

An Observational Study of Placental Changes among Term and Preterm Babies Delivered in Tertiary Care Hospital

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Abstract

Background and Objective: Placental pathology has been implicated in the pathogenesis of preterm neonatal morbidity. However, the role of placental infection in the occurrence of neurological, lung, and infection morbidity among prematurely born infant remains controversial. Furthermore, there is disagreement regarding the association between sepsis in preterm neonate and *in utero* exposure to placental infection.

Objective: The present study was undertaken to investigate the association of placental pathology with the preterm and term delivery.

Materials and Methods: Design: This was a hospital-based observation study. The study included 100 placentas including 60 preterm placenta and 40 term placenta from singleton live birth delivered at Rajarajeswari Medical College and Hospital from November 2018 to November 2019.

Results: As placental weight is one of the key indicators of fetal intrauterine status, among term placenta 26% weighed between 501 and 750 g and 14% weighed between 251 and 500 g. In the late preterm placenta, 6% were within 501–750 g and 38% were within 251–500 g. Among the early preterm placentas, 2% were found to be within 100–250 g and 14% were found to be within 251–500 g. Histopathological findings among term placenta in which 23% of the placentas were found to be with normal morphology, having two arteries and one vein embedded in myxoid matrix and unremarkable, maternal surfaces show mature vascularized villi and fetal parenchyma also shows mature villi and 5% showed features of chorioamnionitis, 8% of the placentas revealed occasional focal areas of calcification on the maternal as well fetal surfaces, 15% showed infarction, and 3% showed hemorrhagic changes. Histopathology findings among preterm placenta in which 14% normal morphology, 21% of chorioamnionitis, 10% shows focal and extensive areas of infarction with increased syncytial knots, 4% had hemorrhagic and perivasculitis changes with focal hyalinized villi, and 5% had villitis with mixed inflammatory infiltrate in the chorionic villi. Histopathology study among term and preterm comparison, it shows chorioamnionitis with Chi-square 19.604 with confidence interval of 35.66–77.04% with $P < 0.0001$, calcification with $P = 0.466$, placental infarction with confidence interval of 41.51–92.47% with $P = 0.0002$, placental hemorrhage with confidence interval of -31.33%–52.31% with $P = 0.613$, and villitis with confidence interval of 38.55–100% with $P = 0.002$. Relative risk with respect to histopathology among term and preterm placenta relative risk is 2.3 which means that preterm group has 2.3 times more risk of abnormal placental histopathology than term group.

Conclusion: Among histopathological study between term and preterm placenta, preterm placentas were most commonly associated with abnormal histopathological findings, among abnormal histopathological finding chorioamnionitis is the most common.

Key words: Gestational age, Placental pathology, Preterm infants;

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INTRODUCTION

A baby born before 37 completed weeks of gestation starting from the 1st day of last menstrual period is defined as a preterm baby. They are divided as late preterm, that is, babies born between 35 and 37 weeks of gestational age and early preterm, that is, babies born <35 weeks of

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gestational age. Preterm births are the second leading cause of death in children under 5 years of age. Of which, late preterm births (70%) being the most common.^[1]

Placenta is the most accurate record of the infant's prenatal experience. It is a unique organ that arises *de novo* and is directly related to growth and development of the fetus. The placenta (Greek, *plaknos* = flat cake) is named on the basis of the gross anatomical appearance.^[2]

Placenta provides a diary of gestational life. The placenta is often the most accessible and readily evaluable component of the triad of mother, infant, and placenta. It shows the cumulative effects of pregnancy-related events, reflects the intrauterine environment, and can be examined to a degree that the infant usually cannot.^[3]

Placental examination has been self-explanatory in solving the litigation faced by the obstetricians during early times when the preterm babies arrived with neurological disabilities over a period of time.^[4] Henceforth, placental examination serves as a key to recognize the underlying cause of preterm delivery. Microscopic examination of the placenta helps to assess lesions such as chorioamnionitis, calcification, infarction, hemorrhage, villitis, and chorangiosis.

Chorioamnionitis is the inflammatory response to infections caused by microorganisms such as *Ureaplasma urealyticum*, *Gardnerella vaginalis*, *Mycoplasma*, *Fusobacterium*, *Chlamydia trachomatis*, *Streptococcus*, *Staphylococcus*, *Toxoplasma*, *Rubella*, *Cytomegalovirus*,^[5] herpes virus, syphilis, malaria, and listeria. Placental tissues deposited with calcium are known as calcification which contributes to preterm delivery, especially in patients who are diagnosed with early preterm placental calcifications under ultrasonography.^[6] Placental infarctions have found to be associated with late preterm with decreased fetoplacental blood supply subsequently causing preterm delivery.^[7] Villitis is the inflammation of the chorionic villi; chronic villitis has association with preterm delivery.^[5]

As the complications and the cost of management of the preterm babies are huge burden for the society as well as the family, identification of the cause for the preterm birth would throw a light to prevent preterm mortality and morbidity. This prospective study was conducted to determine the placental weight and pathological findings corresponding to the gestational age and lays down foundation for the pediatricians as well as the obstetricians by providing guidelines for the pathogenesis preterm delivery. Once the etiopathogenesis of the placental pathology is identified, further studies in this field help in providing interventions.

MATERIALS AND METHODS

Study Design

This was a hospital-based comparative study.

Type of Study

This was an observational study.

Study Site

This study was conducted at the Department of Paediatrics, Rajarajeshwari Medical College and Hospital.

Study Duration

Duration of the study will be conducted over a period of 12 months from November 2017 to November 2018.

Sample Size

$n = 100$ sample size is calculated based on previous years of incidence of preterm delivery in Rajarajeshwari Medical College in which 60 samples are of preterm placenta and 40 samples are of term placenta.

Selection Criteria

Inclusion criteria

The following criteria were included in the study:

1. All babies born with <37 completed weeks.
2. Patient willing to give an informed consent to participate in the study.

Exclusion criteria

The following criteria were excluded from the study:

1. Induced preterm deliveries secondary to:-
 - Scar tenderness
 - Diabetes mellitus
 - Pregnancy-induced hypertension.

After taking an informed written consent to participate in these study from participant and attenders, a detailed maternal history regarding any h/o fever and foul smelling vaginal discharge was taken and look for any fetal tachycardia, maternal tachycardia, and uterine tenderness. As routine workup for preterm deliveries, maternal complete hemogram, C-reactive protein, and high vaginal swab were taken and were noted.

Collection, Storage, and Transport of Samples

Placental samples which include patients with gestational age <37 weeks and term deliveries after completing 37 and within 42 weeks of gestational age (which is considered as control group) were collected immediately after delivery and examined thoroughly after washing under running tap water and were stored in 10% neutral buffered formalin container after obtaining photographs and transported to the laboratory for further investigations.

Gross Examination

Placental weight (using weighing scale) was noted after trimming the membranes. After 48 h of fixation with 10% neutral buffered formalin, placental membranes were examined for rupture and cut from the ruptured site up to the placental margin and kept aside for blocking making a Swiss roll with ruptured site as the starting point and placental margin as the end point. Shape, size, completeness, and consistency are noted.

The umbilical cord is assessed for length, the color, knots, hematomas, and thrombosis, and the cut section of the cord is obtained for blocking. Both maternal and fetal surfaces are examined for the color change, appearance of vessels on fetal surface and number of cotyledons on the maternal surface is noted. Representative tissue bits were obtained from appropriate areas from both normal and abnormal areas, and the placental tissues were sent for processing.

Microscopic Examination

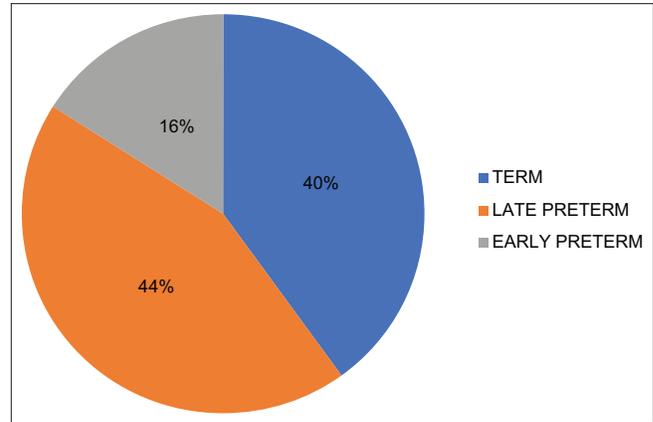
The stained placental slides were examined using compound microscope under $\times 10$ and $\times 40$. Changes such as chorioamnionitis, calcification, villitis, infarction, hemorrhage, chorangiomas, hyalinized villi, and perivascularitis were observed and the final observation were statistically analyzed and recorded accordingly.

DISCUSSION

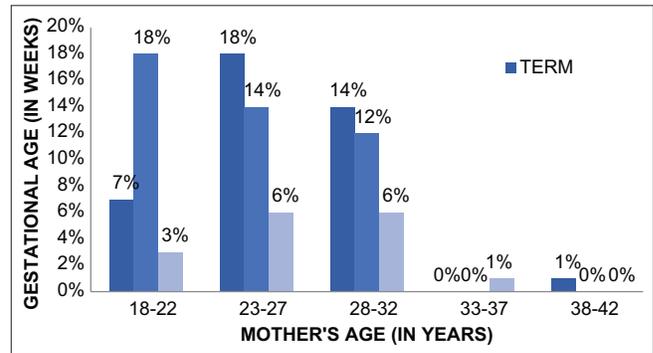
The placenta is a dynamic organ which plays a key role in maintaining fetal and maternal wellbeing. Fetal growth restriction and placental pathology go hand in hand. It is generally accepted that intrauterine events have an important effect on neonatal mortality and the development of long-term morbidity.^[8] Therefore, placental examination may represent a means of investigating the intrauterine past to explain the present condition of the neonate. Timely examination of the placenta may even help in guiding therapies or surveillance of infants deemed at increased risk for mortality or significant morbidity.^[9]

In our study, among 100 placental study, 40 cases (40%) were term and 60 cases (60%) were preterm placentas, in which early preterm were 16 (16%) and late preterm were 44 (44%) [Graphs 1-10].

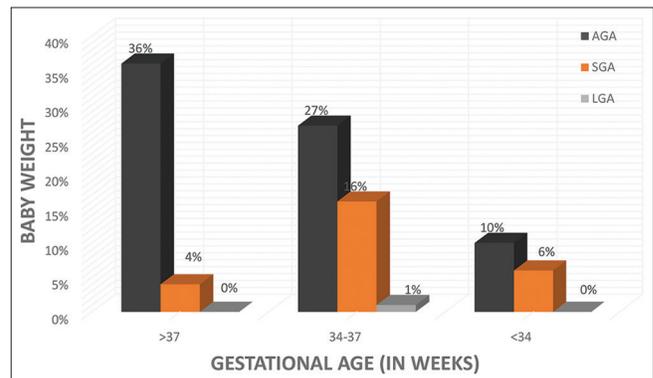
As placental weight is one of the key indicators of fetal intrauterine status, among term placenta, 26% weighed between 501 and 750 g and 14% weighed between 251 and 500 g. In the late preterm placenta, 6% were within 501–750 g and 38% were within 251–500 g. Among the early



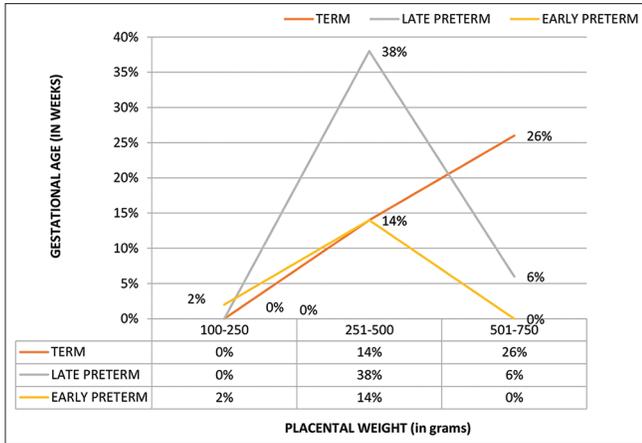
Graph 1: Percentage of gestational age. The study includes 100 cases out of which 40 (40%) cases were term and 60 cases (60%) were preterm including early and late preterm. Among which 44 (44%) were late preterm and 16 (16%) were early preterm



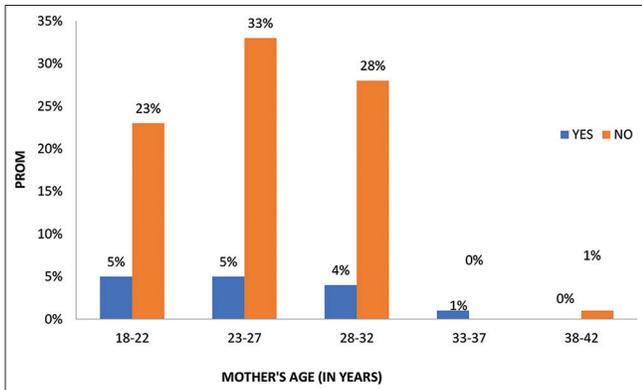
Graph 2: Graph explains the relationship between the age of mother with gestational age in weeks. Among the age group of 18–22 years, 23–27 years, 28–32 years; 7%, 18%, 14% are term deliveries respectively, about 18%, 14%, 12% are late preterm deliveries, respectively, and 3%, 6% and 6% were early preterm deliveries, respectively



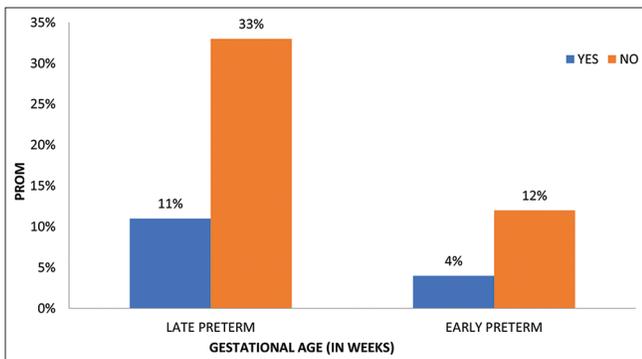
Graph 3: Comparison between gestational age and the weight of the baby. According to Fenton's centile chart, small for gestational age (SGA) $\leq 10^{\text{th}}$ percentile. Appropriate for gestational age (AGA) = 10^{th} – 90^{th} percentile. Large for gestational age (LGA) $\geq 90^{\text{th}}$ percentile. Graph depicts the comparison of gestational age with the weight of the baby, among 40 term babies, 4 was found to be SGA and 36 were AGA. Among 16 early preterm babies, 10 were AGA and 6 were SGA. Out of 44 late preterm babies 16 were SGA, 27 were AGA, and 1 was LGA



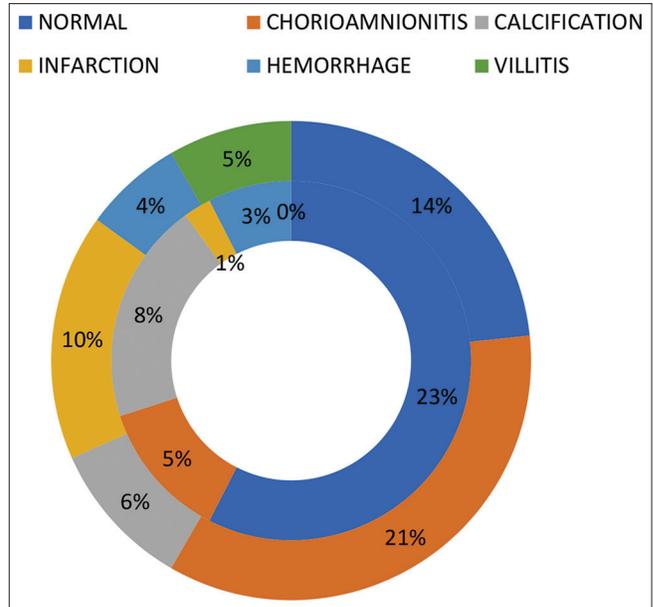
Graph 4: Comparison between gestational age and placental weight. Graph shows the comparison between gestational age and placental weight. Among the term placentas, 26% weighed 501–750 g and 14% weighed between 251 and 500 g. In the late preterm placentas, 6% were within 501–750 g and 38% were within 251–500 g. Among the early preterm placentas, 2% were found to be within 100–250 g and 14% were found to be within 251–500 g. There is increase in placental weight with gestational age of more than 37



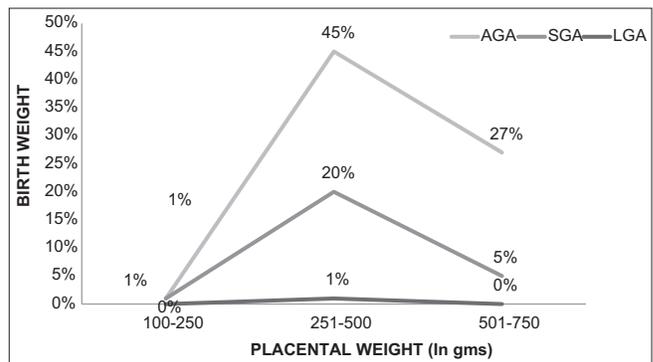
Graph 5: The role of mother's age with premature rupture of membrane (PROM). Mother's within the age group of 18–37 years presented with PROM. Higher at 18–27 years of age



Graph 6: Comparison between gestational age and premature rupture of membrane (PROM). Graph depicts the comparison between gestational age and PROM in early and late preterm delivery. About 11% of cases of late preterm presented with PROM and 4% cases of early preterm presented with PROM



Graph 7: Histopathological findings in term and preterm deliveries. Inner area of the doughnut shows the histopathological findings in term placentas in which 23% of the placentas were found to be with normal placental morphology; having two arteries and one vein embedded in the myxoid matrix and unremarkable, maternal surface shows mature vascularized villi lined by inner cytotrophoblast and outer syncytiotrophoblast with occasional syncytial knots, fetal parenchyma also shows mature terminal villi and 5% showed features of chorioamnionitis, 8% of the placentas revealed occasional focal areas of calcification on the maternal as well fetal surfaces. About 1% showed infarction and 3% showed hemorrhagic changes. Outer area of the doughnut shows the histopathological findings in preterm placentas in which the placental tissue reveals 14% of normal morphology, 21% of chorioamnionitis with inflammatory infiltrate and edema in the membrane with increased syncytial knots, 6% shows focal areas of calcification, 10% shows focal and extensive areas of infarction with increased syncytial knots, 4% had hemorrhagic and perivascular changes with focal hyalinized villi, and 5% had villitis with mixed inflammatory infiltrate in the chorionic villi



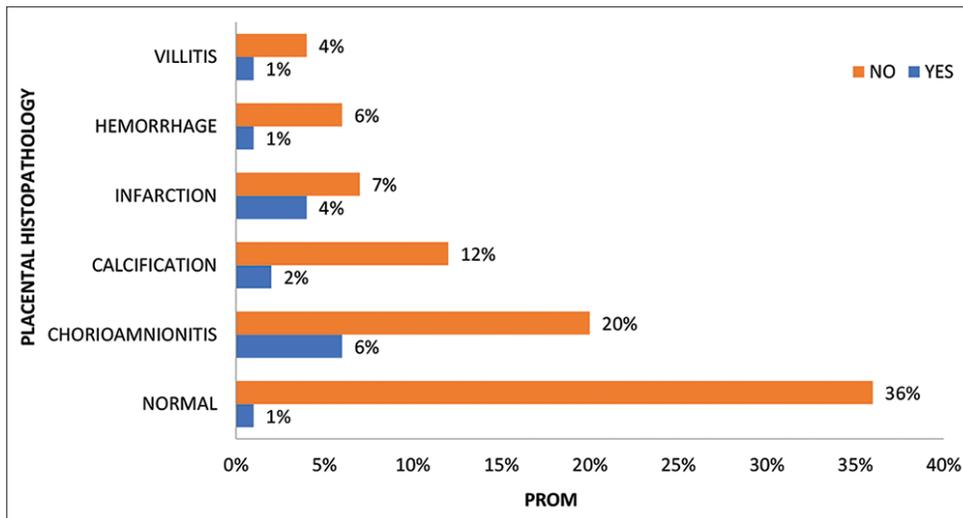
Graph 8: Correlates placental weight and birth weight of the baby. Within 100–250 g of placental weight 1%, 1%, and 0% were appropriate for gestational age (AGA), small for gestational age (SGA), and large for gestational age (LGA), respectively. Within 251–500 g of placental weight, 45%, 20%, and 1% were AGA, SGA, and LGA, respectively. Within 501–750 g, 27%, 5%, and 0% were AGA, SGA, and LGA, respectively. As the placental weight increases, baby's birth weight also increases

preterm placentas, 2% were found to be within 100–250 g and 14% were found to be within 251–500 g [Graph 4].

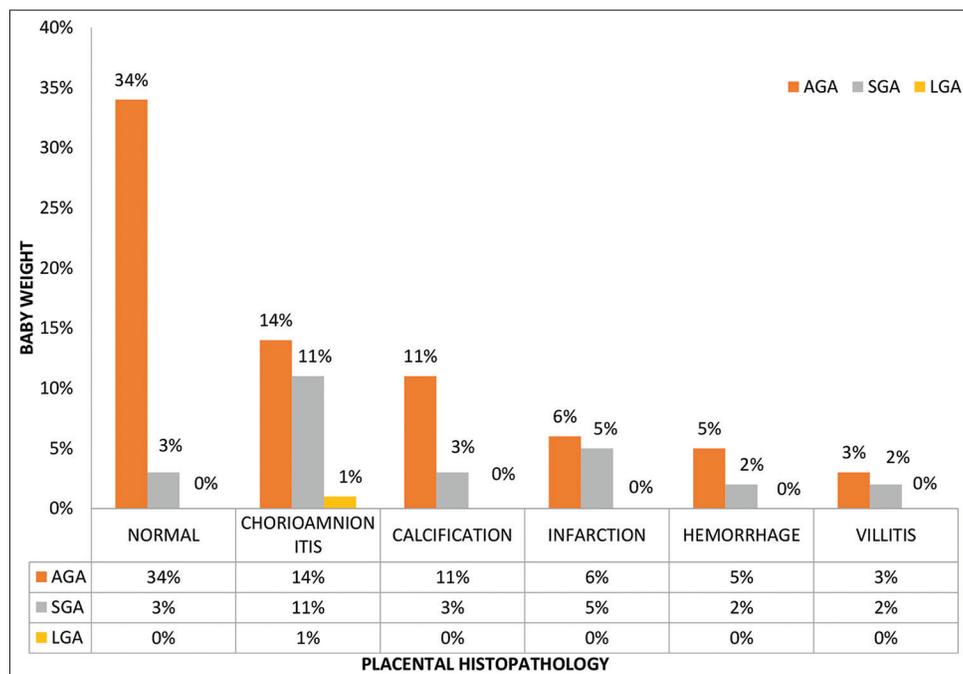
Histopathological findings among term placenta in which 23% of the placentas were found to be with normal morphology, having two arteries and one vein embedded in myxoid matrix and unremarkable, maternal surfaces show mature vascularized villi, and fetal parenchyma also shows mature villi and 5% showed features of

chorioamnionitis, 8% of the placentas revealed occasional focal areas of calcification on the maternal as well fetal surfaces, 15% showed infarction, and 3% showed hemorrhagic changes [Graph 7].

Histopathology findings among preterm placenta in which 14% normal morphology, 21% of chorioamnionitis, 10% shows focal and extensive areas of infarction with increased syncytial knots, 4% had hemorrhagic and perivasculitis



Graph 9: Relationship between premature rupture of membrane (PROM) and histopathological findings in term and preterm deliveries. In the studies of 100 cases, 15 cases presented with PROM with consisted of 1% with normal placental histopathology, 6% with chorioamnionitis, 2% with calcification 4% with infarction, 1% with hemorrhage, and 1% with villitis



Graph 10: Relation between weight of the baby and histopathological findings in term and preterm placentas. It is illustrated that the placentas of appropriate for gestational age baby accounted 34% of normal placental morphology, 11% of chorioamnionitis, 11% of calcification, 6% of infarction, 5% of hemorrhage and 3% of villitis. Small for gestational age babies accounted with 2% of normal placental morphology, 11% of chorioamnionitis, 3% of calcification, 5% of infarction, 2% of hemorrhage, and 2% of villitis. About 1% placentas of large for gestational age baby had chorioamnionitis

changes with focal hyalinized villi, and 5% had villitis with mixed inflammatory infiltrate in the chorionic villi [Graph 7].

Histopathology study among term and preterm comparison, it shows chorioamnionitis with Chi-square 19.604 with confidence interval of 35.66%–77.04% with $P < 0.0001$, calcification with $P = 0.466$, placental infarction with confidence interval of 41.51–92.47% with $P = 0.0002$, placental hemorrhage with confidence interval of –31.33–52.31% with $P = 0.613$, and villitis with confidence interval of 38.55%–100% with $P = 0.002$.

Histopathology among term and preterm placenta relative risk is 2.3 which means that preterm group has 2.3 times more risk of abnormal placental histopathology than term group.

CONCLUSION

Among histopathological study between term and preterm placenta, preterm placentas were most commonly associated with abnormal histopathological finding among

which chorioamnionitis is most common abnormal pathology.

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