CORRELATION OF FOETAL OUTCOME WITH SOME PATHOLOGICAL CHANGES OF PLACENTA*

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Placental morphology varies considerably during its short life span. Alterations in placenta as part of "ageing" phenomenon are probably a part of a maturation process and go hand in hand with continued growth of placenta. Placenta grows till 36th week and as a result immature villi are seen even till term. Hence in any study on placenta Fox (1975) has stressed the importance of analysing the placental pathology quantitatively and has stated that the importance of the lesions can be realised only when assessed in relation to foetal outcome.

Premature ageing of placenta is thought to be responsible for poor foetal outcome in pre-eclamptic toxaemic and for intrauterine growth retardation in cases not associated with any obvious maternal or foetal disorder. In anaemia there is anoxia on the maternal side and compensatory hypertrophy of placenta (Beischer *et al*, 1970). Placental changes in these abnormal situations and in normal term parturient are quantitatively analysed in this study and their correlation with foetal outcome studied.

Material and Methods

In the present study, placentae from 100 cases admitted to labour ward of Lady Hardinge Medical College and Hospital were studied grossly and histologically after formal fixation. Foetal outcome in these cases was noted. Cases selected for study were:

Group-I: Control: Normal term parturients—25.

Group-II: Intrauterine growth retardation; birth weight less than 2500 gms.—25.

Group-III: Toxaemia of pregnancy with blood pressure of 130/90 mm. of Hg. and above with or without edema and/or proteinurea—25.

Group-IV: Anaemia of pregnancy-Hb. less than 8.0 gm%.—25.

Each placenta was trimmed of membranes measured, washed and blood squeezed out, weighed and examined grossly for degree of calcification, extent of infarction and subchorionic fibrin deposit.

Each placenta was sliced and fixed in 10% formalin. From each specimen, 8 whole thickness tissue blocks, 2.5 cms x 0.5 cms in size were taken from definite

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representative sites along an S-shaped area so as to include all areas of placenta. The tissues were processed for paraffin blocking and sections cut, 5-7 u. in thickness, stained with conventional haemotoxylin and eosin stain and with periodic acid Schiff reagent as a special staining procedure. Random microscopic fields were selected from each slide and at least 800 villi were studied for:

1. Intervillous fibrin deposits: This was graded according to the extent of deposit in each high power field (H.P.F.), minimal as Grade-I, moderate as Grade-II, extensive as Grade-III.
2. Intravillous fibrin or fibrinoid change of whole villous.
3. Basement membrane thickening.
4. Villous fibrosis.
5. Syncytial knots.

Foetus

Following data was recorded in each case:

1. Any sign of foetal distress i.e. fetal heart rate outside 120-160/min. range with or without meconium stained liquor, except in breech deliveries.
2. Birth weight.
3. Apgar score at 1, 5 and 10 minutes.
4. Any stillbirth.
5. Neonatal morbidity and mortality till the time of discharge.

Observations

There were 6 (24%) perinatal deaths in toxaemia and anaemia group. Low apgar score i.e. less than 7 at 5 minutes was recorded in 3 (12%) cases in all 3 groups i.e. anaemia, toxaemia and IUGR (Table-I). Incidence of foetal distress was observed maximum in toxaemia i.e. in 11 (44%) out of 25 cases.

Cross Changes

With placenta weighing less than 300 Gms. intrapartum foetal distress was observed in 33.3% of cases (Table II). The

TABLE I
Foetal Outcome in Various Groups

Group	Control	Toxaemia	IUGR	Anaemia
Total No.	25	25	25	25
Foetal distress				
No.	5	11	7	6
%	20	44	28	24
Low Apgar				
No.	—	3	3	3
%	—	12	12	12
Stillbirth				
No.	—	3	—	1
%	—	12	—	4
Perinatal deaths				
No.	1	6	2	6
%	4	24	8	24

Foetal Distress—F.H.R. ranging outside 120—160/min. and/or meconium stained liquor except in breech delivery.
Low Apgar—Apgar less than 7/10 at 5 minutes (Drayge and Berendes 1966).

TABLE II

Correlation of Foetal Outcome With Gross Placental Changes

	Grading	Total No.	Foetal Distress		Law Apgar		Stillbirth		Perinatal Death	
			No.	%	No.	%	No.	%	No.	%
Placental weight	0—300 G.	36	12	33.3	4	11.5	2	5.5	7	19.4
	300—500 G.	51	14	26.6	5	9.5	2	3.8	9	15.2
	Above—500 G.	13	3	23.3	—	—	—	—	—	—
Placental co-efficient	0—15	64	19	30.4	6	9.6	2	3.2	8	12.8
	0.16—0.19	30	8	27.2	2	6.8	1	3.4	6	20.4
	0.2 or above	6	2	33.3	1	16.6	1	16.6	1	16.6
Placental infarction	Absent	63	17	25.6	6	9.6	—	—	7	11.6
	0—4%	27	7	25.9	2	7.4	1	3.7	3	11.1
	5—9%	9	4	44.1	1	11.0	3	33.0	4	44.1
	10% or above	1	1	100%	—	—	—	—	1	100
Subchorionic fibrin	Absent	78	21	27.3	8	10.4	4	5.2	15	19.5
	+	20	1	50.0	1	5.0	—	—	2	10.00
	++	2	6	30.0	—	—	—	—	—	—
Calcification	Absent	65	19	30.4	7	11.2	4	6.4	12	19.2
	+	29	9	32.4	2	7.2	—	—	3	10.8
	++	6	1	16.6	—	—	—	—	—	—

only significant correlation was of low placental weight with foetal distress and of the extent of placental infarction with stillbirth and perinatal deaths (Table III).

TABLE III
Statistical Evaluation of Table—II

		Foetal Distress	Low Apgar	Stillbirth	Perinatal
Placental weight Less than 300 Gms.		Significant	N.S.	N.S.	N.S.
d.f. 1, X^2 =	X^2	3.86	0.83	0.7	2.03
Placental Coeff.		N.S.	N.S.	N.S.	N.S.
d.f. 1, X^2 =	X^2	0.09	0.19	0.0028	0.91
Placental infarction		N.S.	N.S.	Significant	Significant
d.f. 3, X^2 =	X^2	3.92	0.12	18.10	8.99
Subchorionic fibrin.		N.S.	N.S.	N.S.	N.S.
	X^2	0.2	0.16	0.22	0.64
Placental calcification		N.S.	N.S.	N.S.	N.S.
d.f. = 1. X^2 =	X^2	.0046	0.703	2.237	1.74

N.S.—Not significant

No correlation was found with other foetal parameters, nor altered placental co-efficient was found to be significant.

Placental infarction was graded according to percentage of surface area infarcted. Stillbirth and perinatal deaths increased significantly when area infarcted was more than 5 per cent of the total.

Microscopic Changes

The frequency of syncytial knots was graded according to the percentage of villi showing syncytial knot formation; less than 30% was Grade I. 30 to 59% Grade II, 60 to 89% as Grade III, more than 90% as Grade IV. Foetal distress was more frequent with Grade III and Grade IV (Table IV) and stillbirth and perinatal death with Grade IV but this was not found statistically significant (Table V).

All foetal parameters were worse when more than 10% of villi showed fibrinoid necrosis (Table IV) but on statistical evaluation the difference was not found significant (Table V). Separately thickening of basement membrane also was not found significant but when fibrinoid necrosis was associated with thickened basement membrane in more than 2% of villi, 3 out of 4 such placentae were associated with intrapartum fetal distress and this was found to be statistically significant.

Intrapartum fetal distress was significantly increased with Grade II or Grade III of intervillous fibrin deposit i.e. fibrin was present and either was partially or completely filling the intervillous space in high power field. Other fetal parameters i.e. low apgar score, stillbirth and perinatal deaths were also more frequent with Grade III (Table IV) but this was not statistically significant.

Villous fibrosis was graded as 'absent', Grade I, when seen in 0-3% villi, Grade II when seen in more than 3% villi. Highly significant correlation was found, foetal outcome being worse i.e. more frequent foetal distress, stillbirths and neonatal deaths with increased villous fibrosis.

TABLE IV

Correlation of Foetal Outcome With Microscopic Placental Pathology

Pathology Change	Grading	Total No. (100%)	Foetal Distress		Low Apgar		Stillbirth		Perinatal Death	
			No.	%	No.	%	No.	%	No.	%
Syncytial Knot Count	I. 0-29%	38	14	36.4	2	6.2	—	—	6	15.2
	II. 30-59%	36	6	16.8	4	11.2	1	2.8	3	8.4
	III. 60-89%	22	7	32.2	13	13.8	2	9.2	5	23.0
	IV. Above 90	4	2	50.0	—	—	1	25.0	1	25.0
Fibrinoid Necrosis Villi	0- 5%	62	15	24	5	8.0	1	1.6	9	14.4
	5-10%	35	13	36.4	3	8.4	3	8.4	5	14.3
	Above 10%	3	1	33.3	1	33.3			1	33.3
Thickened Basement Membrane	Absent	28	10	35.7	6	21.0	—	—	8	25.5
	0-2%	64	15	22.5	2	3.0	3	4.5	4	6.0
	Above 2%	8	4	50.0	1	12.5	1	12.5	3	37.5
Combined Fib. Necrosis Thickened B.M.	Absent	69	14	19.6	8	11.2	3	4.2	11	15.4
	0-2%	27	12	44.4	—	—	1	3.7	2	7.4
	Above 2%	4	3	75.0	1	25	—	—	2	5.0
Intervillous Fibrin Deposit	Absent	51	8	15.8	3	6	—	—	5	10.0
	Grade—I	21	8	36.4	3	14.4	—	—	4	19.2
	Grade—II	23	11	48.4	1	4.4	3	13.2	4	17.6
	Grade—III	5	2	40.0	2	40.0	1	20.0	2	40.0
Villous Fibrosis	Absent	79	16	19.2	8	9.6	2	2.4	9	10.8
	I	14	6	42.6	1	7.1	—	—	2	14.2
	II	7	5	71.5	—	—	2	28.6	4	57.2

TABLE V
Statistical Evaluation of Table—IV

	Foetal Distress	Low Apgar	Still Birth	Perinatal
Correlation of Syncytial Knots	N.S.	N.S.	N.S.	N.S.
d.f. = 1, X^2	1.83	1.04	2.55	0.029
Fibrinoid Necrosis	N.S.	N.S.	N.S.	N.S.
d.f. = 1, X^2	1.83	0.6	1.06	0.03
Thickened Basement Membrane	N.S.	N.S.	N.S.	N.S.
d.f. = 1, X^2	0.85	1.08	0.48	0.01
Fibrinoid Necrosis with Thickened Basement membrane	Significant	N.S.	N.S.	N.S.
d.f. = 1, X^2	8.2	0.95	0.08	0.02
Intervillous Fibri.	Significant	N.S.	N.S.	N.S.
d.f. = 1, X^2	5.73	0.14	10.71	0.51
Villous Fibrosis	Significant	Highly Significant	Highly Significant	Highly Significant
d.f. = 1, X^2	7.54	0.74	11.83	10.48

N.S. = Not Significant

Discussions

Very little is known about the factors that control placental maturation and placental growth, not necessarily the two processess go hand in hand. Placenta continues to grow till 36th week but throughout intrauterine life foetus grows more rapidly in weight than placenta (Gruenwald, 1963) and thus it outgrows its nutritional supply.

Placenta is significantly smaller in mature growth retarded babies. Fox (1975) states that placenta being a foetal organ is small when foetus is small. Placenta of less than 300 Gms was found in 20 out of 25 normotensive IUGR cases but only in 5 out of 9 growth retarded babies in toxaemia and in 2 out of 12 growth retarded babies in anaemia. Only criterion considered being weight less than 2500 Gms. However, low placental weight does decrease functional reserve, as, though stillbirth and perinatal deaths were not significantly increased in this study but intrapartum fetal distress, was significantly more frequent when placenta weighed less than 300 Gms at term. No such relation was found with low placental co-efficient. Potter (1952) considers that there is little evidence that the foetal death is ever the result of insufficient placental size except in twins.

Placental infarction of more than 5% surface area was considered pathological as it was significantly more frequent in cases of toxaemia. With increased area of infarction, stillbirth and neonatal deaths were significantly more common. Fox (1967) and (1975) is of the opinion that in uncomplicated pregnancy placental infarction plays a little role in perinatal mortality and morbidity. But extensive infarction as found only in hypertensive complications in pregnancy, is associated with high incidence of foetal hypoxia.

Subchorionic fibrin deposition is considered to indicate good placental circulation and placental calcification of no

clinical significance (Fox, 1963 and 1975).

Certain histological changes such as syncytial nuclear aggregation, basement membrane thickening and stromal fibrosis are considered part of ageing phenomen of normal term placenta and occur prematurely in toxaemia. These were shown to be quantitatively increased in toxaemia and IUGR earlier (Mirchandani *et al*, 1979). Syncytial knot formation is seen with increased frequency in last weeks of pregnancy and more villi show syncytial knots in prolonged pregnancy and toxaemia. The nature of these is uncertain but it seems possible that these are a result of ageing changes as suggested by electron microscopic changes seen in nuclei. The loss of nuclei as a result of such sequestration is made up by fresh nuclei from cytotrophoblast (Fox, 1965), hence foetal jeopardy is not increased as found in present study even if syncytial knot formation was found in 60-89% of villi (Grade III) or in 90% or above (Grade IV).

The basement membrane separating the trophoblast from the villous stroma shows a progressive thickening between 34th week of gestation and term; at that stage it measures between 1000 and 3000A° in thickness. Villous fibrinoid necrosis is another change of senescence as it probably is a form of senile amyloidosis, the amyloid being deposited as a result of immune attack on trophoblastic cells with misspecified protein synthesis (Burstein *et al*, 1973). Thickening of basement membrane has been found associated with toxaemia (Tanney, 1935; Fox, 1964; Mehrotra *et al*, 1972; Sayeed *et al*, 1976; Mirchandani *et al*, 1979) and is found more pronounced with increasing severity of toxaemia (Mathews *et al*, 1973). Sen and Langly (1974) found it to be markedly increased in intrauterine growth retardation. There is no earlier report on its influence on foetal outcome. In the present study it was found that foetal distress, low apgar, neonatal and perinatal deaths were increased when thickened basement membrane was seen in more than 2% of villi (Table IV). However, this was found to be statistically significant only when associated with fibrinoid necrosis and was found in more than 2% of the villi (Table V). Separately fibrinoid necrosis also was not found to be significantly associated with increased foetal risk.

Fibrinoid necrosis associated with thickened basement membrane is found increased in toxaemia and IUGR (Sen *et al*, 1974; Bazaz Mallik *et al*, 1979). Various workers on this subject have not commented on the relation of these villous changes with foetal outcome.

Mathews *et al* (1973) found stromal fibrosis in 0-3% of villi in term placenta of normal pregnancy. Stromal fibrosis was found significantly increased in placentae of toxaemia and IUGR (Mirchandani *et al* 1979). The present study shows that foetal jeopardy is increased with stromal fibrosis. The incidence of intrapartum fetal distress, low apgar score at birth and perinatal deaths increases significantly with increased fibrosis of villi. Fibrosis of villi has been reported to be increased in intrauterine growth retardation by Warkany, 1961 and in hypertensive disorders of pregnancy by Paine, 1957; Gruenwald and Minh, 1961 and Fox, 1967.

Severe degrees of intervillous fibrin deposition is also deterimental to foetal survival (Gruenwald, 1961 and 1963; Wigglesworth, 1964) though Little (1961) and Fox (1963 and 1975) are of the opinion that intervillous fibrin may be extensive without eventually affecting the outcome of pregnancy. Fibrin deposits

may be seen often partially filling (i.e. Grade II) or completely filling (Grade III) intervillous spaces under high power in toxaemia and in IUGR. Significant decrease in incidence of intrapartum fetal distress was found in present study in cases where intervillous fibrin deposit was not seen.

Stillbirths were four times more frequent in Grade III intervillous deposit than when none was found. The cause of these deposits, like thrombus formation may be alteration in blood flow or damage to adjacent tissue, both of which may be operative in complications of late pregnancy, or like amyloid deposit could be a sign of 'ageing'. Kirby *et al* (1964); Billingdon (1967) and Bagshaw (1967) consider it to be an immunological barrier.

Summary and Conclusions

Intrapartum fetal distress is more often observed when placenta weighs less than 300 Gms at term and has more than 5% of surface area infarcted.

Fibrosis of villous stroma was most indicative of intrapartum foetal jeopardy. Thickened basement membrane with fibrinoid necrosis of more than 2% of villi also was indicative of foetal risk. Separately, neither of these changes was significant nor was increased syncytial knot count. Increased fibrin deposit in intervillous space increased intrapartum foetal distress.

Quantitative estimation of placental changes is essential as none of the changes are diagnostic either of maternal associated condition or of foetal anoxia.

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