International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2019): 7.583

A Study of Association of Placental Pathology with Neonatal Outcome in Preterm Births: A Prospective Analytical Observational Study

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Abstract: ***Preterm birth is multifactorial and has long term health consequences for the child. Placenta plays a central role in preterm birth and the placental pathology was associated with adverse maternal and neonatal outcomes in various studies, which highlights the importance of placental examination in preterm births. Hence, we studied gross and histopathology of preterm (cases) placentas and their association with neonatal outcome. Controls were term deliveries. A total of 300 placentas, 150 preterm and 150 term were examined and the respective neonates were followed for complications till discharge. Results and conclusion:Abnormal placental pathology found in preterm placentas were infarction (22%), calcification(44%), acute (2.7%) and chronic (5.3%) chorioamnionitis, marginal cord insertion (17.3%), thin cord (6%), false knot(1.3%).Fibrinoid necrosis (1.3%) and fleshy cord (4%) were found in term placentas. Outcomes in preterm neonates observed were low Apgar scores (10.7%), NICU admission (32%), respiratory distress syndrome (28.7%), neonatal jaundice (6.7%), intraventricular hemorrhage (2%), seizures (1.3%), retinopathy of prematurity(0.7%) and sepsis (3.3%). 45.5% of infarction in preterm placentas was associated with RDS and 25% of chronic chorioamnionitis was associated with sepsis were statistically significant, (p<0.05). Thin umbilical cords were significantly associated with IUGR and oligohydramnios.***

Keywords: Preterm birth, Placental pathology, Neonatal outcome, Association

1. Introduction

Preterm births are defined as those delivered before 37 completed weeks according to World Health Organisation(WHO) and International Federation of Obstetrics and Gynaecology (FIGO).[1]Placenta being the central organ of inutero fetal nutrition, plays a central role in preterm birth.Preterm birth is multifactorial, has long-term health consequences on the child. Placental pathology provides important diagnostic information to ascertain the cause of preterm birth[2]. Studies have found association of placental features like histologic chorioamnionitis, funisitis, coagulopathy, malperfusion lesions, etc. with the neonatal complications like Respiratory distress syndrome(RDS), Intraventricular hemorrhage(IVH), sepsis, Necrotisingenterocolitis (NEC), Retinopathy of Prematurity(ROP) and many more [2-17]. Even though pretermlabour has multiple causes identified, 20-30% are of unknown etiology[18]. Our study is designed so as to examine the placentas of preterm and term births for abnormalities and study their association with the neonatal outcomes, which we hope will provide an insight to the unknown etiology of preterm birth too.

2. Review of Literature

Lee J et al.[10] in their study found acute chorioamnionitis in 22.7% of preterm births, but in term births, the incidence is 16.7%. The incidence of Chronic chorioamnionitis was 20.8% in preterm, but in term, it was 10.5%, which were significant statistically.In a study by Mehta R et al[14]., acute chorioamnionitis was found in 67.7% of the extreme preterm and 17% of early preterm placentas, (p< 0.001). Maryamazizi et al.[19] concluded in their study that calcification was present in 90% of early preterm, 14% of late preterm and 15% of full term placentas. Tantbirojn P et al.[20] in their study, found association between gross cord abnormalities and intrapartum complications, stillbirth and intrauterine growth restriction in singleton pregnancies.

3. Materials and Methods

This prospective analytical and observational study was conducted in Rajiv Gandhi government woman and children hospital, Puducherry, India for a period of 1 year. Pregnant women who were admitted in our hospital in preterm labour/PPROM/induced for obstetric reasons, between 24+0 and 36+6 weeks gestation were taken as cases. For every preterm delivery taken as case, the immediate next term (between 37+0 and 41+6 weeks gestation) delivery was taken as control. 300 placentas (150-preterm and 150-term) were examined grossly and histologically. After placentas were delivered, they were weighed and fixed in 10% formalin and examined by a qualified and experienced pathologist of our hospital. The respective preterm and term neonates were followed for complications, tillthey got

discharged from the hospital.The results were obtained and analyzed statistically. Inclusion criteria:1) singleton pregnancies delivered between 24+0 and 36+6 weeks, 2)singleton pregnancies delivered between 37+0 and 41+6 weeks, 3) preterm and term IUGR, 4)preterm and term oligohydramnios. Exclusion criteria: 1) polyhydramnios, 2) multifetal gestation, 3)anomalous babies, 4) maternal complications like PIH, GDM, overt DM, 5) clinical evidence of chorioamnionitis and urinary tract infection.

4. Methods of Statistical Analysis

Data was entered in EpiData software version 4.0 and analysed using SPSS version 24.0. Description of categorical variables was done using frequency and proportion and that of continuous variables using mean and standard deviation. The association between placental abnormality and neonatal outcome were carried out using chi-square test for categorical and t-test for continuous independent variable. All the test were two sided. The p value less than 0.05 was considered statistically significant.

5. Results

In our study, preterm and term were comparable in terms of age, no significant difference was observed between them (p-0.283) and primigravidas were predominant compared to multigravidas (table 1).

Table 1: Demographic characters

	Preterm–cases(%)	Term –controls(%)	Total	p-value
Age:				
18-25 years	86(54.4)	72(45.6)	158(100.0)	0.283
26-30 years	51(44.7)	63(55.3)	114(100.0)	0.283
31-35years	8(40.0)	12(60.0)	20(100.0)	0.283
>35 years	5(62.5)	3(37.5)	8(100.0)	0.283
Obstetric score:				
Primigravidas	87(51.5)	82(48.5)	169(100.0)	0.561
Multigravidas	63(48.1)	68(51.9)	131(100.0)	0.561

The placental pathologies observed in preterm placentas were infarction (22%), calcification (44%), acute chorioamnionitis (2.7%), chronic chorioamnionitis (5.3%), marginal cord insertion (17.3%), thin cord (6%) and false knot (1.3%). Fibrinoid necrosis (1.3%) was found in term placentas.All were statistically significant (p<0.001) except calcification, marginal cord insertion and fibrinoid necrosis. (table 2)

Table 2: Summary of placental pathologies in different categories of preterm and term placentas

Placental pathology	Extreme preterm(n=2)	Early preterm(n=18)	Late preterm(n=130)	Term (n=150)	Total	p-value
Placental infarction	0(0.0)	11 (61.1%)	22 (16.9%)	18 (12%)	33	<0.001
Calcification	1 (50%)	6 (33.3%)	59 (45.4%)	70 (46.7%)	66	0.618
Acute chorioamnionitis	-	1 (5.6%)	3 (2.3%)	6(4%)	4	<0.001
Chronic chorioamnionitis	-	5 (27.8%)	3 (2.3%)	1(0.7)	8	<0.001
Fibrinoid necrosis	-	-	-	2(1.3%)	-	-
Marginal cord insertion	-	4 (22.2%)	22 (16.9%)	25(16.7%)	26	0.693
False knot	-	1 (5.6%)	1(0.7%)	-	2	<0.001
Thin cord	-	1 (5.6%)	8(6.2%)	-	9	<0.001

The neonatal outcomes observed in preterm babies were low Apgar score (10.7%), NICU admission (32%), respiratory distress syndrome (28.7%), neonatal jaundice (6.7%), intraventricular hemorrhage (2%), seizures (1.3%), retinopathy of prematurity (0.7%) and sepsis (3.3%).NICU admission (0.7%), respiratory distress syndrome (0.7%) and neonatal jaundice (2%) were observed in term neonates.All were statistically significant except neonatal jaundice and ROP. (table 3)

Table 3: Summary of neonatal outcomes in different categories of preterm and term neonates

Neonatal outcomes	Extreme preterm(n=2)	Early preterm(n=18)	Late preterm(n=130)	Term (n=150)	Total	p-value
Low apgar score <8/10	2 (100%)	7 (38.9%)	7 (5.4%)	-	16	0.002
NICU admission	2 (100%)	11 (61.1%)	35 (26.9%)	1(0.7%)	48	0.002
RDS/HMD	1 (50%)	11 (61.1%)	31 (23.8%)	1(0.7%)	43	0.004
Hyperbilirubinemia/NNJ	-	3 (16.7%)	7 (5.4%)	3(2%)	10	0.185
IVH/PVL	1 (50%)	-	2 (1.5%)	-	3	<0.001
Seizures	1 (50%)	-	1 (0.8%)	-	2	<0.001
ROP	-	-	1 (0.8%)	-	1	0.925
Sepsis	1 (50%)	3 (16.7%)	1 (0.8%)	-	5	<0.001

45.5% of infarction in preterm placentas was associated with RDS and 25% of chronic chorioamnionitis was associated with neonatal sepsis, which was statistically significant (table 4).

Table 4: Association between placental findings and neonatal complications among cases (n = 150)

Neonatal Outcome	Placental Pathology					
	Thin cord n=9 (%)	Marginal cord insertion, n=26 (%)	Infarction, n=33 (%)	Calcification, n=66 (%)	ACA, n=4 (%)	CCA, n=8 (%)
Low APGAR score	1(11.1)	3(11.5)	7(21.2)	8(12.1)	0(0.0)	3(37.5)
NICU Admission	5(55.6)	9(34.6)	15(45.5)	24(36.4)	2(50)	5(62.5)
RDS	5(55.6)	9(34.6)	15(45.5)*	23(34.8)	2(50)	5(62.5)
Neonatal jaundice(NNJ)	2(22.2)	2(7.7)	4(12.1)	5(7.6)	0(0.0)	2(25)
IVH	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Seizures	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
ROP	1(11.1)	0(0.0)	0(0.0)	1(1.5)	0(0.0)	0(0.0)
Sepsis	0(0.0)	0(0.0)	2(6.1)	3(4.5)	0(0.0)	2(25)*

5.6% of the placental infarction in term placentas was associated with RDS, which was statistically significant (table 5).

Table 5: Association between placental findings and neonatal complications among controls (n = 150)

Neonatal Outcome	Placental Pathology					
	Thin cord	Marginal cord insertion	Infarction	Calcification	ACA n=6	CCA
	n=0	n=25	n =18	n =70		n =1
Low APGAR score	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
NICU admission	0(0.0)	0(0.0)	1(5.6)	1(1.4)	0(0.0)	0(0.0)
RDS	0(0.0)	0(0.0)	1(5.6)*	1(1.4)	0(0.0)	0(0.0)
Neonatal jaundice (NNJ)	0(0.0)	1(4.0)	0(0.0)	2(2.9)	0(0.0)	0(0.0)
IVH	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Seizures	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
ROP	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Sepsis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)

6. Discussion

Preterm deliveries were seen more in 18-25 years and >35 years age group in our study, which is similar to a study by Jamal S etal[21]., where maximum preterm deliveries were observed in teenage (27%) and elderly gravidas (23.9%). Among the preterm deliveries in our study, 87(58%) were primigravidas and 63(42%) were multigravidas. Fernandes SF et al. [22] found in their study, among the primigravidas, preterm deliveries were more frequent than term deliveries (62.5% vs. 37.5% respectively), which favours our study.

88.9% of preterm placentas with thin cord had both IUGR and Oligohydramnios associated with them. This is supported by the following two studies. Raio L et al.[23] in their study said that the proportion of SGA infants was higher among fetuses who had a lean umbilical cord than among those with a normal umbilical cord. (11.5% vs. 2.6% respectively, p<0.05).

45.5% of infarction in preterm placentas was associated with RDS, which was statistically significant (p<0.05). 6.1% ofpreterm placental infarction was associated with culture negative sepsis and 12.1% associated with hyperbilirubinemia. In term group, 5.6% of placental infarction was associated with NICU admission and RDS, which were statistically significant (p<0.05**)**. This is comparable to the study by Chiskolmet al.[24], where they found that 41.8% of RDS was associated with placental infarction and 16.7% of culture positive sepsis was associated with infarction-statistically insignificant.

50 % of acute chorioamnionitis was associated with RDS and NICU admission in preterm babies in our study, which was statistically insignificant.Liu Z et al.[25] in their study found a statistically significant association of 5.7% of ACA was associated with RDS, p<0.05.

Even though chronic chorioamnionitis (CCA) was associated with low Apgar score, RDS, hyperbilirubinemia and Klebsiella positive neonatal sepsis in our study, the association of CCA with sepsis was only found to be statistically significant (p<0.05). Chiskolmet al.[24]in their study found 83.3% of culture positive sepsis was significantly associated with CCA.

7. Conclusion

There were significant associations between infarction and respiratory distress syndrome in preterm and term groups. Chronic chorioamnionitis in preterm placentas was associated with neonatal sepsis. Chronic chorioamnionitis was more frequent than acute chorioamnionitis in preterm birth. Calcification, a sign of placental maturity, might have been the trigger of parturition in late preterm birth. Thin umbilical cord was significantly associated with IUGR and oligohydramnios.

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