Chorangiosis of the Placenta: Association with Maternal Profile and Neonatal Outcome, Experience at our Centre

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Abstract
Chorangiosis is a vascular change of the placenta that involves the terminal chorionic villi. It has been proposed to result from longstanding, low-grade hypoxia in the placental tissue and has been associated with conditions such as pre-eclampsia, diabetes and intrauterine growth restriction (IUGR). The entity has been bracketed with adverse feto-maternal outcome. This interplay of maternal and fetal factors may combine to produce this pathologically distinct entity of clinical significance. To characterize chorangiosis with its related maternal and fetal profile, we identified 15 cases of chorangiosis at our centre.

Material and Methods: Histomorphology of 50 placentas received in a tertiary care hospital were studied for chorangiosis/chorangiomaticus lesions as per the defined criteria. Association with neonatal and maternal profile was determined.

Results: Among the 50 placentas received in a tertiary care hospital, 15 had evidence of chorangiomaticosis/chorangiosis. No Fatal outcome was present in our cases, while the associated neonatal morbidity in the form of IUGR, Low Birth Weight, prematurity and NICU admissions were high. In terms of maternal profile, strong positive association of chorangiomaticus lesions with pregnancy induced hypertension/preeclampsia was noted.

Conclusion: This admonishes the pathologists to identify this entity that elucidate causes of neonatal morbidity and mortality even if they do not directly contribute to it.

Keywords: Chorangiosis, Placenta, pre-eclampsia, chorionic villi, neonatal outcome.

Introduction
Normal chorionic villi should contain no more than 5 vascular channels. Chorangiosis refers to the marked increase in the number of vascular channels in non-infarcted, non-ischemic areas of the placenta. The classic definition is more than 10 capillaries in more than 10 villi in several areas of placenta. It is an uncommon finding that is widely described as a compensatory response to chronic hypoxia\[1\]. Its commonly associated with various feto-maternal and placental conditions such as women living in high altitudes, pre-eclampsia, eclampsia, diabetes mellitus, severe anemia, syphilis, smoking \[2\]. Chorangiosis should be differentiated from congestion, in which vasculature is numerically normal, and from tissue
ischemia with shrinkage of villi. The criteria to evaluate the severity of this process include determining the number of vessels within each villus and the placental area throughout which the vasculature is seen.

Chorangiosis is a placental change that has not been extensively studied. Its etiology is still not clear, but it is believed to result from long-standing placental hypoperfusion or low-grade tissue hypoxemia. This also occurs in pre-eclampsia, a condition in which placental tissue hypoxia causes villous capillary endothelial cell proliferation and capillary hypervascularity[3].

Chorangiosis has been associated with increased perinatal morbidity and mortality, though the ultimate mechanism by which chorangiosis is involved in adverse perinatal outcomes is unknown. The interaction of maternal, placental, and fetal factors may combine to produce this pathologic change. Whatever its cause, it should be considered as a placental sign of potential clinical significance.

This underlines the significance of chorangiosis and related placental vascular lesions as signs of neonatal morbidity and mortality.

Materials and Methods
This study was a prospective observational study in a tertiary care hospital. Total of 50 placentas were studied.

The placentas were collected in a sterile bag with formalin and kept in a thermocol box with ice for transport to the department of Pathology where the following procedures were done

- The placenta was weighed and examined for any anomalies including those of umbilical cord.
- Placenta was kept for fixation for 24 hours.
- Sections were taken from the placenta: 3 representative sections of the placental parenchyma
- 2 cross sections of UC at both maternal and fetal end
- Membrane roll

Any grossly abnormal areas

Haematoxylin and Eosin staining was done as per the protocol. Slides were then interpreted by pathologist to look for chorangiosis.

Maternal and neonatal data was collected as explained in Table 1 and Table 2. Data was also collected on neonatal morbidity and mortality which included requirement of resuscitation, duration of NICU stay, use of CPAP or mechanical ventilation. Neonates requiring NICU admission because of various reasons like RDS, prematurity, LBW and other complications were shifted to NICU. Rest of the neonates were kept with the mother and followed up.

The diagnostic criteria of chorangiosis used in our study was the same as suggested by Altshuler in 1984[1]. A diagnosis of chorangiosis was made when on microscopic examination, with 10x objective, 10 villi, each with ten or more vascular channels were present in ten or more non infarcted areas of at least three different placental areas. Chorangiosis was differentiated from congestion in which the vessels were numerically normal and from tissue ischemia in which shrinkage of villi is discerned.

Results
A total number of 50 placentas were examined, of which fifteen were diagnosed as chorangiosis on histomorphology of the placenta. The average gestation period was of 37 weeks. Ten (66%) cases had premature delivery with gestational ages between 30 and 34 weeks. The various maternal and fetal conditions studied with chorangiosis tabulated below;

| Maternal conditions | Incidence Number | Percentage |
|---------------------|-----------------|------------|
| PIH                 | 12              | 80%        |
| DM/GDM              | 04              | 26%        |
| Smoking             | 0               | -          |
| Tobacco             | 0               | -          |
| High Altitude       | 0               | -          |
| Preterm Labour      | 10              | 66%        |
| Cesarean Section    | 12              | 80%        |
Table No 2. Maternal conditions

| Neonatal outcome       | Incidence Number | Percentage |
|------------------------|------------------|------------|
| CPAP                   | 02               | 13%        |
| Resuscitation          | 04               | 26%        |
| NICU admission         | 04               | 26%        |
| Low Birth Weight       | 10               | 66%        |
| IUGR                   | 08               | 53%        |
| Congenital Anomalies   | 01               | 6%         |

Amongst the maternal profile, Pregnancy induced hypertension/pre eclampsia were present in 80% of the cases while 26% of the patients had associated Diabetes Mellitus/Gestational Diabetes Mellitus. A high rate of cesarean section was seen amongst these cases (80%) with 66% being preterm labour. It is postulated that the high cesarean section rate was on account of chorangiosis, a marker of chronic hypoxia, because of long standing hypoxia coupled with the stress of labor.

Amongst the neonatal profile, 66% of the cases were Low Birth Weight while 53% were IUGR, 26% of the patients required resuscitation and were admitted in NICU while only 13% were put on CPAP. There was no case of neonatal mortality amongst the cases studied.

Discussion
The etiology and clinical associations of chorangiosis are not well understood; however, this finding is associated with fetal, maternal, and placental disorders.

The association of chorangiomatous lesions with high altitude, as elucidated in an earlier report highlights the link between this lesion and hypoxia hypobaric hypoxia at high altitude could be the etiology. Overexpression of angiogenic cytokines such as vascular endothelial growth factor, which is known to be up regulated by this factor in vitro, may mediate this effect. An almost similar explanation goes for its association with preeclampsia wherein placental tissue hypoxia causes villous capillary endothelial cell proliferation

In our study, a total of 50 placentas were sent for histo-pathological examination to look for evidence of chorangiosis. The association of chorangiosis with neonatal morbidity and mortality and maternal profile was analysed.

Out of the total 50 placentas included in our study, 15 placentas showed evidence of chorangiosis on histopathological examination. Thus incidence of this vascular lesion at our centre was 30%. Our study has also identified the antenatal characteristics seen to be associated with chorangiosis as well the pregnancy outcome. At the same time the neonatal outcome was determined for such cases. Amongst the maternal factors, pre-eclampsia was seen to be strongly associated. Amongst the pregnancy outcome, cesarean sections were found to be strongly associated. The rate of cesarean section in this study was 81%. Study done by Shariska S Peterson et al also showed increased trend in cesarean sections amongst patients diagnosed as chorangiosis[7].

Our study reveals that placental chorangiosis is associated with high neonatal morbidity. There was no case of neonatal death, although morbidity in the form of LBW, IUGR, NICU admissions, requirement of CPAP was high. One case showed congenital anomaly in the form of single single kidney on ultrasonography. The findings pertaining to neonatal and fetal morbidity corroborates with the studies conducted by Priyanka et al[8] and Amulyajit et al[9].

The strengths of the study are that it is one of the very few indian studies done on placental chorangiosis that also determines the association with neonatal outcomes as well as the maternal profile. Also, the clinic-pathological associations studied here are relevant in the setting of developing countries.

The limitations of the study were its small sample size and absence of a control group.

Conclusion
Till date, to the best of our knowledge, the exact incidence of Chorangiosis has not been documented and this uncommon and underreported entity imposes diagnostic implications. Although, the study involves a
relatively small number of cases, however the clinic-pathological associations is relevant in the setting of developing countries. We reiterate that a sizeable number of these lesions pose potential implications for neonatal well-being and affect the pregnancy outcome. Therefore, this rare placental vascular pathology is important to diagnose and renders a challenge to the pathologist in view of the associated potential critical complications altering feto-maternal outcome. Follow up of such cases for screening of congenital anomalies can also help the pediatrician in limiting the neonatal morbidity and mortality at least to some extent.

Conflicts of Interest
The authors declare that they have no conflicts of interest.

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