

Evaluation of Aetiopathogenesis of Spontaneous Preterm Parturition Syndrome: A Cross Sectional Study

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How to cite this article:

Surbhi Gupta, Girija Wagh/Evaluation of Aetiopathogenesis of Spontaneous Preterm Parturition Syndrome: A Cross Sectional Study/Indian J Obstet Gynecol. 2022;10(2):97-103.

Abstract

Background: Preterm birth is the multifactorial condition of the pregnancy involving the same parturition pathway as term birth but the different outcome in terms of morbidity for both mother and fetus, various pathological process has been identified and need to be evaluated further.

Aim: To evaluate the aetiopathogenesis of spontaneous preterm labour by analysis of maternal risk factors and placental abnormalities.

Objectives: (a) To study the prevalence of spontaneous pre term labor in tertiary care centre. (b) To identify associated maternal factors both clinical as well as pathological as the probable cause of pre term labor. (c) To examine the placenta for any gross and his to pathological abnormalities associated with spontaneous pre-term labor.

Settings and design: This is the cross sectional observational study carried out in a tertiary health care centre over 2 years from October 2019 to October 2021.

Materials and methods: A cross sectional observational study consist of 255 pregnant women between the 20 weeks to 36 weeks 6 days of gestation fulfilling the inclusion criteria were selected excluding the women iatrogenically induced for preterm birth. The methodology and relevance of the study were explained to the women and valid informed written consent was recorded. The ethical clearance for the study obtained from ethical review committee of the tertiary care centre.

During the study duration, women presenting with preterm labor were observed till delivery whether delivered or not in our tertiary care centre and finally were included in the study. The following data were collected under the heading of age, occupation, height, weight, body mass index, parity, presenting complaints of pain in abdomen per vaginal leak, par vaginal bleed, high grade fever, headache, edema, epigastric pain, blurring of vision, palpitations vomiting, weight gain, gum bleeding breathlessness, burning micturition, increased frequency of micturition, itching over genital region, dark coloured urine also including the co-morbidities such as asthma, anemia, valvular heart disease, diabetes, thyroid disorder and preeclampsia.

Detailed physical examination was done, blood pressure was measured with sphygmometer, detailed per abdominal examination done with the use of measuring tape to measure fundal height, abdominal circumference, all fungal grip were palpated, per speculum examination was done to look for per vaginam discharge, per vaginal bleeding, and the high vaginal swab was taken for further evaluation. In per vaginam examination cervical changes were seen like dilatation, effacement, length. The necessary laboratory findings were done includes complete blood count to look for haemoglobin, total leucocyte count, platelet counts, urine microscopic and culture sensitivity was done to analyse the infection. Later, after the delivery the placenta was send and histopathology examination was done.

Conclusion: In our study we made an attempt to identify the risk factors and associated factors involved in spontaneous preterm labor. The study able to identify the risk factors which can be potentially used for predicting outcome.

Keywords: Spontaneous preterm; Multifactorial.

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Received on: 22.02.2022 **Accepted on:** 19.03.2022

Introduction

Preterm delivery leads to serious perinatal morbidity and mortality worldwide and accounts for 75% of neonatal deaths and 50% of long-term morbidity, including respiratory disease and neurodevelopment impairment. Preterm birth is defined as the delivery of a newborn between 20

weeks to 36 weeks 6 days of gestation. Incidence being 5% to 8%, it is still increasing worldwide. The millions of babies born preterm every year. The etiology of preterm birth is multifactorial and many contributor issues have been identified, looking at the diverse etiopathogenesis and its maternal factors called it as a PPS. This study address this fall and tries to analyse the multiple etiologies, factors and syndrome pathways.

Recently certain pathological processes have been identified to be assessed with preterm birth.

- Anemia especially in the 1st trimester Hb<10g/dl.(if available)
- Maternal BMI <18kg/M2,> 30kg/M2. (if available)
- USG associated short cervix <25mm at 19wk scan. (if available)
- Co-morbid condition such as preeclampsia/ heart disease/ diabetes.
- Maternal infection such as high grade fever/ urinary/ respiratory/ vaginal infection/ periodontal infection during pregnancy.

The crucial point is that the signs and symptoms that define the preterm parturition syndrome are caused by multiple aetiologies or pathological processes.

Unlike sickle cell disease, which is caused by a single base pair mutation in the nucleotides encoding for hemoglobin, may be expressed with a wide range of phenotypes which depend to a large extent on environmental factors. There are various mechanism associated with the disease like allergies, uterine infections, cervical infection or inflammation.²

The majority of preterm birth occur as spontaneous onset of labor while remaining are indicated preterm birth. The term "indicated" refer that labor and/or delivery has been the result of induction and/or abdominal delivery for maternal or fetal indications. The most common maternal indication is preeclampsia, and the fetal indication is a small-for-gestational-age fetus with evidence of compromise. Other causes of "indicated preterm birth" include congenital anomalies or maternal diseases that require delivery (e.g. acute fatty liver of pregnancy or other disorders, which would improve after delivery). This distinction between spontaneous and indicated preterm birth is based upon the clinical circumstances which determine preterm delivery, namely, the presence of spontaneous labor. It is important to note that this

classification does not take into account the cause of the "spontaneous" or "indicated preterm birth", and indeed, there may be an overlap between the two.

The risk of death of a preterm neonate is 120 times greater than that of an infant born at term. Moreover, survivors are at risk of short-term morbidity (respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, sepsis, retinopathy of prematurity) and long-term morbidity such as cerebral palsy learning disabilities blindness and crippling respiratory disease. Recent evidence suggests that preterm neonates may also be at risk for altered metabolic states in adult life.

Preterm births have been classified according to the gestational age at which they occur, into very early (those with a gestational age at delivery of ≤ 28 weeks), early (≤ 32 weeks), and late preterm birth (33–36 weeks). The frequency of these three types is 0.82%, 2.2%, and 8.9%, respectively. Therefore, most preterm births occur late, yet serious morbidity and mortality affect disproportionately those born before.

Recent observations suggest that late preterm births are at a higher risk for health and developmental problems than infants born at term. Indeed, infant mortality, defined as "deaths at the age of one year" is significantly greater in late preterm birth than in term birth³. The clinical implications of these observations is that late preterm birth should not be neglected as unimportant, or a short-term neonatal problem.

Keeping in mind the multifactorial nature of the problem, this study was done to evaluate the etiopathogenesis of spontaneous preterm labor by analysis of maternal risk factors and placental abnormalities.

Materials and Methods

A cross sectional observational study was carried out in 255 women visiting gynaecological wards and opd in spontaneous preterm labor. The data was collected from Bharati Hospital, wards and opd, department of Obstetrics and Gynaecology, Pune between October 2019 October 2021. The purpose and the procedure of the study was explained to them and a written consent was obtained.

Inclusion Criteria

Women presenting with spontaneous preterm labor were included

Exclusion Criteria

Women who were iatrogenically induced for preterm onset of labor.

Methodology

During the study duration, women presenting with preterm labor were included in the study. These women were observed till delivery and finally all the women who underwent spontaneous labor were included in the study .After an informed consent of each participant ,the following data were collected

- Age
- Occupation
- Height ,weight and BMI
- Parity

Presenting complaints such as Pain ,Per vagina leak, Per vaginal bleed, Per vaginum discharge, High grade fever, Headache, Edema, Epigastric pain, Blurring of visison, Palpitation, vomiting, weight gain, Gum bleeding, Breathlessness, Burning micturation, Increased frequency of micturation, Itching over genital region, Dark coloured urine.

Co-morbidities such as Asthma,anemia, valvular heart lesion, diabetes, thyroid disorders, pre-eclampsia, etc.

Physical examination was done for obtaining the systolic blood pressure and diastolic blood pressure. For all patients pallor, edema, lymphadenectomy, uterine contractions, per vaginal leak, fetal heart sound and per vaginal bleeding were observed. Laboratory investigation were done for obtaining hemoglobin levels, Total leucocyte count, C-reactive protein as well as Urine microscopy and culture were performed. Ultrasounds were done to obtain the uterine height, cervical changes, AFI, fetal weight and location of placenta. All placenta were evaluated after delivery and sent for histopathology study.

Table 1 and figure 1 depicts the incidence of spontaneous labor among preterm delivery cases which is 87.5%. Out of the 255 preterm cases, 223 (87.5) present with spontaneous labor while 32 (12.5) were induced for labor.

Table 2: Distribution of presenting complaints (N=223)

	Dark colored urine	Frequent micturition	Burning micturition	Weight gain	Edema	Hea dache	High grade fever	P/V meco nium	P/V bleed	P/V leak	Pain
Dark colored urine		13 (5.8)	14 (6.3)	0 (0.0)	0 (0.0)	3 (1.3)	1 (1.3)	4 (1.8)	0 (0.0)	9 (0.4)	22 (9.9)
Frequent micturition	13 (5.8)		11 (4.9)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	3 (1.3)	0 (0.0)	5 (2.2)	18(1.8)

Statistical Analysis

The data was recorded in the proforma and it was transferred to a spreadsheet in Microsoft excel. Qualitative data was expressed in form of percentages while quantitative data were expressed as mean _+SD and range values. The relationship between qualitative data were tested using Chi-squae or Fisher’s exact test and for quantitative data independent sample “t” test was used. Lastly, univariate and bivariate analysis were to done to calculate odds ratio with confidence interval and p-value that depicted the strength of association. For analysis, p<0.05 was considered statistically significant. The data were subjected to statistical analysis using the SPSS (Statistical Package for the Social Sciences) version 24.0 software.

Results

Table 1: Parity of participants (N=223)

Parity	Frequency	Percentage
Primigravida	43	19.3
Multiparous	180	80.7
Total	223	100.0

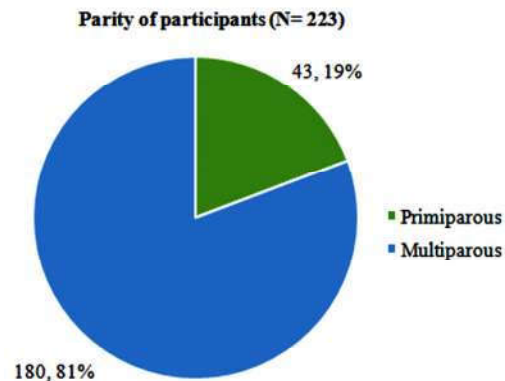


Fig. 1: Incidence of labor.

Burning micturition	14 (6.3)	11 (4.9)		1 (0.4)	0 (0.0)	2 (0.9)	1 (0.4)	4 (1.8)	0 (0.0)	7(3.1)	23 (10.3)
Weight gain	0(0.0)	0 (0.0)	1 (0.4)		1 (0.4)	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	3(1.3)	4(1.8)
Edema	0(0.0)	0 (0.0)	0 (0.0)	1 (0.4)		1(0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	2(0.9)
Headache	3(1.3)	2 (0.9)	2(0.9)	1(0.4)	1 (0.4)		0 (0.0)	1 (0.4)	2(0.9)	4(1.8)	24(10.8)
High grade fever	1(0.4)	0(0.0)	1(0.4)	0 (0.0)	0 (0.0)	0(0.0)		0(0.0)	0(0.0)	0 (0.0)	2(0.9))
P/V meconium	4(1.8)	3(1.3)	4(1.8)	1(0.4)	0(0.0)	1(0.4)	0 (0.0)		0(0.0)	0(0.9)	15(6.7)
P/V bleed	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(0.9)	0(0.0)	0(0.0)		0(0.0)	9(4.0)
P/V leak	9(4.0)	5(2.2)	7(3.1)	3(1.3)	1(0.4)	4(1.8)	0(0.0)	2(0.9)		0(0.0)	79(35.4)
Pain	22(9.9)	18(8.1)	23(10.3)	4(1.8)	2(0.9)	24(10.8)	2(0.9)	15(6.7)	9(4.0)	79(34.4)	

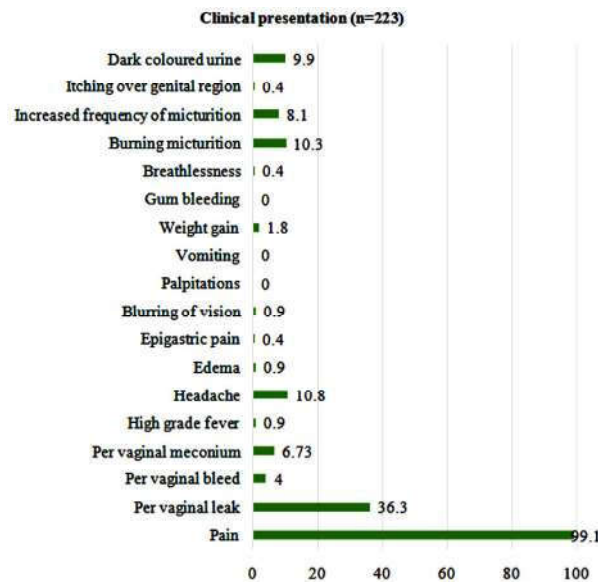


Fig. 2: Clinical Presentation.

The above table depicts that the most common symptom is pain in abdomen in 99.1% women presenting in preterm labor followed with premature rupture of membrane, burning micturation in 36.3% and in 10.3% women.

Table 3: Obstetric Risk Factor (N=223)

Obstetric risk factor (Current & previous pregnancy)	Frequency (N=223)	Percentage
PPROM	77	30.2
Twin pregnancy	1	0.4
Previous preterm delivery	99	44.4
IVF conception	12	5.4
Gestational hypertension	15	6.7
Preeclampsia	23	10.3
Eclampsia	—	—
Previous abortions	13	5.8
Diabetes	33	14.8
Thyroid disorders	15	7.7

Table 3 depicts the obstetric risk factors observed in both previous and current pregnancy. Preterm delivery was observed as a risk factor in majority of the cases 99(44.4) followed by PPRM 77(30.2), diabetes 33 (14.8) and preeclampsia 23 (10.3).

Table 4: Examination findings of cases (N=223)

Examination Findings	Present	Absent	Total
Pallor	92 (41.3)	131 (58.7)	223 (100.0)
Edema	33 (14.8)	190 (85.2)	223 (100.0)
Lymphadenopathy	0 (0.0)	223 (100.0)	223 (100.0)
Uterine contractions	223 (100.0)	0 (0.0)	223 (100.0)
Per vaginal leak	70 (31.4)	153 (68.6)	223 (100.0)
Fetal heart sound	223 (100.0)	0 (0.0)	223 (100.0)
Per vaginal bleeding	2 (0.9)	221 (99.1)	223 (100.0)

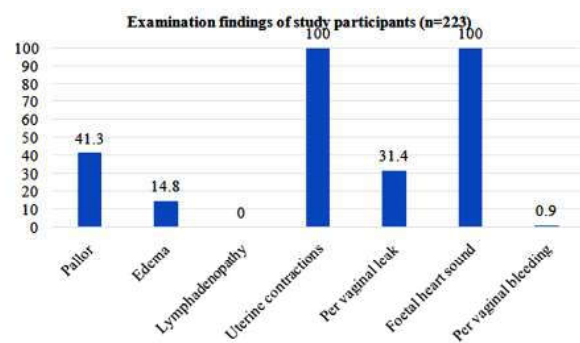


Fig. 3: Frequency Graphs of Examination Findings.

Table 5: Descriptive statistics on ultrasound findings (N=223)

Ultrasound findings	Frequency (N)	Mean ± S.D	Minimum	Maximum
Uterine height	223	32.1 ± 2.7	24	36
Cervical length	223	2.8 ± 0.2	1.8	3.8
AFI	223	9.9 ± 1.9	4.0	14.0
Fetal weight	223	2.2 ± 0.2	1.0	2.9

Table 5: Shows the mean uterine height, Cervical Length, AFI and fetal weight as per ultrasound to be 32.1, 2.8, 9.9 and 2.2 respectively.

Table 6: Morphology of placenta (N= 223)

Placenta details		Frequency	Percentage
Placenta gross	Normal for gestation	200	89.7
	Necrotising	6	2.7
	Calcification	16	7.2
	Haemorrhagic	1	0.4
Total		223	100.0

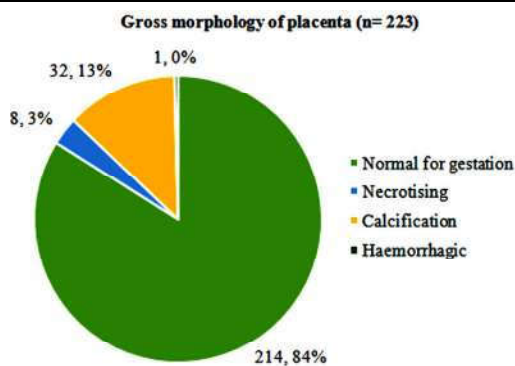


Fig. 4: Pie chart distribution of cases on morphology of placenta.

Table 6 and figure 5 shows the distribution of cases based on histopathology of placenta. Majority (83.9) placenta was normal in histopathology while among the rest, calcification was observed in maximum (13.0) cases.

Table 7: Histopathology of placenta (N= 223)

Placenta details		Frequency	Percentage
Placenta histopathology	Normal for gestation	200	89.8
	Intra- placental clot	3	1.3
	Placental fibrin deposition	17	7.6
	Placental lakes	2	0.9
	Calcification	1	0.4
Total		223	100.0

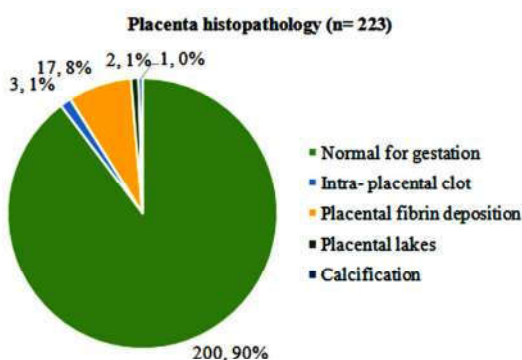


Fig. 5: Pie chart distribution of cases based on histopathology of placenta.

Table 7 and figure 6 shows the distribution of cases based on histopathology of placenta. Majority (89.8) placenta was normal in histopathology while among the rest, placental fibrin deposition was observed in maximum (7.6) placenta.

Discussion

The preterm labor is mediated by multifactorial conditions leading to increase morbidity and mortality in perinatal period. The various emerging obstetric risk factors and medical morbidities lead to the onset of preterm parturition syndrome.

The present hospital based observational study aimed to determine the multi factorial causes contributing to preterm birth. The study includes 223 women delivered preterm between (20 weeks to <36 weeks 6 days weeks) of gestation in a tertiary care centre or have been followed up in antenatal clinic, fulfilling the eligibility criteria. After informed written consent of each patient, data was collected which include parity, gestational age, disparity in gestational age, significant history of previous preterm deliveries (recurrent cause evaluated), medical past history (focusing on diabetes, chronic hypertension, cardiovascular disease).

The detailed physical examination was done at the time of presentation with preterm labour. The body mass index, temperature, pulse rate, blood pressure, respiratory rate, pallor, edema, deep tendon reflex, urine albumin assessment, detailed abdominal examination (uterine height, symphio-fundal height, abdominal girth and the pelvic grips), per speculum examination to look for genital infection, per vaginal leaking, per vaginal bleeding. The per vaginal examination also document cervical changes such as effacement, short cervix and dilatation.

All patients were subjected to investigation such as complete blood count, urine routine assessment, urine culture and sensitivity, high vaginal swab to rule out genital infection, C-reactive protein. It is done to consider anemia, leucocytosis, genitourinary infection or inflammation as a cause of preterm labor. The fifth month ultasonography was done to co relate the clinical cervical length and cervical status, the length less than 2.5 mm plays a good predictor for diagnosis of spontaneous preterm labor.

After the delivery, placenta was send for histopathological examination and detailed microscopic and gross study done to evaluate the placental causes contributing to preterm birth.

The incidence of spontaneous preterm labor was 87.5% in the current study among the 255 women underwent preterm delivery which is similar to the study done by Romero R et al and Phillips C et al where the incidence of spontaneous labor in preterm birth is, 75 % and 70 % respectively^{4,5}

The parity plays its own significant role in preterm delivery, the previous preterm deliveries and low birth weight history seen predisposing mother for recurrent preterm birth with subsequent pregnancies, as the nutrition value decreases hence prove that multigravida are more prone for pre term birth, but the primigravida under the effect of environmental factors and other genital and urinary infections also prone to premature delivery. Though in present study multigravidas (80.7 %) underwent more preterm deliveries than primigravida (19.3%).

Mariana Buen in her study stated that bleeding during pregnancy is significantly associated with spontaneous preterm labor however we found that only 27.6% of the women in present study had per vaginal bleeding.⁶ In the present study most common presentation is pain in abdomen (99.1%), followed by PPRM (34.5%) and burning micturation (10.3%).

Anemia is like an evil eye to pregnant women which increases the risk of preterm birth to many folds. Theresa O Scholl in her study stated that maternal anemia is associated with two fold increase in risk of spontaneous preterm birth.⁷ In the present study 18.8% of the women were anemic who underwent spontaneous preterm birth.

The multiple gestation, oligohydramnios, premature rupture of membranes, diabetes, pre eclampsia, assisted reproductive techniques, antepartum hemorrhage and other obstetric risk factors counted to be major risk factor for preterm parturition syndrome.

Robert L Goldenberg state that almost all multiple gestations will deliver as preterm, although 40% of them have spontaneous preterm labor. The uterine over distension, result in increasing contractions and rupture of membranes, is causative mechanism for the increase rate of spontaneous preterm births. In the present study, of all the participants who underwent spontaneous preterm labor, only 0.4% were twins. The history of previous preterm labor increases the risk of spontaneous preterm labor as stated in the study of Courtney Phillips [23 (13-33)], Mariana Buen [3.88 (2.53-5.97)] and Kwang-Sig-Lee (4.62 (3.52-5.86)). Similar results were observed in our study where 44.4% of the women gave a history

of preterm delivery in the past.

As per the results of Sarah D McDonald, Tanja Premru-Srsen, and P Cavoretto there was an increased incidence of spontaneous preterm labor in pregnancies conceived after reproductive assisted technique (IVF/ ICSI). But in this study, 5.4% of the total pregnancies were conceived after IVF and they underwent spontaneous preterm labor.^{8,9,10}

In the present study it was observed that only 6.7% of the women had gestational hypertension, 10.3% had preeclampsia and none had eclampsia. These results were similar to that of the study conducted by Mariana Buen where only 4.3% of the women had preeclampsia or Eclampsia and it depicted that pregnant women with presence of factors like gestational hypertension, Preeclampsia and Eclampsia were less likely to have spontaneous preterm birth.⁶

According to Michal A. Elovitz, only 7.5% of the female who underwent spontaneous preterm labor had diabetes whereas in our study 14.8% had diabetes¹¹

Placental implantation plays a major role, the posterior and lateral localization significantly associated with preterm labor. The failure of migration of placenta progress to placenta previa which is one of the dreaded obstetric condition leading to preterm labor . In present study 37.7% of cases , placenta lie posteriorly followed by anterior location.

In the prospective review conducted by Shumaila Zia, the results state that posterior placental implantation was significantly associated with preterm labor.¹² While another observational study conducted by EF Magann states that low placental implantation had greater risk of preterm labor [13]. Tak Yuen Fung in the retrospective study stated that lateral placenta placentation were at increased risk of developing spontaneous preterm delivery before 34 weeks.¹⁴

However, in the present study no such association could be seen as majority of the placenta was normal for gestation both grossly (89.7%) and his to logically (89.9%). Thrombosis was seen in 1.3% and necrosis in 2.7%.

Conclusion

Spontaneous preterm labor is a heterogenous condition with many triggers .Different mechanism have been described for pathogenesis of preterm labor. Though we have made great advances in

the understanding of human labor and causes of preterm labor, we have still not been able to correctly predicts spontaneous preterm labor. The present study able to identify risk factors. It is a big challenge of preventing preterm labor and the risk factors associated with it. The new technique and intervention by far has made it easy to study and identifying this multi factorial conditions to prevent morbidity and improving outcome of preterm labor. But still the preterm birth /labor is like a sea surrounding all the obstetric risk factor, so it need to be studied and observed meticulously.

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