

# FREQUENCY OF SPONTANEOUS MISCARRIAGES IN EARLY PREGNANCY COMPARISON BETWEEN OBESE VERSUS NORMAL WEIGHT WOMEN

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## ABSTRACT

*Background:* Miscarriages are one of the most common complications of pregnancy, affecting approximately 15% of all pregnancies in the general population. It is suggested that obese women have greater risk of early miscarriage as compared to women with normal weight. This study was performed to compare the frequency of spontaneous miscarriages in early pregnancy in obese versus normal weight women.

*Materials and Methods:* It was a prospective cohort study, conducted at the department of Obstetrics and Gynaecology, Bahawal Victoria Hospital Bahawalpur from July 2012 to January 2013. After taking written and informed consent from the patients meeting inclusion criteria, they were divided in two groups. In group – A, patients were obese and in group – B, age – matched and gravid – matched normal weight women.

*Results:* A total of 206 patients were included in the study, 103 in each group. Mean age of patients was 22.52 years with standard deviation of 4.118 years. Nine primigravida had miscarriages and 11 multi-gravida had a miscarriage. Among these, sixteen (15.5%) patients were from group – A (obese) while 4 (3.9%) patients were group – B (normal weight) with a significant p value of 0.005.

*Conclusion:* Obesity is associated with a higher spontaneous miscarriage in early pregnancy in women who conceive spontaneously and this is a sound reason for advocating weight reduction in overweight and obese women who are planning to have more children.

*Keywords:* Obesity, pregnancy, miscarriage.

## INTRODUCTION

Miscarriages are the most common complication of pregnancy, affecting approximately 15% of all clinically recognized pregnancies in the general population. The exact frequency of miscarriages is, however, unknown as miscarriages frequently occur before the woman is aware of her pregnancy. It is estimated that more pregnancies are lost spontaneously than are actually carried to term.<sup>1</sup> Most of the miscarriages are sporadic and non-recurrent, and are often caused by chromosomal abnormalities in the fetus. Recurrent miscarriage (RM), defined as three consecutive pregnancy failures, is estimated to affect 1% of all couples trying to conceive.<sup>2</sup>

There are numerous factors that may cause miscarriages, but the underlying problem often remains undetected. Although much work has been done to identify the underlying mechanisms, the cause of miscarriage can be identified in only 50% of cases. The known causes of RM include maternal age, history of miscarriage, infertility, chromosomal and metabolic abnormalities, uterine anomalies, obesity and immunologic factors. Even though RM is a heterogeneous condition and the progress in identifying causative factors has been slow, the repetitive pregnancy losses in some couples and the high percentage of unexplained

RM indicate that there are specific underlying causes yet to be identified.<sup>3</sup>

Earlier reports suggested that obese women have an increased risk of early miscarriage both after spontaneous conception and infertility treatment. The body mass index (BMI), also known as the Quetelet index, is used far more commonly for measuring obesity. BMI is closely correlated with the degree of body fat in most settings. BMI between 18.5 – 24.9 kg/m<sup>2</sup> is regarded as normal whereas BMI between 26 – 29.9 kg/m<sup>2</sup>, 30 – 34.9 kg/m<sup>2</sup> and 35 – 40 kg/m<sup>2</sup> are considered as overweight, obese and morbidly obese respectively.<sup>4,5</sup>

Overweight women are known to be at a higher risk of menstrual dysfunction, anovulation and early pregnancy loss, possibly due to altered secretion of pulsatile gonadotrophin releasing hormone, resulting in altered sex hormone binding globulin, ovarian and adrenal androgens and Luteinizing hormone. The excess risk of miscarriage in the overweight and obese population is independent of embryonic aneuploidy. The increased risk may be because obese women often have polycystic ovarian syndrome (PCOS) or isolated insulin resistance, which have been associated with a higher frequency of early pregnancy loss. An unfavorable hormonal environment resulting in poorer endometrial receptivity is considered to play a role.<sup>6</sup>

**MATERIALS AND METHODS**

**Study Design:** Prospective cohort study.

**Setting:** This study was conducted at the department of Obstetrics and Gynaecology, Bahawal Victoria Hospital / Quaid-i-Azam Medical College Bahawalpur.

**Duration of Study:** From Jul. 2012 to Jan. 2013.

**Sample Size:** Sample size was calculated as 206 patients.

A total of 103 patients were obese pregnant women (Group – A) served as exposed cases and 103 patients were age – matched and parity matched normal weight pregnant women (Group – B) who served as non-exposed.

**Sampling Technique:** Non-probability consecutive sampling.

**Inclusion Criteria**

1. Age between 16 years and 30 years.
2. Primigravida or multigravida obese women having pregnancy in first trimester, presenting to the obstetrics and gynaecology OPD served as exposed group.
3. Age – matched and primigravida or multigravida matched normal weight women having pregnancy in first trimester, presenting to the obstetrics and gynecology OPD served as non-exposed group.

**Exclusion Criteria**

1. Diabetes mellitus.

2. Hypertension.
3. Grand multiparity.
4. Patients with cervical shortening.
5. Cervical fibroid.

**DATA COLLECTION PROCEDURE**

The study was approved from hospital ethics committee. Only miscarriages occurring after 6 weeks of gestation were recorded to avoid confusion with early pregnancy loss. A written and informed consent was taken from the patients prior to participation in the study. Pregnancy was confirmed by measuring serum BHCG (level of  $\geq 5$  mIU/ml taken as positive pregnancy). For final outcome, both exposed and non-exposed were asked to report back to researchers in OPD at 12 week of pregnancy. They were examined for spontaneous miscarriage (history of vaginal bleeding and abdominal pain) and viability of pregnancy was confirmed on ultrasonography of pelvis which was performed by senior radiologist. A proforma was used to collect the pertinent information from every patient. Data was entered and analysed with SPSS version 15.0. Frequency of miscarriages in early pregnancies was compared in two groups by chi square test. P-value of less than 0.05 was taken as significant. Tables and graphs were used to present data.

Effect modifiers were controlled by stratification of data with reference to age, gravida and socioeconomic status to see above mentioned outcome. Chi square test was applied to see the effect of these on outcome variables. P-value of less than 0.05 was taken as significant.

Table 1: *Obese and normal weight patients in different age group.*

Age groups	Study groups		Total	P-value
	Group – A (Obese)	Group – B (Normal wt.)		
16 – 20 years	35 (46%)	41 (54%)	76 (100%)	0.971
21 – 25 years	44 (51%)	42 (49%)	86 (100%)	
26 – 30 years	24 (50%)	20 (50%)	44 (100%)	
Total	103 (54%)	103 (46%)	206 (100%)	

Table 2: *Primigravida and multigravida in obese and normal weight patients.*

Gravidity	Study Groups		Total	P-value
	Group – A (Obese)	Group – B (Normal wt.)		
Primigravida	51 (48%)	55 (52%)	106 (100%)	1.00
Multigravida	52 (52%)	48 (48%)	100 (100%)	
Total	103 (50%)	103 (50%)	206 (100%)	

**OPERATIONAL DEFINITIONS**

**Spontaneous miscarriage in early pregnancy:** The miscarriage that occurred spontaneously between 6 – 12 weeks of pregnancy was termed as spontaneous miscarriage in early pregnancy. It was diagnosed by history of vaginal bleeding and abdominal pain and was confirmed on ultrasonography of pelvis.

**RESULTS**

The mean age of patients in group – A was  $22.52 \pm 4.12$  (16 – 30) years. According to age stratification, 76 patients were in 16 – 20 years age group, 86 patients were in 21 – 25 years of age group and 44 patients were in 26 – 30 years of age group as shown in Table 1. It is clear from the table that both study groups were age – matched (p value = 0.971).

Out of 206 patients, 106 (51%) patients were primigravida and 100 (49%) patients were multigravida. In study group – A and B, almost equal proportion of primi- and multigravid women was observed as shown in Table 2.

In total, 20 (9.71%) patients had miscarriages out of which 16 (15.5%) patients were from group A while 4 (3.9%) patients were from group – B as shown in Table 3. In 16 – 20 years of age group, 4 patients had miscarriages and 72 patients had no miscarriage, in 21 – 25 years of age group, 12 patients had miscarriages while 72 patients had no miscarriage, in 26 – 30 years of age group, 4 patients had mis carriages while 40 patients had no miscarriages as shown in Table 4.

Nine primigravida and 11 multigravida had miscarriage while 97 patients in primigravida had no miscarriages and 89 patients in multigravida had no miscarriages as shown in Figure 1.

**DISCUSSION**

Maternal obesity, based on a Body Mass Index (BMI > 29.9 kg/m<sup>2</sup>),

Table 3: Comparison of miscarriages in early pregnancy in study groups.

Study Group	Miscarriages		Total	P-value
	Yes	No		
Group – A (obese)	16 (15.5%)	87 (84.5%)	103 (100%)	0.005
Group – B (normal wt.)	4 (3.9%)	99 (96.1%)	103 (100%)	
Total	20 (9.7%)	186 (90.3%)	206 (100%)	

Table 4: Miscarriages in early pregnancy in different age groups.

Age Group of Patients	Miscarriages		Total	P-value
	Yes	No		
16 – 20 years of age group	04 (5.3%)	72 (94.7%)	76 (100%)	0.174
21 – 25 years of age group	12 (14.0%)	74 (86.0%)	86 (100%)	
26 – 30 years of age group	04 (9.1%)	40 (90.9%)	44 (100%)	
Total	20 (9.7%)	186 (90.3%)	206 (100%)	

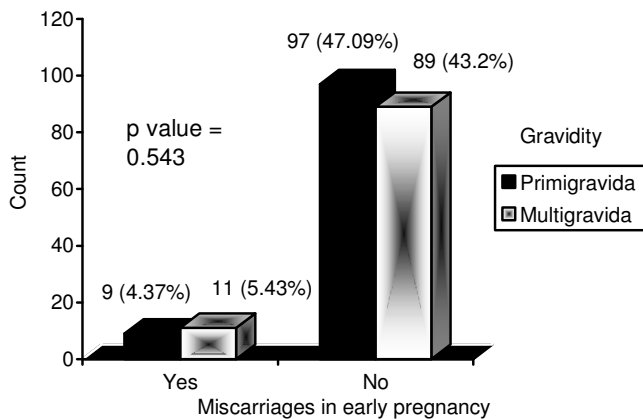


Fig. 1: Frequency of miscarriages in different gravida.

has emerged as an important risk factor in modern obstetrics worldwide and has been seen to be associated with an increase in pregnancy complications such as miscarriages in early pregnancy, gestational diabetes mellitus (GDM), preeclampsia, congenital malformations and fetal growth abnormalities, resulting in an increase in obstetric interventions such as caesarean section and induction of labour.<sup>7</sup> Besides the coexistence of pre-existing diabetes mellitus and chronic hypertension, obese women are more likely to have pregnancy – induced hypertension, gestational diabetes, thromboembolism, macrosomia, and spontaneous intrauterine demises in the latter half of pregnancy. Obese women also require instrument or Cesarean section delivery more often than average – weight women. Following Cesarean section delivery, obese women ha-

ve a higher incidence of wound infection and disruption. Obesity represents a low – grade inflammatory state that is associated with metabolic and cardiovascular complications. The rates of hypertensive diseases of pregnancy and gestational diabetes among morbidly obese women are significantly increased.<sup>8</sup>

Spontaneous miscarriage is the commonest complication of pregnancy. Earlier reports suggested that obese women have an increased risk of early miscarriage both after spontaneous conception and infertility treatment. In A large study which included 1644 obese primigravida but not multigravidas showed that obesity may increase the risk of miscarriage. In this study only historical miscarriages after six weeks gestation from previous pregnancies were recorded.<sup>9</sup>

The mean age of patients in our study was 22.52 years. In a study conducted by Lashen showed that the mean age of patients was 26.6 years.<sup>9</sup> This study also showed the frequency of miscarriages was significantly higher in obese women as compared to non-obese women. The frequency of miscarriages in obese women was 12.5% and in non-obese women it was 10.5%. These results were comparable to our study. In our study the frequency of miscarriages in obese women was 15.5% and in non-obese women it was 3.9%.

A recent meta analysis involving 16 studies concluded that obesity may increase the risk of miscarriage after spontaneous and assisted conception. Patients with a body mass index of ≥ 25 kg/m<sup>2</sup> had significantly higher odds of miscarriage, regardless of the method of conception (odds ratio, 1.67; 95% confidence interval, 1.25 – 2.25). Subgroup analysis from a limited number of studies suggested that this group of

women may also have significantly higher odds of miscarriage after oocyte donation (odds ratio, 1.52; 95% confidence interval, 1.10 – 2.09) and ovulation induction (odds ratio, 5.11; 95% confidence interval, 1.76 – 14.83). Only two of the 16 studies were prospective and both were in women who had ovulation induction.<sup>10</sup>

An other study conducted by Tuener et al. showed that the overall miscarriage rate was 2.8% (n = 33).<sup>11</sup> The mean gestational age at enrolment was 9.9 weeks. In the obese category (n = 217), the miscarriage rate was 2.3% compared with 3.3% in the overweight category (n = 329), and 2.3% in the normal BMI group (n = 621). In this study the difference of miscarriage between normal weight and obese women was not significant but the frequency of miscarriage in normal weight women was comparable to the result of our study.

A study conducted by Wang et al. showed that the overall incidence of spontaneous abortion was 20% (476 of 2349).<sup>12</sup> The effect of BMI on the risk of spontaneous abortion was significant after adjusting for several independent risk factors. Compared with the reference group (BMI 18.5 to 24.9 kg/m<sup>2</sup>), underweight women had a similar risk of spontaneous abortion, whereas there was progressive increase of risk in overweight, obese, and very obese groups (p < 0.05, p < 0.01, and p < 0.001, respectively).

Study conducted by Boots et al. showed higher miscarriage rate of 13.6% in 3800 obese versus 10.7% in 17,146 normal – BMI women (OR: 1.31; 95% confidence interval, 1.18 to 1.46).<sup>13</sup> Although the cohort was small, there was a higher prevalence of recurrent early miscarriage in obese versus normal – BMI women (0.4% versus 0.1%; OR: 3.51; 95% confidence interval, 1.03 to 12.01). In women with recurrent miscarriage, there was a higher miscarriage rate in the obese versus non-obese women (46% versus 43%; OR: 1.71; 95% confidence interval, 1.05).

Similar results were found in another study conducted by Bellver et al.,<sup>14</sup> that showed that the rates of implantation, pregnancy, miscarriage, and ongoing pregnancy were not similar among the different body mass index groups. There was a negative trend when body mass index increased. Ongoing pregnancy rates per cycle were poorer in the overweight and obese groups than in the underweight and normal groups. In addition, women under 25 kg/m<sup>2</sup> presented an ongoing pregnancy rate per cycle of 45.5%, compared with 38.3% for those with > or = 25 kg/m<sup>2</sup>.

There are many sound reasons for advocating weight reduction in overweight and obese women who are planning to be pregnant.<sup>15</sup> The problems associated with obesity, such as diabetes, hypertension, thromboembolism and coronary heart disease are well documented in the non-pregnant population, but the condition itself holds specific risks during the antepartum, intra-partum and postpartum periods.<sup>16</sup> Of particular

concern is the intra-partum period. The risk of congenital anomalies is also increased. Several studies report not only an increased incidence of neural tube defects but also an incremental increase in the upper ranges of maternal BMI. Increased risks for various other defects have been described, including heart defects and facial clefting. Diagnosing fetal anomalies prenatally remains challenging in the obese gravida, as a full anatomic survey is often incomplete or sub-optimal.

Complications such as miscarriages in early pregnancy, slow progress during labour and increased rates of caesarean section are best addressed proactively. For this reason all morbidly obese women are referred for evaluation of the pregnancy and planning of labour and delivery by an anesthetist and an obstetrician, as suggested by Saravanakumaretal.<sup>17</sup> Epidural anaesthesia during the active phase of labour is always a part of this plan.<sup>18</sup>

It is **concluded** that obesity is associated with a higher spontaneous miscarriage in early pregnancy in women who conceive spontaneously and this is a sound reason for advocating weight reduction in overweight and obese women who are planning to have children.

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