Placental Parameters and Fetal Outcome: Implications on Routine Evaluation of Placental Histology

PLASENTAL PARAMETRELER VE YENİDOĞAN BULGULARI: PLASENTA HİSTOLOJİSİNİN RUTİN DEĞERLENDİRİLMESİ ÜZERİNE GÖRÜŞLER

Hulusi Bülent ZEYNELOĞLU* Esra KUŞÇU*, Ebru TARIM**,
Hakan DURAN***, Mehmet Hulusi ERGENELİ*, Sertaç BATIOĞLU****

* Yrd.Doç.Dr..Başkent Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğrun AD,
** Ara.ş.Ciör.Dr.,Başkent Üniversitesi Ttp Fakültesi Kadın Hastalıktan ve Doğum AD,
*** tiz.Dr.Başkent Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum AD,
**** Doç.Dr,Başkent Üniversitesi Ttp Fakültesi Kadın Hastalıkları ve Doğum AD. ANKARA

-Summarv-

Objective: To assess the relations/lifts between the fetus and /daccuta.

Institution: Department of Obstetrics, Baskent University, Ankara.

Materials and Method: Prospective longitudinal analysis of fetal and placental parameters oj 293 women who delivered live newborn in the maternal ward of Department of Obstetrics. Baskent University.

Results: There were significant correlations between placental weight, newborn weight; placental diameter and newborn weight 46. i>A), 001; r=0.30, p<0.0()l). There was a weak correlation between placental weight and fifth Apgar scon- which was again significant (r- 0.22, p- 0.005). When we consider only newborns who were admitted into newborn intensive care unit, the babies with fiasittvc /i/aceulal />atho/ogy were signilicantlv lower in btrthweight when compared to babies with normal placental histology (¡925.()(h 1059.48 gin vs. 3167.04±59(). 17 gm, /i<0.()5). The logarithmic transformation of the mean multiples of median for maternal total human chorionic gonadotropin in the second trimester was similar in pregnancies with positive placental histology and in /iregnuncics without positive placental histology (1.01=0.66 vs 0.67=0.32).

Conclusion: Placental growth is well correlated with fetal growth, however, nomine histological examination may not be a cost-effective compleinetitaiy tool in the evaluation of the early fetal outcome.

Key Words: Placenta. Birth weight, Placental pathology

T Klin J Gynecol Obst 1999. 9:3 1-36

Geliş Tarihi: 20.04.199S

Yazışma Adresi: Dr.Hulusı Bülent ZCYNELOGLU
Başkent Üniversitesi Tıp Fakültesi
Kadın Hast. ve Doğum AD
Kubılay Sok 36 Maltepe, ANKARA

Ozet.

Amaç: Fetus ile plasenta parametreleri arasındaki ilişkileri incelemek.

Çalışmanın yapıldığı yer: Başkent Üniversitesi Kadın Hastalıkları ye Doğum Bölümü.

Materyel ve Metodlar: Başkent Üniversite Hastanesi 'ndc doğum ya/muş 293 kadının fetal ve placeıital parametreleri daha önceden hazırlanmış formlara doldurularak prospekll,f olarak incelendi.

Bulgular: Plasenta! ağırlık, yenidoğan ağırlığı; plasenta! çap ve yenidoğun ağırlığı arasında anlamlı korelasyon suptandı (r=0.46, p<0.001; r=0.30, p<O.0(H). Plasenta ağırlığı ve 5. dakika Apgar skoru arasında zayii ancak istatistiksel anlamlılık içeren bir korelasyon safiiaudt (r=0.22, p<0J)05). Yenidoğan ünitesine vat t rıhın bebeklerden plasenta incelemesinde bir sorun görülenler, sorun görülmeyenlere göre daha düşük doğum ağırlıklı idiler (¡925.00=1059.48 gnı vs. 3107.04=590. 17 g,,,. p<0.()5). Bunun yanında 2. tritnester üçlü testi oluşturan kısımlardım biri olan HCG'nin logaritmik transformasyon değeri plasenta histolojisinde sorun olanlarda, olmayanlara göre dalla yüksek bulundu (-0.06iO.23 ile -0.22=0.2), p<0.00l).

Sonuç: Plasenta! gelişim ketal gelişim ile beraber gitmektedir ancak, plasentanın rutin histolojik incelenmesi erken yenidoğan değerlendirmesinde ekonomik bir ek araç olmayabilir.

Anahtar Kelimeler: Plasenta, Doğum ağırlığı
Plasenta patolojisi

T Klin Jinekol Obst 1999. 9:31-36

Maternal-Fetal Tıp ve Ohstetrtk ve Üreme Bilimleri Konusunda Türk-Yunan Bilimsel Toplantısı 'nda tebliğ olarak sunulmuştur (Nevşehir 9-12 Ekin, ¡991).

Evidence indicates that placental growth is correlated with total growth (1). As normal gestation advances, there is a greater increase in fetal weight than in placental weight and as a result, there is a decrease in the placenta I-fetal weight ratio in the second half of the pregnancy. In human pregnancy, both small maternal pelvic diameter (a possible marker of poor nutrition during development) and shortness of babies in relation to head circumference and birth weight (possibly indicating mid-pregnancy nutrient deprivation) arc associated with significantly raised placental weight to birthweight ratios (2).

In addition, the examination of the placenta may discover the hidden complications of the pregnancy which may give insight into the pathogenesis of neurologic and other developmental disorders. The National Collaborative Perinatal Project, conducted during 1959-1966, examined associations between placental findings and preterm delivery, stillbirth, neonatal death, cerebral palsy, mental retardation, epilepsy, and speech, hearing and vision problems; it is the largest study of placental abnormalities to dale (3). However, these data were collected before the technologic advances currently used in clinical perinatal management and pathologic diagnosis. Selected placental lesions may represent acute and chronic causes of perinatal asphyxia (4). Rcdline and Patterson (5) examined patterns of placental injur)' in pregnancies complicated postmaturity, intrauterine growth retardation, and other clinical syndromes associated with fetal outcome in the immediate postnatal period. Few epidemiologic studies have related placental abnormalities to gestational age or adverse outcome of the newborn. The data provide an opportunity to examine placental signs of intrauterine conditions that are potentially hazardous to fetal and later development. Thus we aimed to assess the impact of the placental parameters at birth and relevance of its routine pathologic examination to the pregnancy outcome.

Materials and Methods

Feial and placental parameters of 297 consecutive women who delivered from June 1995 to August 1997 in Department of Obstetrics, Baskcnt University were evaluated. Data were collected rctrespectively from patients' charts. Preterm newborns were defined as those born before 37 completed weeks' gestation, and term neonates as .37-41 weeks. Placental weight was recorded in the chart after the delivery and placentas were sent to pathology department for the histologic examination.

The histopathologic abnormalities included placental ischemic change, chorioamnionitis. abruptio placentae, infarction, chronic villitis, and chorioangiosis. These entities arc described comprehensively and arc well indexed, (6) but arc described in brief here: Histopathologic ischemic changes are signs of low uteroplacental blood flow. They include villous agglutination, shrinkage of villi, numerically increased syncytiotrophoblastic knots, increased perivillous fibrin, infarcts, sclerotic or avascular villi and fibrinoid material with abundant histiocytes. When uteroplacental blood How deficiency is severe, fetal placental response manifests increased nucleated red blood cells, occlusive thrombi, hemorrhagic endovasculopathy, and intravillous hemorrhages (7). For ibis study, both acute and chronic ischemic changes were included.

Chorioamnionitis is defined as inflammation of the cxtraplaccntal membranes and the placental amnion and chorion. Many such placentas also had inflammation in the vessels and supporting tissue of the umbilical cord. Our investigation did not differentiate those cases nor did it evaluate correlations with various patterns or severity of inflammation. Abruptio placentae refers to the separation of all or part of the placenta from the wall of the uterus before delivery of the fetus. Chorioamnionitis or localized decidual inflammation is often present with placental abruption as arc light microscopic signs of low uteroplacental blood flow. Placental infarction denotes ischemic villous necrosis. In chronic infarction, the process may be diffuse and difficult to recognize with the naked eye. The accompanying light microscopic changes include diffuse fibrinoid material. Our diagnosis of infarction required light microscopic confirmation of grossly diagnosed lesions.

Statistical zJ net I vsis

Values are given as mean and standard deviations unless stated otherwise. Onc-way-Anova with

posl-lioc Bonferroni correction, Pearson correlation coefficient, linear regression tests and. Student's T tests were employed. Statistical significance was present if p was <0.05.

Results

Of 293 newborn, 38 (12.9%) were delivered preterm, 5 being between 28-32 weeks and only one being before 28 weeks of gestation. Table 1 depicts the demographic data of the preterm deliveries compared to term deliveries. The newborn weight and length were significantly smaller in the premature group when compared to the term group. The placental weight was significantly lower in the premature group, however, the diameter of the placenta did not show significant change. Moreover, the 1, 5 and 10 minute Apgar scores tended to be lower in preterm deliveries, although it did not reach statistical significance.

There were significant correlations between placental weight and newborn weight (Figure 1); and placental diameter and newborn weight (r=0.45, p<0.001: r=0.28, p<0.()01, respectively). Placental weight and height of the newborn were also significantly correlated (r=0.26, p<0.001). There was a weak correlation between placental weight and fifth minute Apgar score which was again significant (r=0.22, p<0.005). The placental weight to birth weight ratio was inversely, but significantly correlated to the birth weight (r=-0.42, p it.on 1 ! (Figure 2). However when the ratios of placental weight to newborn weight were compared newborn babies over 2500 gin to babies under 2500 gm, there was a trend for lower birth weight babies to have a larger ratio (0.18-0.04 vs 0.24±().()6, p=0.053). Furthermore this ratio correlated inversely with the gestational age at delivery (r=-0.418, p<0.001).

Placental Histology

Of the 274 patients whose babies had a 5 minute Apgar score of 9 and 10, 6 had placental infarcts, 3 had focal necrosis, 6 had ischemic changes, 8 had perivillous fibrin deposition, 8 had chorioamnionitis and 1 had fetal-maternal bleeding. Of the 12 patients whose babies had an Apgar score of 8, 2 had chorioamnionitis. One of two mothers having babies with an Apgar score of 7, had placental infarcts. One patient, whose baby had an Apgar score of 4, had chorioamnionitis.

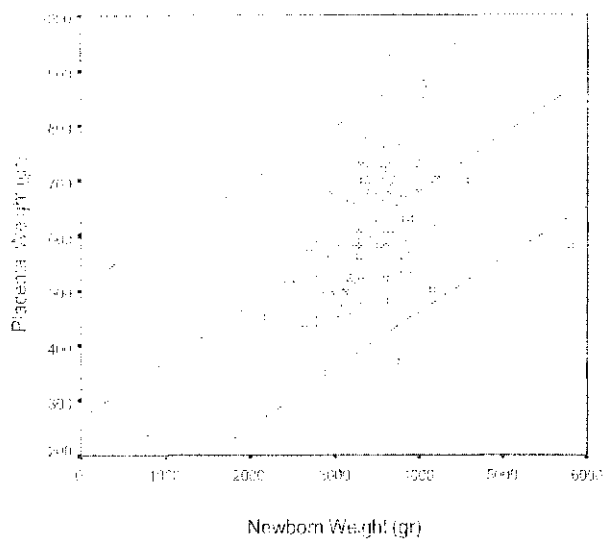
Tabic 2 shows the Apgar score, placental abnormality and neonatal weight distribution of the babies. Placental infarcts were mostly found in babies large for gestational age. Acute chorioamnionitis was mainly detected in preterm babies. Tabic 3 shows the distribution of newborn admission to NICIJ (newborn intensive care unit) according to pathological findings of their placenta.

However, when wc consider only newborns who were admitted into NICU, the babies with positive placental pathology were significantly lower in birthweight when compared (o babies with normal placental histology (1925.00A 1059.48 gm vs. 3167.04±590.I7 gm, p<0.05). Although these babies had lower Apgar scores when compared to babies with normal placental histology, it did not reach statistical significance.

The mean multiples of median for maternal total human chorionic gonadotropin in the second trimester was similar in pregnancies with positive

Table 1. The demographic data and comparison of the preterm deliveries with term de iverics

	- 37wecks (n=A0)	>37weeks (n-26.3)	P
Aye (years)	213.±-4.76	28.95x4.84	0.844
C Iravulitv	2.30.14.80	2.2211.83	0.813
Newborn Weight (gri	2>22.00+738.67	3360.48±459.28	<0.()0I
Newborn Length (cm)	45.0()±3.6()	48.37r3.47	-"0.001
Apgar Scores (1 mm.)	8.00±1.80	8.59.1-0.98	0.0X8
Apgar Scores (5 nun.)	9.3 Oi1.42	9.7610.57	0.088
Apgar Scores (10 mm.)	9.4711.28	9.90.10.41	0.072
Mean Placental Diameter (cm)	I6.02±1.80	16.23i 1.80	0.536
Placental Weight (gr)	522.86J.456.I3	618.09x117.77	0.006
Placenta! Weight." Newborn Weight	0.2310.05	0.1810.03	(1.085



l-'ijiure I. Tlie eorrelation of placental weigh) 10 newborn weiidit and its 95% confidence intervals.

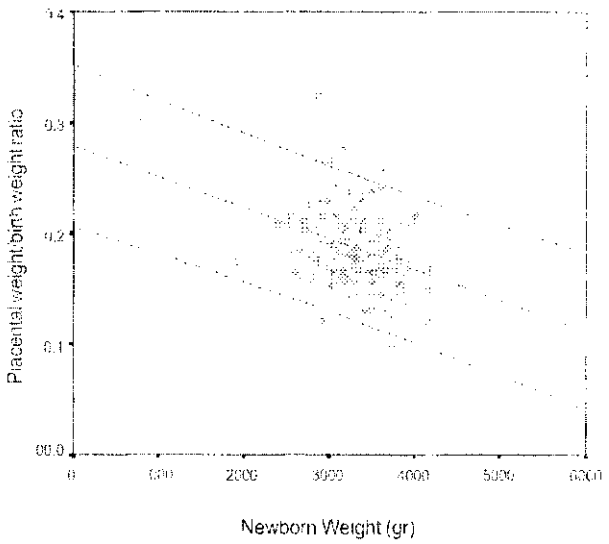


Figure 2. The correlation of placental weight to ncwbon weight ratio with newborn weight and its 95% confidence intervals.

Table 2. The distribution oh Apgar scores, placental histology and birth weight

5 mill. Apgar Score (n)	Pathologies (number)	Birth Weight (gm)
9-10 (274)	placental infarct (6)	4250. 3150. 4220, 3050. 5804. 3600
	focal necrosis (5)	1300*, 3490. 2850
	chonoamnionitis (8)	3860, 3150. 2760, 2950, 3080, 3100*. 2900. 3250
	perivillous fibrin deposition (8)	3600, 3370, 2530. 2900, 3200, 2500*
	fetal-maternal bleeding (1)	2800
8 (8)	chonoamnionitis (2)	1500*, 2770
7 (3)	placental infarct (1)	4270*
4 (1)	chonoamnionitis (1)	800*
0 (2)	placental infarct f 1)	1900
	chonoamnionitis (1)	2830

'ticnoies NK'Uadmission

placental histology and in pregnancies without positive placental histology (1.01 ±0.66 vs 0.67a-.0.32). However, when we computed the log transformation of this parameter, these were significantly higher in pregnancies with positive placental histology than pregnancies with normal placental histology (-0.06a_0.23 vs -0.22a0.21, p--0.001). We could not delect such relationships for other components of triple lest with placental histology.

Discussion

There has been heightened interest in clinical-pathologic correlation between placental abnormalities and adverse pregnancy outcome. Skilled and systematic examination of the umbilical cord, membranes, and placenta is performed on properly prepared specimens, insight into antepartum pathophysiology may be gained under certain circumstances. In most of these instances, such as chonoamnionitis, the diagnosis already will have been made on clinical grounds, with the placental examination providing confirmation. In other eases of poor outcome, a disorder that was not suspected clinically may be revealed by placental pathology. Examples of pathologic findings and the disorders they suggest include the microabscesses and am-

Table 3. The distribution of placental histology according to the newborns admitted in NICU

	NICU Admission		Total
	no	yes	
Acme chorioainniomtis. focal villitis	3		3
Fetomalernal hemorrhage, manire placenta	1		1
Focal necrosis	2	1	3
Fibrinoid deposits, ischemic changes	1		I
Hematoma and multiple infarct	I		1
Intel \ illous thrombosis	5	I	6.
C'horangiosis	1		I
Chorioamuionitis	6	3	9
Mature plaeenla	229	28	257
Mature placenta, pcrivillous fibrinoid deposits	2		2
Mature, squamous metaplasia in amnion membrane	1		1
Placental infarct, mature placenta	7	I	8
Total	259	34	293

nion nodosum suggesting long-standing oligohydramnios. The underlying pathophysiology of these lesions has been confirmed by laboratory testing or consistent and specific clinical, associations. The significance of other findings, such as villoirs edema, hemorrhagic cndovasculitis, and chronic villitis, has not been as well delineated. These lesions, among others, have been variously reported to correlate with poor short-term and long-term neonatal outcome. The paucity of properly designed studies of adequate size with appropriate outcome parameters has prevented universal agreement as to positive predictive values, underlying pathophysiology, or even the consistency of clinical correlations with these findings. Furthermore, the distribution of pathologists with the expertise to interpret more subtle placental findings is uneven from region to region. Although a protocol for obtaining routine placental pathologic examination under certain obstetric and neonatal conditions has been recommended (8), there are few data to support the clinical utility of this approach (')).

This study investigated the necessity of routine placental examination in a university-based obstetrics clime. However, it failed to show that the benefit from the analysis did not outweigh the confirmation of the complications of the pregnancy. That is, only 13.3% of newborns admitted to NICU had abnormalities in the placental histology. However, babies with positive placental pathology who were admitted to NICU had significantly lower birth weight than babies with negative placental histology.

College of American Pathologists suggested that routine placental examination may not be feasible on either a cost or manpower basis, and a small portion of placenta obtained at random would be unlikely to provide useful information and they added that the practice of saving all placentas unfixed at 4°C for 1 week after delivery would permit ascertaining most neonatal problems in which pathologic examination of the placenta may be appropriate. However, the scientific basis for clinical correlation with placental pathology is still evolving, and the benefit of securing specimens on a routine basis is as yet unproven. Continued research and education in this field should be encouraged. Research should be designed with the goal of defining clinical indications for placental examination. In contrast, pathologic examination of the stillborn Ictus and placenta is always potentially informative.

It has been suggested that poor nutrition before and during pregnancy is a major factor determining the birth weight relative to placental weight and altering fetal metabolism such that there is a predisposition to hypertension in adult life (2, 10). A higher placental weight to birthweight ratio has been found in association with women who have lower external conjugate pelvic diameters (indicating possible poor nutrition during development) and anemia (possibly indicating current poor nutritional status) (2).

As expected, our data has also demonstrated that placental weight and birth weight were highly correlated. An increased placental weight to birth-

weight ratio could not be predicted by birth weight or placental weight alone. In particular, a high placental weight to birthweight ratio did not imply an infant small for gestational age. Gestational age has a large influence on the ratio, even within the range of term deliveries. Prospective studies in which fetal growth and placental function are measured directly are needed in this exciting topic to determine the role of intrauterine development as an antecedent of adult hypertensive disease.

Raised levels of second trimester maternal serum alpha-feto protein and hCG in women who are subsequently delivered of an extremely small for gestational age infant arc related to the presence of pathological changes in the placenta, detectable at birth (11). It is speculated that these placental pathological changes, which frequently accompany small for gestational age pregnancies, have their origin in the second trimester, when the normal physiological changes of the placenta occur.

In this study, although we detected a correlation between the ratio of placental weight to fetal weight, this did not show any relationship with maternal weight or maternal weight gain during the pregnancy. Moreover, placental weight to birth weight ratio was not significantly associated with first visit, second or third trimester hemoglobin concentration. Williams et al(l) analyzed 2900 pregnancies and the placental parameters. They found strong correlation between placental weight to birth weight ratio and fetal weight and they detected a weak relationship between placental weight to birth weight ratio and body components, and other markers, such as maternal ethnic origin, socioeconomic class, duration of gestational age and smoking. As a marker of fetal growth the potential usefulness of the placental weight to birthweight ratio is diminished because the ratio is influenced by a multiplicity of factors.

Our data has detected a very weak, but significant correlation between maternal weight and fetal weight. However, we could not detect any relationship between maternal weight gain and birth weight. Edwards et al (12) have argued that maternal nutrition (excepting extreme malnutrition) has little importance in fetal and placenta] growth, instead suggesting that raised placental ratios reflect increased fetal exposure to maternal glucocorticoids.

Conclusion

Placental weight is dependent on gestational age and although placental sampling may reveal some hidden factors affecting the newborn, the routine investigation of the placental pathology in low risk population is not necessary as our data shows little benefit, nor did cord blood gases (13). The ratio of placental weight to birth weight may not be an accurate marker of fetal growth. However, babies with a greater ratio of placental to birth weight should be followed. Determining the role that relative growth rates of the fetus and placenta requires further prospective study.

REFERENCES

1. Williams L A. Evans SF, Newnham J P. Prospective cohort study of factors influencing the relative weights of the placenta and the newborn infant. B M J 1997; 314:1864-68.

2. Barker D, Bull A, Osmond C, Simmonds S. Fetal and placental size and risk of hypertension in adult life. B M J 1990: 1990:259-62.

3. Niswander K R. Gordon M. The women and their pregnancies. Philadelphia: WB Saunders, 1972.

4. Altshulcr G. Herman A A. The medicolegal imperative: Placental pathology and epidemiology. Fetal and neonatal brain injury: Mechanisms, management and the risks of practice. Philadelphia: BC Decker, Inc, 1989: 250-63,

5. Rcdlinc RW, Patterson P. Patterns of placental injury: Coirc-lations with gestational age, placental weight and clinical diagnoses. Arch Pathol Lab Med 1994; 118:698-701.

6. Benirsehke K. Kaufmann P. The pathology of the human placenta. New York: Springer-Verlag, 1995.

7. Altshulcr G. The placenta. In: Sternberg SS. ed. Diagnostic surgical pathology. 2nd ed. New York: Raven Press, Ltd.. 1994: 1993-2015.

8. College of American Pathologists Conference XIX. Idle examination of the placenta: patient care and risk management. Arch Pathol Lah Med 1991: 115:641-732.

9. A C O C i Committee Opinion Committee on Obstetrics: Maternal and Fetal Medicine Number 125: Placental Pathology 1993.

Ki.Langlcy SC, Jackson A A. Increased systolic blood pressure in adult rats induced by fetal exposure to maternal low protein diets. Clin Sci 1994: 86:217-22.

1 LMorssink LP dc Wolf lST, Koruman Lit, Beekluns JR. van der Hall TP. Mantingh A. et al. The relation between serum markers in the second trimester and placental pathology. A study on extremely small for gestational age fetuses. Br J Obstel Gynaecol 1996: 103:779-83.

12.Edwards CRW, Bcnediktsson R, Lindsay RS, Seekl JR. Dysfunction of placental glucocorticoid barrier: link between fetal environment and adult hypertension? Lancet 1993; 341:355-7.

l.YErgeneli ME. Duran Ell, Gürakaıı B. Kuşçu E, 1 Liberal A. Batıoğlu S. Perinatal. Obstetric parameters and umbilical cord blood acid-base status: results of Başkent University. Türkiye Klinikleri Journal of Obstetrics and Gynecology 1997: 7:197-201.