

## Evaluation of Perinatal Outcomes in Women with a History of Recurrent Consecutive Spontaneous Abortions: Retrospective Cohort Study

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Cite this paper as: Mahmoud F. Hassan, Yahia Z. Ali, Enas A. A. Abdallah, Nehal Moussa, Ahmed Sewidan, (2025) Evaluation of Perinatal Outcomes in Women with a History of Recurrent Consecutive Spontaneous Abortions: Retrospective Cohort Study. *Journal of Neonatal Surgery*, 14 (32s), 3649-3657.

### ABSTRACT

**Objective.** To assess how recurrent consecutive spontaneous abortion (RCSA) affects the mother and baby in future pregnancies.

**Materials and Methods.** A retrospective cohort study was carried out at Suez Hospital in Egypt. It examined the electronic medical records of pregnant women between the ages of 15 and 49 years who had non-anomalous singleton pregnancies. The study looked at 7,718 women, of whom 172 had a history of recurrent consecutive spontaneous abortion (defined as two or more consecutive pregnancies that ended in abortion). The outcomes for mothers and their newborns were compared for those in the RCSA group versus a control group of women who had  $\leq$  one abortion. A multivariate logistic regression analysis was carried out to adjust for possible confounding variables that could have influenced the study's results.

**Results.** Women with a history of RCSA had significantly higher risks of early-onset-preeclampsia [Adjusted odds ratio (aOR) = 3.13; 95% confidence interval (CI): 1.12–8.72], placenta-previa (aOR = 2.73; 95% CI: 1.09–6.81), placental-abruption (aOR = 3.3; 95% CI: 1.18–9.23), preterm-birth (aOR = 1.79; 95% CI: 1.1–2.91), and small-for-gestational-age infants (aOR = 1.72; 95% CI: 1.03–2.87). These associations remained significant after adjusting for potential confounders.

**Conclusion.** A history of RCSA is linked to an increased risk of adverse obstetric and neonatal outcomes, likely due to underlying placental dysfunction. Therefore, women with a history of RCSA need closer monitoring during subsequent pregnancies to optimize pregnancy outcomes.

**Keywords:** Perinatal outcomes; placenta previa; preeclampsia; preterm birth; recurrent miscarriage.

### 1. INTRODUCTION

Pregnancy loss remains a major worry in obstetric care, particularly when it happens repeatedly. Recurrent spontaneous abortion poses serious challenges not just to maternal health, but also to perinatal health [1]. Recurrent consecutive spontaneous abortion (RCSA), defined as the loss of two or more consecutive pregnancies before the point of viability, affects approximately 1–5% of women who are attempting to conceive [2]. Although most present literature concentrates on the psychological consequences and the associated risk factors of RCSA, there is an emerging necessity to delve into the issue of physiological impact during subsequent gestations [3]. Many studies have addressed the adverse maternal and perinatal outcomes in women with a history of RCSA. Research highlighted the association between RCSA history and significantly higher odds of complications such as preeclampsia, gestational diabetes mellitus (GDM), preterm birth, foetal distress, and neonatal morbidity [4-6]. Understanding the risks associated with recurrent consecutive spontaneous abortion during a subsequent pregnancy creates opportunities for improved clinical interventions aimed at improving pregnancy outcomes in such high-risk populations [7].

Despite of all these well-documented risks of RCSA, information on RCSA and its effect on perinatal outcomes in the Egyptian community is still not sufficient providing an opportunity to explore the effects of RCSA on pregnancy outcomes in a large and diverse patient cohort in the distinct demographic and healthcare setting of Egypt [8]. Gaining insight into these risks for an Egyptian cohort is vital for the configuration of clinical guidelines, the betterment of prenatal care, and the achievement of more favourable perinatal health results. The current aims to assess the perinatal outcomes of women with consecutive spontaneous abortion within Suez Hospital, Egypt.

## 2. MATERIALS AND METHODS

We conducted a retrospective cohort study using electronic records of all the pregnant women who attended the Obstetric Department of Suez Hospital in Egypt. We included all the women aged 15 to 49 years with a non-anomalous singleton pregnancy. The study received approval from the local institutional review board and ethics committee (SUEZ Med-IRB/2024-No. 37). The ethics board waived the need for patient consent since this was a retrospective study.

This study concentrated solely on the initial subsequent childbirth after a diagnosis of recurrent consecutive spontaneous abortion. In addition, to avoid the possibility of within-person correlation, we chose the first delivery record for each mother in the study. We defined a viable pregnancy as one that resulted in a birth after 24 weeks. We routinely had access to our in-house, comprehensive medical health records for births occurring at or beyond 24 weeks. We included in our study only those women who had their deliveries at our institution. We had excluded from our investigation any pregnancy that was more than a singleton, any pregnancy that resulted in a birth of a child with a major congenital anomaly, or any pregnancy for which there was missing hospital medical records data on the subject's age, socioeconomic status, obstetric history, or the gestational age and outcomes of the pregnancy.

### *Study Population*

The cohort studied consisted of two sets of women. The first set (study group) had given birth and had a history of two or more losses during pregnancy. The second set (control group) had given birth but did not have the diagnosis of recurrent pregnancy loss. We regarded the women as having recurrent pregnancy loss when they had two or more prior losses as per the guidance from the European Society of Human Reproduction and Embryology, the American Society of Reproductive Medicine, and the American College of Obstetricians and Gynecologists [1,9,10].

We obtained details from hospital medical records regarding the demographic characteristics of mothers: age, body mass index (BMI), parity, race, and residence; education; and smoking and medical history. As well, we accessed information on use of infertility treatment or assisted reproductive technologies. The methods of assisted reproductive techniques comprised of intrauterine insemination and various forms of in vitro fertilization. The medical histories of the women studied recorded chronic health problems, including hypertension, diabetes, heart disease, asthma, anaemia, hypo- or hyperthyroidism, and polycystic ovary syndrome.

### *Outcomes*

The present study assessed a set of maternal and neonatal results. Among the outcomes for mothers, they were: gestational diabetes mellitus, preeclampsia and its early onset form, anaemia, disorders of the amniotic fluid volume (low or excessive), placental abruption, placenta previa, induced labour, foetal distress, and caesarean or operative vaginal delivery. Among the outcomes for neonates, they were: birth weight, preterm birth, intrauterine foetal death (IUFD), small for gestational age (defined as birth weight < 10th percentile for gestational age), Apgar score <7 at 5 minutes, admission to neonatal ICU, and male gender.

### *Statistical Analysis*

All analyses were performed using the Statistical Package for Social Science (SPSS) version 23 for Windows (IBM Corp., Armonk, NY, USA). We used 2-tailed tests for these analyses and established our significance level at  $P < 0.05$ . The initial exploration of the data distribution used the Shapiro Wilk test to assess normality. Variables that continuously vary with a normal distribution were depicted using the mean and standard deviation; non-parametric variables were represented using the median and interquartile range; and the categorical variables were articulated as number and percentage. The categorical variable group differences were compared using the chi-squared test or Fisher's Exact test where appropriate. The continuous variable differences between groups were compared using Student's t-test, while the non-parametric group differences were assessed using the Mann-Whitney U test.

We computed the odds ratios (ORs) with 95% confidence intervals (CIs) to yield the risks of poor maternal and neonatal outcomes associated with a history of recurrent consecutive spontaneous abortion. Confounding factor adjustment was obtained via a multiple logistic regression analysis and using the stepwise method. The odds ratios reported in this study were computed as adjusted odds ratios (aORs), which provide a more accurate measure of the relationship between the key independent variables of interest and our outcomes. We included in the regression model factors that have a known or presumed association with the risk of having an RCSA and the study outcomes of interest. Factors included in the study were maternal age at delivery, BMI, parity, smoking habits, type of infertility treatment, use of assisted reproductive technology,

chronic hypertension, and pre-gestational diabetes.

### 3. RESULTS

From January 1, 2018, to December 31, 2023, there were 9,592 infants delivered at our institution, each having reached at least 24 weeks of gestation, which satisfies the minimum legal viability threshold. The study included a total of 7,718 women (80.5%) of these individuals [Figure 1]. Within this group of women who qualified for the study, 172 (2.2%) had a past history of two or more consecutive spontaneous abortions. We compared maternal and neonatal outcomes between women experiencing recurrent abortion and the 7,546 women who had either one or no prior abortion.

The demographic and medical histories of the women are summarized in Table 1. In contrast to women having either one or no abortions, those with a history of recurrent consecutive spontaneous abortion tended to be older and had an average age of 32.6 years ( $\pm 5.2$ ) compared to 31.8 years ( $\pm 4.7$ ) for the control group ( $P = 0.0277$ ). The average BMI for women who had recurrent abortion was higher at 30.9 ( $\pm 11.4$ ), compared to 29.2 ( $\pm 10.9$ ), for the other group ( $P = 0.0434$ ). The data revealed that patients with recurrent abortion had a higher chance of being overweight or obese ( $P = 0.0371$ ), having a lower parity ( $P = 0.034$ ), undergoing infertility treatment (18.6% vs. 9%;  $P = 0.0001$ ), and utilizing assisted reproductive techniques (5.23% vs. 2.44%;  $P = 0.0203$ ). The RCSA group had a greater history of chronic hypertension (4.65% vs. 2.16%;  $P = 0.0282$ ) and pre-gestational diabetes (5.23% vs. 2.33%;  $P = 0.0139$ ) than the control group.

Table 2 presents the obstetrical and delivery results for the two groups. The rate of GDM was 6.4% in the RCSA group, while the controls had a rate of 3.41% ( $p = 0.0342$ ). We determined that patients in the recurrent consecutive spontaneous abortion group had a greater incidence of early-onset preeclampsia (2.33% vs. 0.69%,  $p = 0.0357$ ), placental abruption (2.33% vs. 0.6%,  $p = 0.232$ ), and placenta previa (2.91% vs. 0.98%,  $p = 0.0311$ ). Table 3 compares the neonatal outcomes of women with a history of recurrent abortion with those of the control group. There was a significantly higher rate of preterm delivery (11.05% vs. 6.24%,  $p = 0.0106$ ) and an increased rate of small-for-gestational-age babies (9.88% vs. 5.72%,  $p = 0.0212$ ) among those in the recurrent consecutive spontaneous abortion group. However, the control group had higher rates of average birth weight ( $2.97 \pm 0.72$  kg vs.  $3.12 \pm 0.86$  kg,  $p = 0.0233$ ).

The outcomes of multivariate logistic regression analyses are shown in Table 4. These analyses assess the association between pregnancy-related RCSA and obstetric and neonatal outcomes. The association is analysed after statistically controlling for the influence of significant covariates. Recurrent consecutive spontaneous abortion had a consistent independent relationship with several adverse conditions related to pregnancy. These include: early onset preeclampsia (adjusted odds ratio [aOR] 3.13; 95% confidence interval [CI] 1.12–8.72), placental abruption (aOR 3.30; 95% CI 1.18–9.23), placenta previa (aOR 2.73; 95% CI 1.09–6.81), preterm birth (aOR 1.79; 95% CI 1.10–2.91), and small-for-gestational-age infants (aOR 1.72; 95% CI 1.03–2.87).

### 4. DISCUSSION

This retrospective study attempts to investigate the influence of having had recurrent consecutive spontaneous abortion on pregnancy and neonatal outcomes after 24 weeks. Recurrent consecutive spontaneous abortion was found in 2.2% of the subjects enrolled in the study. The study found that women with a history of RCSA have a greater chance of experiencing adverse obstetric and perinatal outcomes in a following pregnancy than do women without a similar history. Adverse outcomes encompass disorders of placental function (such as preterm birth, early-onset preeclampsia, and small-for-gestational-age outcomes), and abnormal placentation (including placenta previa and placental abruption). These associations remained in place even when we controlled for possible confounding variables.

Our findings of associations between a history of RCSA and placental dysfunction disorders support a prior study found that the partially shared pathogenesis of abortion and placental function disorders centres on the failure of early placentation [7]. Researchers have proposed that if the early stages of placental formation go completely awry, this can cause the pregnancy to not persist [11]. Nevertheless, if the failure is partial, the pregnancy might remain viable but with insufficient uterine spiral artery remodelling and a continued imbalance in angiogenic activity during the remaining process [12].

Some other studies did not show a link between having a history of recurrent abortion and the development of preeclampsia [6,13]. Indeed, previous studies did not differentiate between early-onset and late-onset preeclampsia. Preterm or early-onset preeclampsia, which occurs before 34 weeks of gestation, is thought to be caused mostly by dysfunction of the placenta. In contrast, late-onset or term preeclampsia occurs generally around 37 weeks' gestation and is considered to be due more to maternal factors. Term preeclampsia has been strongly associated with the presence of one or more maternal conditions that impair vascular health such as obesity, diabetes, and chronic hypertension [14].

Maternal circulation shows an increased level of soluble vascular endothelial growth factor receptor 1 (sFlt1) before symptom onset of preeclampsia [15]. Moreover, other studies observed elevated sFlt1 levels in serum and enhanced sFlt1 expression in chorionic villus of women with recurrent abortions [16]. Women who have had multiple abortions might have a tendency to high placental sFlt1 expression during viable pregnancies, putting them in a potential risk group for preeclampsia, stillbirth, small-for-gestational-age birth, or placental abruption [17]. Here, we differentiated early-onset preeclampsia from term

preeclampsia and found that women with a history of RCSA were likely to have a higher incidence to develop early-onset preeclampsia (aOR = 3.13), small-for-gestational-age (aOR = 1.72), placental abruption (aOR = 3.3) in the subsequent pregnancy.

Because all these aforementioned complications have been linked in previous studies to trophoblastic abnormalities and decidual invasion [5,18,19], it was hypothesized that women with RCSA may have underlying abnormal placentation [20]. In our study, women with a history of RCSA had an increased risk of placenta previa compared with women in the control group (aOR = 2.73), even when taking their CS history into account. This observation aligns well with many earlier studies [21,22]. Damage to the myometrium or endometrium can lead to problems with placentation in the next pregnancy and can cause abnormal placenta previa to occur. Therefore, the association between a history of miscarriage and these adverse obstetric outcomes could be driven partly by a common cause, perhaps originating in suboptimal endometrial repair and decidualization [3]. On the other hand, our study findings showed that a history of RCSA in currently pregnant women was associated with a greater likelihood of preterm delivery (aOR = 1.79). Similar associations were found using different RCSA definitions [6,23]. It has been suggested that both pregnancy loss and preterm delivery may be due to genital infections [4,24].

There were inconsistent reports regarding the association between GDM and recurrent abortion. While many earlier studies have found a heightened occurrence of impaired glucose tolerance (22.8%, Tulppala et al., 1993 [25]; 22.6%, Cozzolino et al., 2019 [26]), we were not able to confirm such an event in our study after adjusting for various confounding factors. Along with our data, Ali et al. demonstrated no significant difference in the rates of GDM between women with a history of an RCSA and those without such a history. The rates were 24.2% in women with a history of RCSA and 26.1% in women without a history of RCSA ( $p = 0.557$ ) [24]. Too, Jivraj et al. found that there were no differences in the rates of gestational diabetes between the RCSA and control groups [27]. For an explanation for the occasional association of GDM with RCSA, it has been reported that women with abnormal glucose metabolism before pregnancy will have an increased risk of miscarriage in the following pregnancy, which may explain the increased risk of GDM after spontaneous abortion [28,29]. Another possible explanation of the increased incidence of impaired glucose intolerance is simply a result of observational bias, i.e. with increased surveillance of women with a history of repeated pregnancy loss [24].

This study possesses many strengths. Chief among them, it employs a massive sample size of 7,718 deliveries. Besides, it adheres to standard definitions for repeat pregnancy loss and adjusts for key confounders like maternal age, body mass index, smoking, and chronic diseases. Another strength is the concentration on disorders of placental dysfunction and the clear delineation between early- and late-onset preeclampsia, which provides remarkable insights into the possible mechanisms underlying RCSA. Finally, this study considers the effects of assisted reproductive technology (ART) on RCSA and identifies and trends changes in BMI and chronic conditions, which together inform a more comprehensive understanding of RCSA and its associated risks. Notwithstanding, the research contains several limitations, such as a retrospective design, a sole-centre setting in Egypt, and an accordingly restricted generalizability. Additionally, the current study lacks data on different ethnic or geographic representation. Lastly, its focus on short-term outcomes, limits insights into long-term health consequences for both mothers and infants.

## 5. CONCLUSION

This study points out that having a past history of recurrent consecutive spontaneous abortion raises the stakes regarding adverse maternal and neonatal outcomes. These include: early-onset preeclampsia; placenta previa; placental abruption; preterm birth; small for gestational age infants. These results imply that underlying placental dysfunction is likely to be a key driver of these complications. These findings highlight the requirement for improved prenatal monitoring and specific interventions for women with past history of RCSA, so as to lessen the chances that pregnancy problems will occur. A multidisciplinary group of maternal-foetal medicine specialists, endocrinologists, and experts in reproductive health could greatly improve perinatal care and outcomes for this at-risk population.

### 1. Authors' contribution

M.F.H.: Conceptualization, Methodology, Writing – original draft. Y.Z.A., A.H.Y., E.A. A.A.: Resources, Validation, Supervision. N.M.: Formal analysis, Software. A.S.: Data curation, project administration, Writing – review & editing.

### 2. Funding

None.

### 3. Study registration

N/A.

### 4. Disclosure of interests

The authors declare that they have no conflict of interests.

### 5. Ethical approval

Ethical approval was obtained from the local institutional review board and ethics committee (SUEZ Med-IRB/2024-No. 37), Suez Hospital, Suez university in Egypt.

6. Informed consent

N/A.

7. Data sharing

Data are available under reasonable request to the corresponding author.

8. Figure legend

Figure 1. Flow diagram of eligible patients.

9. Table legend

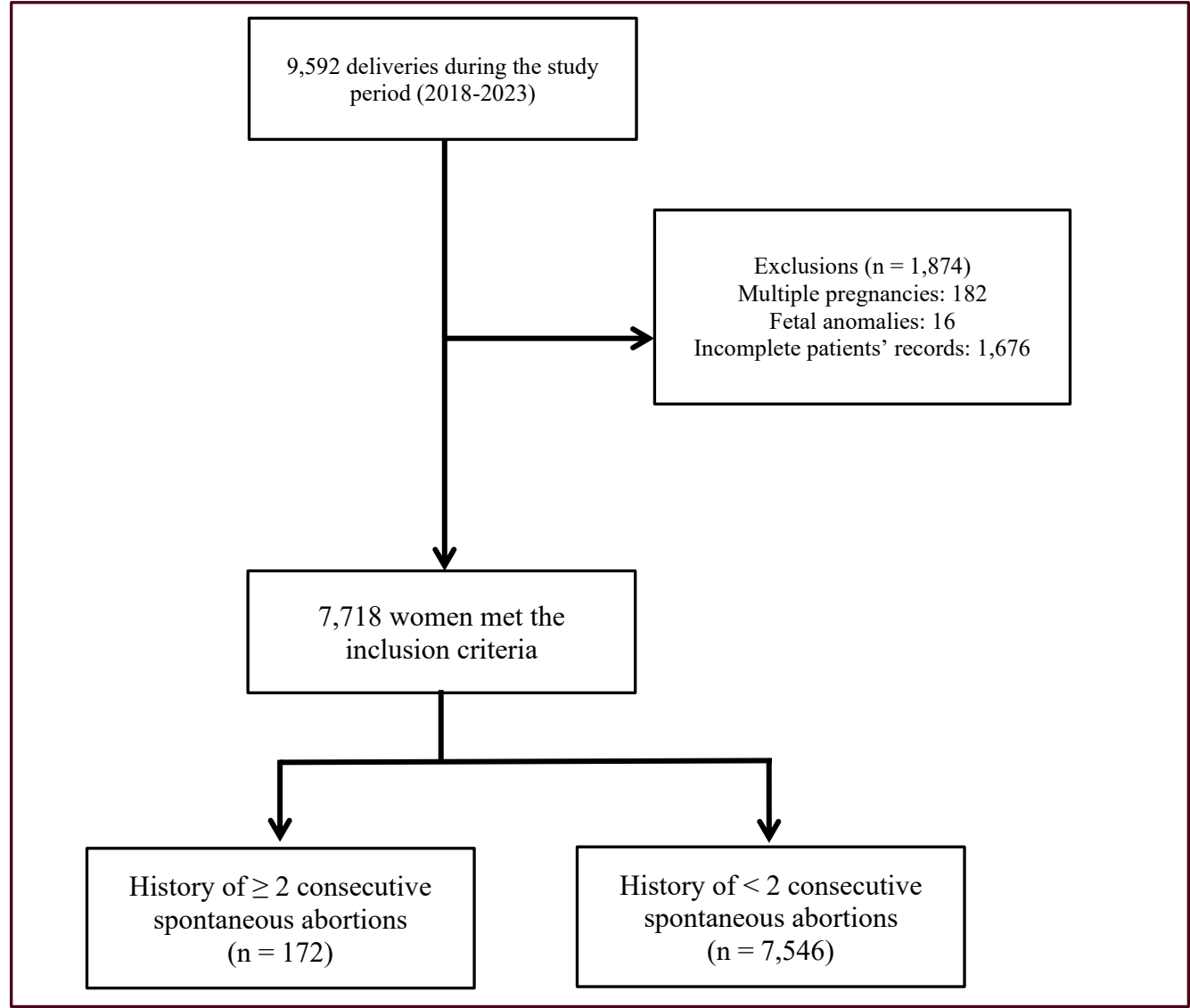
Table 1. Demographic characteristics and medical history of all participants.

Table 2. Obstetrics and delivery outcomes among the study groups.

Table 3. Neonatal outcomes among the study groups.

Table 4. Association between recurrent consecutive spontaneous abortion and maternal and neonatal outcomes.

Figure 1. Flow diagram of eligible patients.



**Table 1. Demographic characteristics and medical history of all participants.**

Variables	RCSA (n=172)	Control (n= 7,546)	P-value
Age, year	32.6 ± 5.2	31.8 ± 4.7	0.0277 *
BMI, kg/m <sup>2</sup>	30.9 ± 11.4	29.2 ± 10.9	0.0434*
BMI > 30	24(13.4)	649 (8.6)	0.0371 †
Parity	2(1-3)	3(1-4)	0.034**
Previous CS	37 (21.5)	1728 (22.9)	0.3533 †
Race			0.2378 †
Black	76 (44.19)	2998 (39.73)	
White	96 (55.81)	4548 (60.27)	
Residence			0.2768 †
Rural	71 (41.3)	3430 (45.46)	
Urban	101 (58.7)	4116 (54.54)	
Education			0.2575 †
School	113 (65.7)	4637 (61.45)	
University	59 (34.3)	2909 (38.55)	
Smoking	2 (1.16)	47 (0.62)	0.2985 †
Infertility Treatment	32 (18.6)	679 (9.0)	0.0001 †
IVF/ICSI	9 (5.23)	184 (2.44)	0.0203 †
<b>Medical History</b>			
Chronic Hypertension	8 (4.65)	163 (2.16)	0.0282 †
Pre-gestational Diabetes	9 (5.23)	176 (2.33)	0.0139 †
Hypothyroid	7 (4.07)	219 (2.9)	0.3692 †
Hyperthyroid	0	12 (0.16)	1 †
Heart Disease	1 (0.58)	8 (0.11)	0.1837 †
Bronchial Asthma	0	8 (0.11)	1 †
PCOS	4 (2.33)	146 (1.93)	0.5783 †
Gender			0.706 †
Male	84 (48.84)	3795 (50.29)	
Female	88 (51.16)	3751 (49.71)	

RCSA, recurrent consecutive spontaneous abortion; BMI, body mass index; IVF, in vitro fertilization; ICSI, intracytoplasmic sperm injection; PCOS, polycystic ovarian syndrome.

Data are presented as mean ± standard deviation, median and interquartile range, or number (percent).

\* Unpaired student t test was used; \*\*Mann Whitney U test was used; †Chi-square or Fisher Exact test was used as appropriate.

P value < 0.05 is significant.

**Table 2. Obstetrics and delivery outcomes among the study groups.**



Variables	RCSA (n=172)	Control (n= 7546)	P-value*
Anaemia	13 (7.56)	662 (8.77)	0.5771
Assisted Vaginal delivery	8 (4.65)	266 (3.53)	0.43
Caesarean Section	49 (28.49)	1871 (24.79)	0.2678
Preeclampsia	9 (5.23)	276 (3.66)	0.2788
Early Preeclampsia	4 (2.33)	52 (0.69)	0.0357
GDM	11 (6.4)	257 (3.41)	0.0342
Labor Induction	29 (16.86)	1424 (18.87)	0.5048
Oligohydramnios	18 (10.47)	551 (7.30)	0.1165
Placental Abruption	4 (2.33)	45 (0.60)	0.0232
Placental Previa	5 (2.91)	74 (0.98)	0.0311
Polyhydramnios	1 (0.58)	34 (0.45)	0.5464

RCSA, recurrent consecutive spontaneous abortion; GDM, gestational diabetes mellitus.

Data are presented as number (percent).

\*Chi-square or Fisher Exact test was used as appropriate.

P value < 0.05 is significant.

**Table 3. Neonatal outcomes among the study groups.**

Variables	RCSA (n=172)	Control (n= 7,546)	P-value
Birth weight (kg)	2.97 ± 0.72	3.12 ± 0.86	0.0233*
Foetal Distress	23 (13.37)	727 (9.63)	0.1017†
IUFD	1 (0.58)	38 (0.50)	0.5857†
low Apgar Score < 7 at 5 minutes	5 (2.91)	146 (1.93)	0.3919†
NICU admission	23 (13.37)	726 (9.62)	0.1003†
Preterm Birth (< 37 weeks)	19 (11.05)	471 (6.24)	0.0106†
SGA	17 (9.88)	432 (5.72)	0.0212†

RCSA, recurrent consecutive spontaneous abortion; IUFD, intra uterine foetal death; NICU, neonatal intensive care unit; SGA, small for gestational age.

Data are presented as mean ± standard deviation, or number (percent).

\* Unpaired student t test was used; †Chi-square or Fisher Exact test was used as appropriate.

P value < 0.05 is significant.

**Table 4. Association between recurrent consecutive spontaneous abortion and maternal and neonatal outcomes.**

Variables	Crude OR (95% CI)	P-value	Adjusted OR* (95% CI)	P-value
Early-onset Preeclampsia	3.431 [1.23 - 9.60]	0.0188	3.13 [1.12 - 8.72]	0.0292
GDM	1.94	0.0375	1.85	0.0532

	[1.04 - 3.61]		[0.99 to 3.45]	
<b>Placental Abruption</b>	3.97 [1.41, 11.16]	0.090	3.30 [1.18 - 9.23]	0.0226
<b>Placental Previa</b>	3.02 [1.21 - 7.58]	0.0182	2.73 [1.09 - 6.81]	0.0319
<b>Preterm Birth (&lt; 37 weeks)</b>	1.87 [1.15 - 3.03]	0.0119	1.79 [1.10 - 2.91]	0.0185
<b>SGA</b>	1.81 [1.09 - 3.01]	0.0231	1.72 [1.03 - 2.87]	0.0368

OR, odds ratio; CI, confidence Interval; GDM, gestational diabetes mellitus, SGA, small for gestational age.

\* Odds ratio were adjusted for maternal age, body mass index, parity, infertility treatment, use of assisted reproductive technology, chronic hypertension, and pre-gestational diabetes.

P-value< 0.05 is significant.

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