Original Research Article

Study of Risk Factors Associated With Term Low Birth Weight Neonates and its PlacentalHistopathological Correlation

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Abstract

Aims: The study was aimed to assess the risk factors leading to low birth weight in term neonates and correlate them with placental histopathology in cases of term LBW. **Material and Methods**: The study was conducted as a cross sectional study, at tertiary care centre on females delivering term neonates with LBW. All the females were subjected to detailed history, examination and blood investigations. Following delivery, baby details were recorded and placentae collected were subjected to gross and histopathological examination. **Results**: Incidence of term LBW was 13.39%. Anemia (33.5%) and hypertensive disorders of pregnancy (29.75%) were noted to be major high-risk factors. Shift in centrality of cord insertion was found to be a significant risk factor for LBW (P value =0.001 and 0.021). Baby weight and placental weight were both reduced in the presence of risk factors. Higher number of placental lesions were significantly associated with low birth weight ($p<0.05$) and it was found that more the number of placental lesions, greater was the decrease in the birth weight of the neonates. All the histopathological findings of placentae correlated with high risk ($p<0.05$). **Conclusion**: Examination of placentae conducted in present study proved to be a useful adjunct in finding the pathogenic mechanism resulting in LBW and can be helpful in timely detection, planning and management including desired interventions in future pregnancies.

Keywords: Histopathological examination, risk factors, placenta, term LBW.

Introduction

The antenatal health care given to pregnant women has great influence on the rates of perinatal mortality and morbidity. Amongst the different causes of perinatal mortality, low birth weight (LBW) is the single most significant factor and accounts for about 2/3 deaths among infants.[1] Low birth weight babies are always at risk of getting serious complications such as hypothermia, neonatal sepsis, meconium aspiration, metabolic and hematological disorders, cognitive birth dysfunction, respiratory and gastrointestinal disorders. Some studies also report higher incidence of coronary diseases, hypertension and diabetes mellitus in adult life.[2] Incidence of LBW varies from 5-40% of live births. However, in India, one-third of all infants weigh less than 2500gms. Prevalence of LBW varies widely worldwide, ranging from 7-18%.[2]

Placenta is a unique organ that arises denovo, and is important for the growth and development of fetus. The word placenta has been derived from Greek word plakuos meaning flat cake (due to its gross anatomical shape).[3]

The triad of placenta, fetus and mother work together throughout the pregnancy to achieve a composite functional equilibrium during prenatal period and dysfunction of any one of them can jeopardise the others.[4] The placenta has not been given much attention and understudied by the scientific community. Improper functioning of this vital and critical organ leads to fetal abnormalities, preterm labor, preeclampsia and IUGR.[5] Placental causes associated with low birth weight include placental infarcts, microscopic chorionic cysts, decidual arteriopathy, chronic villitis, placental hemangiomas, placenta abruptio, circumvallate placenta and umbilical cord abnormalities.[6-8]

Pathological examination of placenta is seldom performed in institutions and thus the etiology for low birth weight in such infants are not much highlighted. Histopathological study of placenta can reveal certain changes in placenta occurring due to these high-risk factors and thus we can correlate various high-risk factors and placental changes explaining adverse fetal outcome that is LBW in full term pregnancy. As there is a clear relationship between placental pathology and fetal growth restriction, a thorough study of placenta is of significant importance to evaluate possible etiological factors. This study aimed to assess the risk factors leading to low birth weight in term neonates and correlate them with placental histopathology in cases of term LBW.

Materials and methods

The study was conducted as a cross sectional study in the Department of Obstetrics and Gynaecology, Sultania Zanana Hospital, during the study period of 1 year i.e. from 23rd January 2019 to 22nd January 2020. All the females delivering term neonate (at or after 37 weeks of

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pregnancy), with birth weight of less than or equal to 2500gms (LBW), irrespective of mode of delivery (caesarean section or vaginal delivery) and giving consent for the study were included whereas patients with multifetal gestation or delivering congenitally malformed fetus were excluded.

After obtaining clearance from the Institutional Ethical Committee, admitted patients fulfilling the inclusion criteria were taken in the study and written consent was obtained from all of them. These patients underwent a detailed history including sociodemographic data such as age, address, education, income etc. and details were noted in questionnaire. Obstetric history was documented from all the study participants. Past history of medical and surgical illness if any was also obtained. History of any high-risk factor associated with previous pregnancy or any high-risk factor identified in present pregnancy was also documented.

All the females were then subjected to detailed clinical examination, general condition of females along with vitals were recorded. Following delivery, baby details including the weight, sex of baby and general condition of the baby was recorded. Placenta of each case was washed with tap water and collected in clean container. The specimen was examined with regard to following gross examination features such as size, shape of placenta, weight of placenta, attachment of umbilical cord and number of vessels. Circular, spherical, discoid shape were taken as normal. Oval and irregular shape as abnormal. Central umbilical cord attachment was taken as normal and eccentric and marginal (shift more than 2cm.) was taken as abnormal. Membranes were looked for any changes in color and site of rupture of the membrane and transparency, no. of cotyledons, presence of infarction, calcification, meconium staining and retroplacental hematoma.

Placentae were preserved with 10% formalin solution and sent to department of pathology for histopathological examination. Different histological findings were observed and quantified.

Observation Chart

Table 1: Distribution According to Baseline Variables

Baseline variables		No. of case (n=400)	Percentage
Age of mother	<20	19	4.75%
	20 to 24Yrs	234	58.50%
	25 to 29	98	24.50%
	30 to 34	41	10.25%
	35 and above	8	2.00%
Parity	Primi	230	57.50%
	Multi	170	42.50%
Birth order	1	230	57.50%
	2	103	25.75%
	3	46	11.50%
	4 and above	21	5.25%
Antenatal visit	<4	163	40.75%
	4 and above	237	59.25%
Sex of neonate	Male	198	49.50%
	Female	202	50.50%
Gestational age	37-40	787	94.25%
	>40	23	5.75%
Complications in neonate	Yes	66	12.50%
	No	334	87.50%

Table 2: Percentage of The High-Risk Factors in LBW Neonates

High risk factors	Number (n=400)	Percentage
Anemia	134	33.5
Mild and moderate anemia	123	30.75
Severe anemia	11	2.75
Hypertensive disorders of pregnancy	79	29.75
GHTN	20	5
Pre-eclampsia	41	20.25
Eclampsia	18	4.5
Abruptio Placentae	5	1.25
IUGR	15	3.75
Hypothyroidism	18	4.5
Oligohydramnios	14	3.5
Drug addict (Tobacco)	23	5.75
Short stature	5	1.25
Others	16	4
Two high risk factors	57	14.25

More than two high risk factors	15	3.75
No high risk identified	19	4.75

Table 3: Relation Between Umbilical Cord Insertion With Baby Weight and Placental Weight

Type of Cord Insertion	Number	Weight of Baby	Weight of Placenta	Average Weight of Baby	Average Weight of Placenta
Centric	278	594 Kg	100.908 Kg	2136	362
E-Centric	98	197 Kg	31.57 Kg	2011	322
Marginal	24	43 Kg	7.128 Kg	1804	297
P value		-	-	**0 .001**	**0 .021**

Table 4: Relationship Between High Risk Factors, Mean Baby Weight, Mean Placental Weight and Baby to Placental Weight Ratio

High risk factors	Mean baby weight(gm)	Mean placental weight (gm)	Baby to placental weight ratio
Mild and moderate anemia	2173	370	5.869
Severe anemia	1900	323	5.867
GHTN	2190	355	6.175
Pre-eclampsia	2080	332	6.266
Eclampsia	2027	324	6.244
Abruptio Placentae	1800	298	6.040
IUGR	2120	351	6.03
Hypothyroidism	2172	364	5.959
Oligohydramnios	2221	356	6.23
Drug addict (tobacco)	2091	340	6.13
Short Stature	2060	339	6.076
Others	2175	363	5.986
Two high risk factors	1985	326	6.07
>2 high-risk factors	1740	276	6.299
No high risk identified	2184	360	6.058
Total	2097	347	6.03
P value	**0.032**	**0.002**	**0.014**

Table 5- Gross and Histopathological Findings of Placenta

		Number (n=400)	Percentage
Gross	Infarction	38	9.5
	Calcification	152	38
	Meconium Staining	8	2
	Retro placental Hematoma	12	3
	Subchorionic Fibrin Deposition	19	4.75
Microscopic findings	0-1	6	1.5
	2 and 3	113	28.25
	4 and 5	196	49
	≥6	85	21.25
	Syncytial Knots	231	57.75
	Fibrinoid Necrosis	223	55.75
	Cytotrophoblastic Proliferation	124	31
	Hyalinized Villi	197	49.25
	Stromal Fibrosis	148	37
	Medial Coat Proliferation of Medium Sized Vessels	60	15
	Perivillous Fibrin Deposition	98	24.5
	Calcification	276	69
	Infarction	233	58.25
	Avascular Villi	72	18
	Blood Vessels Abnormality	57	14.25

Above table represents gross and microscopic findings of placenta.

Table 6: Relationship Between Birth Weight of The Baby and Number of Microscopic Lesions

BIRTH WEIGHT	0-1 lesions		2-3 lesions		4-5 lesions		≥6 lesions		P value
	NO.	%	NO.	%	NO.	%	NO	%	
2-2.4	5	1.58	105	33.22	171	54.11	35	11.07	0.001
1.5-1.9	1	1.53	7	10.76	22	33.84	35	53.84	
<1.5	0	0	1	5.26	3	15.78	15	78.94	

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Table 7: Distribution of Histo-Pathological Lesions in Different High-Risk Groups

	TOTAL	WITH 2 HIGH RISK FACTO R	>2 HIGH RISK FACTORS	ANEMIA	HDP	ABRUPTIO PLACENTAE	IUGR	HYPO TH YROIDISM	OLIGO HYRAM INOS	SHORT STATU RE	DRUG TOBA CCO	OTH ERS	NO HIGH RISK IDENTIFIED
Syncytial Knots	57.75	70.17	66.66	54.47	65.82	40	66.66	55.55	42.85	20	47.82	37.5	52.63
Firbrinoid Necrosis	55.75	78.94	80	30.59	87.34	100	80	66.66	42.85	60	78.26	31.25	31.57
Cytotrophoblastic Proliferation	31	28.07	26.66	38.8	22.78	40	20	33.33	28.57	40	21.73	25	42.1
Hyalinized Villi	49.25	54.38	40	53.73	54.43	60	60	38.88	50	20	26.08	31.25	36.84
Stromal Fibrosis	37	36.84	53.33	43.28	36.7	20	33.3	33.33	14.28	80	30.43	6.25	31.57
Proliferation of Medium size Vessels	15	29.82	33.33	5.22	30.37	80	20	5.55	7.14	80	8.69	56.25	10.52
Perivillous Fibrin Deposition	24.5	35.08	40	16.41	29.11	40	40	33.33	14.28	0	21.73	6.25	21.05
Calcification	69	70.17	66.66	64.17	79.74	60	73.3	61.11	64.28	20	73.91	0	63.15
Infarction	58.25	80.7	80	47.01	73.41	100	46.6	55.55	50	20	56.52	37.5	23.31
Avascular Villi	18	21.05	33.33	3.73	20.25	20	53.3	5.55	7.14	60	43.47	18.75	36.84
Blood Vessels Abnormality	14.25	24.56	20	2.98	34.17	60	40	5.55	4	0	8.69	0	5.26
P value	0.011	0.001	0.001	0.022	0.023	0.001	0.001	<0.001	0.014	0.02	0.001	0.012	

In present study, all the histopathological findings of placenta correlated with high risk ($p<0.05$).

Results

A total of 15590 neonates were born during the study period at our study centre, of them 4073 were low birth weight and among them 2087 were term L.B.W babies (13.39%). Out of these term born L.B.W during the study period of one year; 400 cases were taken with mean gestational age of 38.3 weeks.

Majority of the women delivering term Low Birth Weight belonged to the age group 20 to 24 years (58.50%). Occurrence of LBW was lower in females with increasing birth order. Majority of women had 4 or more antenatal visits (59.25%) as compared to 40.75% women with less than 4 antenatal visits. About 12.5% of term neonates who were low birth weight developed complications.[Table 1]

Anemia (33.5%) and hypertensive disorders of pregnancy (29.75%) were noted to be major high-risk factors in the women delivering low birth weight babies, together accounting for 63.25% of the high-risk factor. In our study, shift in centrality of cord insertion was found to be a significant risk factor for LBW (P value =0.001 and 0.021). The more the shift, the less was the mean baby weight and mean placental weight. This finding can be utilized in future for antenatal screening through ultrasonography to predict any adverse fetal outcome.

In present study, baby weight and placental weight was reduced in presence of risk factors. Both these weights further decreased with increase in the severity of the high-risk factor. Higher number of placental lesions were significantly associated with low birth weight ($p<0.05$)[Table 4-6]

Statistical Analysis

Collected data was entered in Microsoft Excel. Data was finally tabulated, analyzed and interpreted by using IBM SPSS ver.20. Data comparison was done by applying Chi-Square test and ANOVA to find the statistical significance of the comparison. Significance level was fixed at $P<0.05$.

Discussion

Weight of a baby at term depends on gestational age and rate of fetal growth in uterus. Birth weight is one of the important determining factors of an infant's survival and future development.[6] Birth weight less than that expected from the genetic potential might be caused by fetal, maternal or placental factors or a combination of certain risk factors, leading to an impaired placental transport of nutrients or reduced growth potential of the fetus.[7] The morbidities of term LBW are mainly related to uteroplacental insufficiency and poor energy substrate transfer. Present study shows that anemia (33.5%) and hypertensive disorders of pregnancy (29.75%) are the major high-risk factors found in the women delivering low birth weight babies, together accounting for 63.25% of the high-risk factors, which is in accordance with Bhaskar et al study.[12] Anemia was one of the common problems in study of Deshpande et al, where almost 42.5% of mothers who delivered LBW babies were anemic.[13]

The adverse effects of maternal smoking for human pregnancy have been studied since long. Use of smoking and illicit drugs during pregnancy was said to be associated with pregnancy complications and low birth weight. In our study, we found total 23 cases (5.75%) involved in drug addiction, mostly tobacco chewing, affecting both primipara (60.86%) and multipara (39.14%). Similar results were observed in a study by Gupta et al, in which he observed that smokeless tobacco use was associated with an average reduction in birth weight by 105gm. and reduction in gestational age of 6.2days.[8]

In our study, about 4.5% pregnant women had hypothyroidism, where birth weight of baby and placental weight were reduced. Similarly, Glenoer et al documented that thyroid during pregnancy affects both mother and fetus with a potential role in development of child.[9] Our study findings were consistent with findings of previous studies.[10,11]

Placental changes included are related to placental morphology including both gross and microscopic changes in placenta. In our study, oval and irregular shaped placentas were considered as

abnormal shaped placenta. Normal shaped placentae were 74.5% and abnormal shaped placentae were 25.5% in our study. Also, the incidence of altered shaped placenta was 2.6 times more as compared to the previous studies.[14,15] In our study, increased abnormal shaped placenta may be due to different high- risk factors. Mode of insertion of the umbilical cord on the placenta is essential for the growth of the fetus and its development in the uterus of the mother. In our study, eccentric attachment was significantly associated with low birth weight. More the shift less is the baby weight and placenta weight. Brett et al has suggested that a shift in the centrality of the umbilical cord insertion on the chorionic plate reflects the level of vasculature available for nutrient supply.[16] Salafia et al showed that a great shift leads to lower level of vasculature distribution for nutrient exchange and vice versa leading to low placental weight and LBW neonates.[17]

The present study attempted to correlate baby's birth weight and placental weight and showed that weight of new born baby and placentae were significantly low in all high-risk groups and further decreased according to severity of high-risk factors. Birth weight/placental weight ratio mostly decreased in all high-risk groups except in Anemia. Also it was found that birth weight to placental weight ratio was less in anemia (5.869) while it was more in hypertensive disorders of pregnancy groups. Fox et al specified that increased size of placenta in maternal anemia was indicative of compensatory mechanism by which the placenta attempts to overcome decreased oxygen in maternal blood.[18] Majumdar et al[19] and Salmani et al[20] observed that placental weight was lower in cases of pre-eclampsia, macroscopic features like retro-placental hemorrhage, infarction and calcification were found to be more in the placenta of mothers suffering from HDP. The fetoplacental unit was adversely affected in HDP due to placental insufficiency.

Present study showed that most common gross examination finding was calcification which was seen in 38% of the placentas, infarction in 9.5%, and retro-placental hematoma in 3% placentas. In the study of Nkwabong et al, significant placental lesions observed such as placental infarcts and chronic villitis.[21] Nigam et al observed calcification and subchorionic fibrin deposition in significantly higher numbers of placenta infarction from patients than controls ($P<0.01$).[22] We also studied the association of fetal birth weight with the microscopic changes in the placenta. We found that higher no. of placental lesions was significantly associated with low birth weight, suggesting that single lesion might not be enough to induce intrauterine growth retardation unless it is widely spread throughout the whole placenta. So, it is likely that it is the accumulation or total burden of lesions on placenta that when present for a sufficient time leads to LBW baby. Similar association between placental changes and birth weight have been observed in previous studies, where multiple placental lesions can contribute to retarded growth of the fetus.[23,24]

Syncytial knots occur due to reduced perfusion of villi and morphologically it was the reflection of decreased utero-placental blood flow.[25] Dhall et al[26] observed increased stromal fibrosis in anemia that was 42.65%, similarly in our study we found it to be in 43.28% cases of anemia. In our study, we noted that in cases of tobacco chewing, syncytial knot was seen in 47.82% cases, fibrinoid necrosis in 78.26% cases, calcification in 73.91%cases and infarction in 56.52% cases. Majumdar et al[19] noted stromal and villous histopathological changes in placenta like stromal fibrosis, medial coat proliferation of the medium sized blood vessels and hyalinized villi were significant in the hypothyroidism. In hypothyroidism, a significant increase is seen in syncytial knot formation which may indicate a disturbance in the hormonal factors which may probably lead to altered morphology of the placenta. In our study we observed syncytial knotting in 55.55% cases, fibrinoid necrosis in 66.66% cases, cytotrophoblastic proliferation in 33.33% cases, calcification in 61.11% cases and infarction in 55.55% cases of hypothyroidism. In our study, percentage of syncytial knotting and fibrinoid necrosis was 42.85%. Calcification 64.28%, infarction 50%, and avascular necrosis 7.14% in cases of oligohydramnios. Our findings are consistent with the study of Spinillo et al[27]

Present study has some limitations in terms of small sample size which may not replicate the actual population. Also, we did not evaluate all the potential risk factors for low birth weight like marital status, micronutrient deficiencies among mothers, urinary tract/genital infections and the quality of antenatal care received by them others.

Conclusion

There is an identifiable group of women with high-risk for LBW baby. Full term LBW babies were found to be significantly associated with many risk factors, namely maternal age, socio-economic status, area of residence, parity, ANC visits, Anemia, HDP, IUGR, hypothyroidism, oligohydramnios and drug abuse (Tobacco chewing). The majority of placentas revealed presence of gross as well as histo-pathological lesions. Severity of LBW is related to the severity of microscopic changes found in the placenta.

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