	55	9.09	3	19.9	0.76	0.6	.24,2.44	0.93	0.89	.23, 3.67
Age of the husband	<25	301	14.62	10.8	19.1	ref	ref	ref	ref	ref	ref
	25-29	292	9.59	6.4	13.5	0.62	0.08	.35, 1.08	0.63	0.04	.40, .98
	30-34	332	11.75	8.4	15.7	0.78	0.2	.48,1.25	0.84	0.45	.48, 1.45
	35-39	245	7.35	4	11.3	0.46	0.06	.20,1.05	0.5	0.19	.16, 1.58
	>=40	171	18.64	13.1	25.3	1.34	0.29	.72,2.5	1.62	0.47	.35, 7.46
Education of the husband/partner	No education	178	12.36	8	18	ref	ref	ref	ref	ref	ref
	Primary incomplete	277	6.14	3	9	0.46	0.09	.18,1.17	0.45	0.16	.13, 1.54
	Primary complete	188	13.3	8	19	1.09	0.75	.59,2	1.18	0.54	.19, 9.85
	Secondary incomplete	388	12.11	9	15.7	0.98	0.91	.6,1.6	1.02	0.95	.21, 8.94
	Secondary complete or higher	310	16.19	12.1	20.7	1.37	0.37	.62,3.05	1.52	0.44	.2, 8.36

						OR	p	95% CI	AOR	p	95% CI
Profession of Husband	Not involved in income generating activity	41	12.2	4.1	26.2	ref	ref	ref	ref	ref	ref
	Involved in income generating activity	1,300	12.02	10.2	13.9	0.98	0.96	.37,2.62	1.21	0.6	.46, 3.2
Wealth	Lowest	250	9.2	5.9	13.4	ref	ref	ref	ref	ref	ref
	Second	275	9.09	5.9	13.4	0.99	0.9	.52,1.89	0.9	0.7	.45, 1.79
	Middle	314	13.06	8.8	16	1.48	0.2	.68,3.23	1.38	0.4	.56, 3.41
	Fourth	346	12.14	9.8	18.1	1.36	0.3	.67,2.76	1.32	0.4	.61, 2.87
	Highest	287	13.59	8.1	12.7	1.55	0.24	.68,3.53	1.47	0.3	.58, 3.75

Table 5 Relationship between spontaneous abortion and background characteristics, among women with LMP between September and December 2021 (N=1472), presented in Odds Ratio and Adjusted Odds Ratio with 95% confidence intervals

We also identified that spontaneous pregnancy loss is strongly associated with the history of having a previous pregnancy loss (AOR 2.35, 95% CI 1.36,4.04, p=0.0085) (based on a separate logistic regression model).

Chapter 4
Discussion

DISCUSSION

The definitions of pregnancy loss vary and due to this variation, it can be difficult to compare the scientific results from different studies (15). In our study we found that the proportion of pregnancy loss is 11.4%. Here, we have considered pregnancy loss as both early pregnancy loss (up to 12 weeks of gestation) and late pregnancy loss (28 weeks of gestation). All of the pregnancy losses considered are occurring before the 28th week of gestation (which is the age of viability in Bangladesh). They include miscarriage/ spontaneous abortion as well as menstruation regulation and induced abortions. A systematic review of nine studies consisting of 463874 pregnancies, found that the pooled risk of miscarriage was 15.3 % (95%CI 12.5-18.7) of all recognized pregnancies (1). In Bangladesh the proportion of miscarriage is not very well known. A study conducted in 2014 revealed that, the estimated abortion rate in Bangladesh is around 29 abortions per 1000 women of reproductive age (16). However, there is no one estimate explaining the overall burden of pregnancy loss.

We also found that the proportion of early pregnancy loss (1st trimester/less than 12 weeks) is 6.7% and 59% of the pregnancy losses occurred before the 12th week of gestation concluding that the risk of pregnancy loss is highest in 12 gestational weeks. As the gestational age advances, the risk of pregnancy loss due or miscarriage/spontaneous abortion decreases (17). Which is also evident in our study however, other studies have shown that after 8 weeks of gestation the risk of miscarriage decreases substantially (1) and in our study after 13th gestational week the number of pregnancy loss events have substantially dropped and only 5% of pregnancy loss events occurred after 22 weeks of gestation. A number of risk factors contribute to early pregnancy loss occurring as a result of miscarriage/spontaneous abortion. These can be due to a combination of factors, including chromosomal abnormalities in the developing fetus and issues with implantation of the fertilized egg in the uterus or dual factors such as a high-risk pregnancy and previous history of pregnancy loss (17). Additionally, hormonal and structural issues in the mother can also contribute to an increased risk of early pregnancy loss. Biological factors that can contribute to early pregnancy loss can be embryonic chromosomal errors that have been found to occur in 60% of miscarriages. Among these, autosomal trisomy is the most frequently found abnormality (18).

Anatomical factors in the pregnant woman, such as incompetent cervix, uterine anomalies or maternal illness can also contribute to early pregnancy loss (19).

In addition, there are many demographic, lifestyle, clinical and environmental risk factors that contribute to pregnancy loss. Our study reports that ***advancing maternal age***, their ***education*** and a ***previous history of pregnancy loss*** were associated with pregnancy loss. ***Advancing maternal age*** is associated with an increased risk of miscarriage/spontaneous abortion. According to a Norwegian study, the risk of miscarriage was lowest for women between the ages of 25 and 29 (10%) and rose quickly after that, reaching 53% for those over the age of 45 (5). Another study revealed that in spite of prior miscarriages, parity, or calendar period, high maternal age constituted a major risk factor for miscarriage/spontaneous abortion. With rising maternal age, the probability of an ectopic pregnancy and stillbirth also increased. Regardless of reproductive history, fetal loss is more common in women in their late 30s or later and therefore it is recommended that planning and counseling for pregnancy should take this into account (7). Furthermore, women who delay childbearing may also have other risk factors for miscarriage, such as smoking, alcohol consumption, and obesity, which can further increase the risk of miscarriage. It is important to note that while the risk of miscarriage increases with maternal age, majority older women do experience healthy pregnancies. To assess any possible risks and manage any complications that may occur during pregnancy, it is crucial for women to receive counseling and recommended antenatal care. A study conducted in Bangladesh revealed that the prevalence of MR also increased with increasing age of women, where highest prevalence in older age group (30+ years) was 15.6% (95% CI: 14.0– 17.2%) (20) .

In women who have a ***previous history of pregnancy loss***, the odds of experiencing an early pregnancy loss event is 1.66 times (p=0.0015) than the odds among pregnant women with no history of pregnancy loss and a systematic review of nine studies consisting of 4638974 pregnancies reveals that risk of miscarriage is lowest in women with no history of miscarriage (11%), and then increases by about 10% for each additional miscarriage, reaching 42% in women with three or more previous miscarriages (1). We did not have information regarding the number of previous pregnancy loss. Therefore, we could not check potential dose-response relationship of previous pregnancy loss on subsequent pregnancy loss.

In terms of *education*, our study found that women with who have reached the secondary education level were less likely to have a pregnancy loss. This could be due to their awareness on the danger signs that may occur during pregnancy and better lifestyle overall. It's also important to mention that education level is not the only factor that determines the risk of miscarriage, factors such as age, health status, lifestyle, and access to healthcare also play a role in determining the risk of miscarriage and more research is needed to fully understand the underlying mechanisms of this association and to confirm these findings. On the contrary an association was found with paternal education and pregnancy loss (AOR 1.42, p=0.04). It is possible that more educated men in developing countries may have a better understanding of the economic burden of having more children, and as a result, may influence women to consider abortions. Education can play a crucial role in increasing awareness and understanding of the economic and social consequences of having many children, as well as the availability of family planning methods. However, it is important to note that men's education level is not the only factor that determines their support for family planning. Cultural and societal norms, as well as access to information and services, also play a significant role in shaping men's attitudes and behaviors towards family planning and abortion.

The *impact of COVID-19* on miscarriage is an area of ongoing research and there is currently limited data available. In our study we did not find any significant effect of Covid-19 on the proportion of pregnancy loss. Also, another systematic review of 17 studies found that the overall miscarriage in pregnant women with COVID-19 was 15.3 % (95 % CI 10.94–20.59) and 23.1 (95 % CI 13.17–34.95) using fixed and random effect models, respectively. Based on the data in the current literature, the miscarriage rate (<22 weeks) in women with Covid-19 infection is in the range of normal population (21). However, in this study the women had Covid-19 and out study it is not confirmed if the woman had Covid-19. On the contrary, some studies have suggested that pregnant women with COVID-19 may be at an increased risk of miscarriage (22) and it has also been found that the proportion of women seeking abortion services due to social factors during COVID-19 lockdown was significantly higher than that of the pre-COVID-19 sample (1349/1700[79.4%] vs 1275/1999[63.8%]; P < 0.001) (23).

In Bangladesh, the majority of pregnant women come into **contact with ANC** (Antenatal Care) services during pregnancy. According to BDHS 2017, the coverage of at least one ANC from a medically trained provider was 82% in Bangladesh (24). However, the coverage of 4 plus ANC was still relatively low as it was 47% in 2017-18 (24). This shows that there is still a gap in providing comprehensive ANC services to pregnant women, and further efforts are needed to increase the coverage of adequate ANC and improve the quality of the services provided during the ANC visits. Also, counseling on miscarriage and spontaneous abortion together with high-risk pregnancy is important during the first trimester as this is the time when the risk of miscarriage is highest. By providing counseling during the first trimester, healthcare providers can help women to understand the potential risks and causes of miscarriage, as well as the danger signs to look out for. Additionally, counseling on high-risk pregnancy during the first trimester can help to identify any potential risk factors, such as a history of miscarriage, age, chronic health conditions, and lifestyle factors. By identifying these risks early on, healthcare providers can develop a management plan to reduce the risk of complications and improve maternal and fetal outcomes. In addition, counseling on high-risk pregnancy can also help women to understand the importance of regular prenatal care, including the recommended number of ANC visits and what to expect during these visits. This can help women make informed decisions about their pregnancy.

The proportion of spontaneous pregnancy loss among all pregnancy loss is high and we have also found in our study that as the pregnancy order increases, the risk of miscarriage increases. It signifies, it was unwanted pregnancy loss and interventions should be targeted towards this. The effects of a miscarriage can be psychological, such as a rise in the risk of anxiety, sadness, post-traumatic stress disorder, and suicide, as well as physical, such as bleeding or infection. Due to a lack of knowledge about the reasons of miscarriage, couples may feel guilty and place the responsibility on themselves. We also want to emphasize how crucial it is to recognize high-risk pregnancies and receive the proper couple counseling.

STRENGTHS AND LIMITATIONS:

I conducted secondary analysis with data from icddr,b's Baliakandi HHDS site. icddr,b has more than 50 years of experience of conducting HDSS in multiple regions of Bangladesh. Therefore,

the quality of demographic data from the Baliakandi HHDS site was high. In addition, Baliakandi HDSS also maintains a pregnancy surveillance system with well-trained data collectors through quarterly rounds. This has significantly improved the accuracy of LMP reporting. After identification, the outcome of each pregnancy is followed up through the surveillance system. Therefore, there is less chance of reporting and recall bias, which improves the overall validity of pregnancy loss reporting. Although using HDSS data added significant strengths to my study, I have several limitations in my study. HDSS collects minimum demographic and socio-economic data to ensure efficiency. I could not assess the effect of several biological and social risk-factors due to the unavailability of data. Moreover, Baliakandi HDSS started collecting data regarding spontaneous and induced abortion since September 2021. Therefore, we could not report the burden of spontaneous and induced abortion among all pregnant women, that we used for reporting the overall pregnancy loss burden. Also, we could not report the determinants (logistics regression model) of induced abortion due to the small sample size.

CONCLUSION AND RECOMMENDATIONS:

In rural Bangladesh the burden of pregnancy loss in relatively high. Majority of them happen spontaneously and during the first trimester. Therefore, the maternal health program should take special initiatives for reaching out to pregnant women in the first trimester to effectively prevent and protect the pregnancy loss. Moreover, if there is a history of previous pregnancy loss, subsequent pregnancies should be considered high risk and rigorous monitoring should be insured to prevent further losses.

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