Umbilical blood flow and placental pathology

A. ZACUTTI (*) -F. BORRUTO (**) - G. BOTTACCI (*) - M. L. GIANNONI (*)
A. MANZIN (*) - M. PALLINI (*) - A. ZACUTTI Jr. (*)

Summary: The aim of the study was to establish whether or not placental morphostructural damage correlates with umbilical artery Doppler waveform and neonatal condition. To this end, seriated ultrasonographic monitoring, flowmeter tests on the cord artery and computerized cardiotocography were carried out in a population of 93 pregnant women in the second half of pregnancy. After birth placentas were subjected to macroscopic and microscopic examination. The Resistance Index showed a good correlation with pl cental vascular lesions, characterized by a distinct reduction in terminal villi and muscular wall ar erioles. Two types of intrauterine growth retardation were discernible, the first of genetic origin with a low-profile growth curve and therefore not amenable to treatment, but with a positive fet l-neonatal prognosis, and the second with a pathologic placental component, presenting a late flattening growth curve with evolution towards fetal distress and a negative fetal-neonatal prognosis.

Key words: Placental damage; Doppler umbilical flowmetry; Intrauterine growth retardation.

Before the introduction of ultrasonography, studying the fetoplacental unit was rather limited to the direct data, that could be obtained through morphological evaluation after birth ([3, 30, 31]).

The antenatal diagnosis of placental pathological alterations is now possible with the availability of reliable and immediate evaluation parameters ([16, 22]). The significance of biochemical data has been largely reduced with time. The degrees of placental maturation, as described by Grannum ([14]), express development stages ([10]). Their alteration has a pathological significance and the ultrasonographic features of a pathological placenta are by now codified ([2, 15, 17, 19, 24, 25, 26, 29]).

The studies carried out on Doppler waveform at the funicular artery during pregnancy have proved to be an indirect measurement of placental vascular resistance ([11, 20, 27, 31, 33, 34]). Up to now few studies have been performed in order to identify lesions associated with pathological flow values and retarded fetal growth ([4, 18, 23]).

As gestational age goes on, the increase in the placental bed, the increase in tertiary villi and vascular changes cause a progressive decrease in placental resistance under physiological conditions ([21]).

It would seem that a decrease in the number of tertiary villi and a reduction of their vascular component accompany growth retardation; such a phenomenon, which had already been pointed out by Brosens in 1977 ([5]) in pathological placentas, was related by Giles in 1985 ([13]) to umbilical artery flows.

(*) Department of Obstetrics and Gynecology
Ospedale Civile "S. Andrea",
La Spezia, Italy
(**) Obstetric and Gynecologic Institute
University of Verona

In our opinion, the morpho-structural changes of the placenta may have a role in the pathogenesis of IUGR. The purpose of this research is to prove such a hypothesis.

MATERIAL AND METHODS

Seriated ultrasonographic monitoring, flowmeter tests on the cord artery and computerized cardiotocography were carried out on a population of 93 pregnant women in the second half of pregnancy.

The ultrasonographic biometrical parameters investigated were:

- Biparietal Diameter (BPD);
- Transverse Abdominal Diameter (DTA);
- Femur length (Fl);
- Estimated Fetal Weight, following Shepard [28] (EFW);
- Ponderal Index = EFW/3Fl (IP).

The placental ultrasonographic structural features considered were:

- Placental volume in cm^3 according to the Hellmann [16] technique;
- Echographic placental grading (Grannum) [14];
- Gray scale histogram, expressed in terms of Skewness;
- Vascular resistances (umbilical artery doppler flow), expressed in terms of resistance index (RI).

In normal pregnancies the gray scale histogram (Ansaldo AU 940) shows that Skewness (Fig. 1) increases up to the 24th week, then it keeps steadily correlated to the degree of placental maturation following Grannum.

The flowmeter test was performed by analyzing the waveform obtained on the funicular artery by a continuous-wave Doppler apparatus (Multigon 500A); results are expressed in terms of Resistance Index (RI).

As to cardiotocography, the mean range, evaluated by computerized analysis (System 8000 - Sonicaid), was used to express heart rate variability (normal value > 30, borderline 30-20, pathological < 20) [8, 35].

Data concerning delivery and neonatal conditions (Apgar score, pH) were recorded as usual.

After birth placentas were subjected to gross pathological examination following Bartholomew's criteria [1]:

- Ischemic necrosis with fibrin deposition (INFD);
- True acute infarct (D-E Bartholomew);
- True subacute infarct (B-C Bartholomew);
- True chronic infarct (A Bartholomew);
- Placental caverns.

Parameters considered by microscopic examination are:

- Trophoblast surface (Syncytial Layer, Syncytial Sprouts, Cytotrophoblastic proliferation);
- Intervillous Spaces (Villi Agglutination, Intervillous Thrombosis, Fibrin Deposition);
- Villi Vascular Component (Thrombosis, Capillary Caliber Tertiary Villi, Muscular Arteriolar Number).

Specific immunohistochemical stains for actina were performed to show the muscular fibrocells of small vessel walls, and the number of muscular arterioles was counted (Fig. 2).

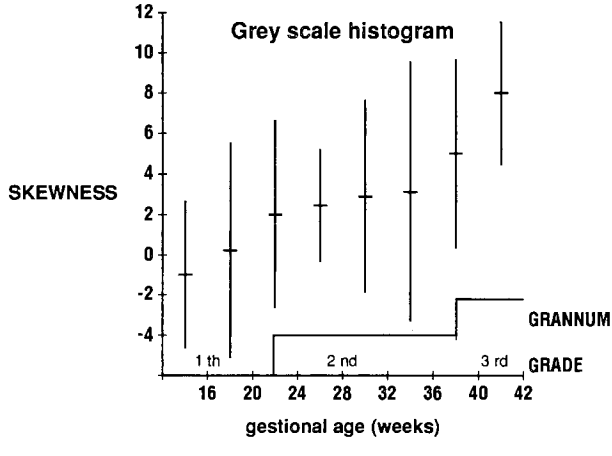

Fig. 1. — The values of skewness increase with gestational age and correlated with placental grading of Grannum.

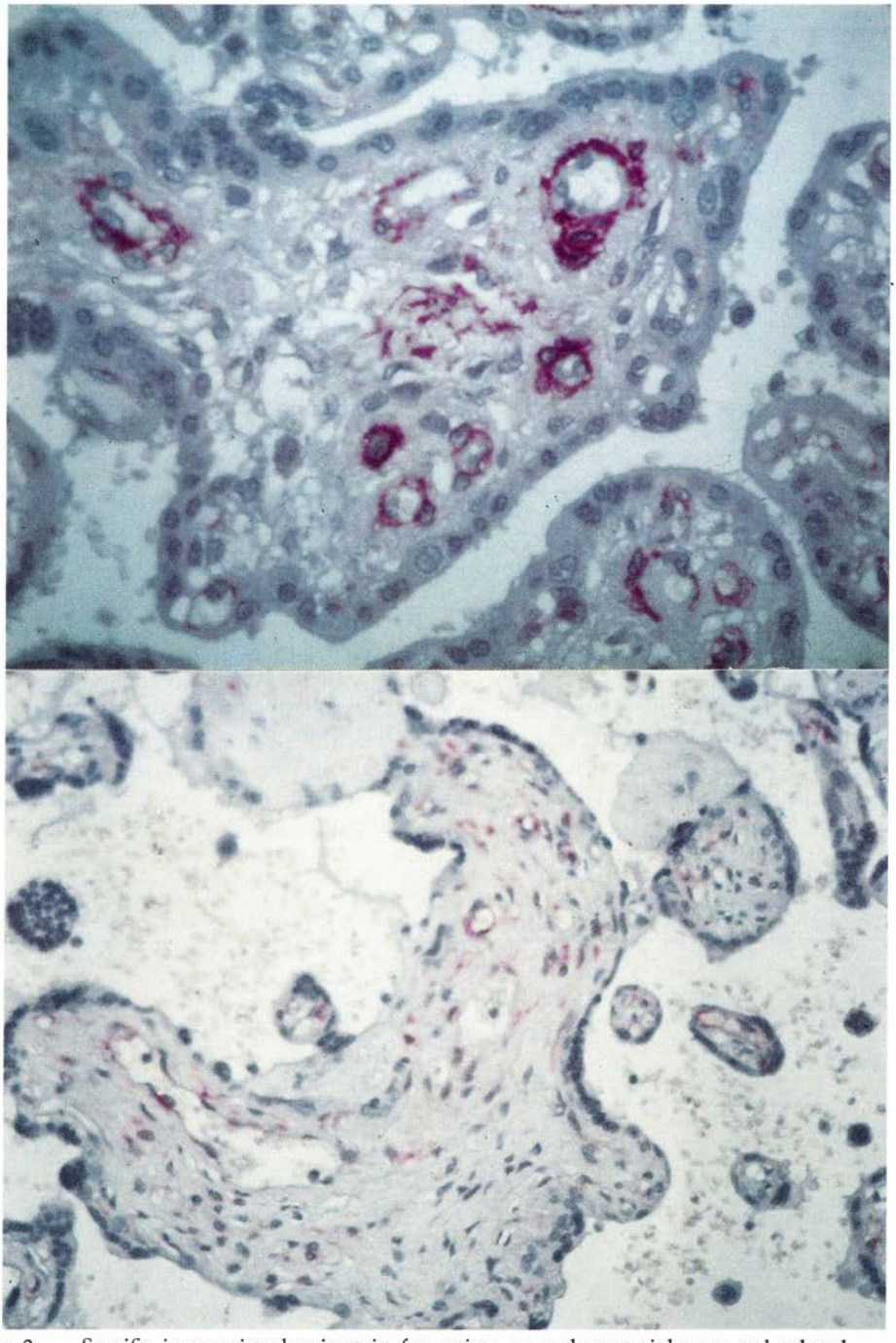

Fig. 2. — Specific immunoistochemic stain for actina: muscular arterioles are red colored.
Fig. 3. — Reduction of tertiary villi and muscular arterioles in a pathologic case (specific stain for actina).

Table 1. – *Gestational age distribution of estimated fetal weight and neonatal weight.*

Gestational age	Percentile	No. cases	Estimated fetal weight M±SD	Neonatal weight M±SD
20 - 25 weeks	< 10	1	900± 0	850± 0
25 - 30 weeks	< 10	2	1450±105	1190± 80
30 - 35 weeks	AGA	8	2850± 50	2625±225
	< 10	9	1900±295	1585±289
35 - 40 wteks	AGA	13	3653±420	3222±398
	< 10	18	2250±370	1850±252
> 40 weeks	AGA	41	3889±467	3581±388
	< 10	1	2900± 0	2580± 0

RESULTS

The population examined (93 cases) concerned four groups of patients.

I) Clinically normal pregnancies (56 cases).

II) Gestosis or pregnancy-induced hypertension (PIH) with AGA fetuses (6 cases).

III) Clinically primitive IUGR, that is, without any maternal complications (10 cases).

4) Clinically secondary IUGR, with gestosis or PIH (21 cases).

All cases of neonates less than 10th percentile were among the 31 cases of IUGR screened by means of echo-biometry (Tab. 1).

They exhibited a different profile of growth curves: 10 cases with low-profile curves, included in the third group, and 22 cases with late-flattening curves, all but one, included in the fourth group.

Placental features found during the antenatal ultrasonographic test proved to be correlated to the anatomo-pathological examination after delivery (Tab. 2).

Table 2. – *Correlation between antenatal ecographic patterns and postnatal anatomopathologic evaluation of placental characteristics.*

	PLACENTAL CHARACTERISTICS						
Antenatal echographic patterns	AGA	IUGR	PIH	Postnatal anatomopat. evaluation	AGA	IUGR	PIH
Volume (cm^3)	603 ± 144	520 ± 113	476 ± 163	Weight (gr)	657 ± 113	510 ± 138	460 ± 39
III Grannum grading (N)	11	1	2	Macroscopic lesions (%)	13%	15%	29%
Grey scale histogram (Skewness)	6.8 ± 5	6.0 ± 6	6.0 ± 5	Microscopic lesions (%)	5%	10%	22%
Doppler (RI)	56 ± 5	56 ± 12	67 ± 2	Mean small arterial vessel (n. count)	82	77	44

Table 3. – *Fetal and neonatal conditions in ca es with normal and pathological placenta.*

	No.	FETAL STATUS				NEONATAL STATUS			
		Doppler RI		Comp. CTG m.r.		Apgar'1	pH umb. art.		C.S.
		m ± ds	> 2 ds No. (%)	m ± ds	<30 No. (%)	<7 No. (%)	m ± ds	<7.15 No. (%)	No. tot. dist. No. (%)
Norm. plac.	64	56±	7 (1.6%)	43.5 ±10	7 (14%)	1 (1.6%)	7.17 ±0.12	12 (19.3)	14 5 (9%)
Pathol. plac.	19	68±	9 (47.8%)	41.2 ±14	8 (25%)	2 (6.4%)	7.16 ±0.14	8 (25.5%)	7 4 (12%)

The ultrasonographic evaluation of placental volume correlated with the weight at birth, with a clear reduction in IUGR cases.

The Grannum grading proved related to gestational age and not to growth retardation, since it showed up only after the 39th week.

Skew showed no statistically significant difference between normal cases and IUGR.

Doppler flow data proved pathological in 13 cases: in only one case in normal pregnancy (1.7%), in 2 cases in primitive IUGR (20%) and in 10 cases in secondary IUGR (45.7%).

The Resistance Index showed a good correlation with the vascular lesions detected by the microscope, characterized by a clear reduction in the number of terminal villi and muscular wall arterioles (Fig. 3).

Placental alterations detected before birth by means of Doppler ultrasonography and which were confirmed by the anatomo-pathological examination after delivery, proved to be significantly correlated (Tab. 3) to the occurrence of fetal distress, as shown by the increased incidence of mean range values below 30 m.sec.

In this group the incidence of cesarean sections with fetal distress proved to be higher. Neonatal conditions showed a small, though higher, incidence of altered pH and Apgar score.

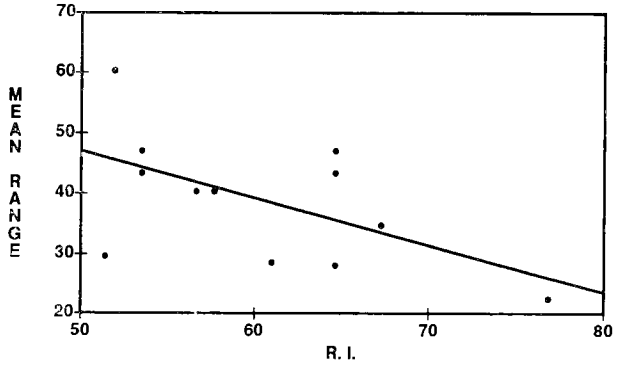

Fig. 4. — Correlation between mean range of computerized cardiotocography and Resistance Index of cord artery evaluation.

CONCLUSIONS

The results of our research show the existence of two IUGR groups, differing in regard to clinical phenomena and even more in regard to placental alterations.

In the primitive IUGR group, the etiologic factor is likely to be intrinsic to the fetus and of a genetic type. From the point of view of antenatal evaluation, the growth curve is of the low-profile type, generally speaking there are no maternal pathological conditions associated, the placenta is normal or slightly altered, fetal neonatal prognosis is good, newborns are small but healthy.

On the contrary, in the second group, the growth curve is of the late-flattening type. The fetal neonatal prognosis is worsened by tendency towards fetal distress. In this group it is possible to detect, besides small placental volume, microscopic placental alterations, characterized by the lost neoproduction of tertiary villi and muscular arterioles.

The consequent increase in placental resistance accounts for an increase in the Resistance Index. Besides uteroplacental ischemia, shown by Campbell ([6]) on the maternal circulatory side, placental alterations may also have their origin in the haemodynamic changes which set up as a compensation on the fetal side ([7]).

The vicious circle of placental damage and feto-placental circulatory failure steadily worsens.

The further evolution of the damage expresses itself in the correlation between the increase in placental resistance and the decrease in heart rate variability (Fig. 7), leading to the occurrence of fetal distress ([9]).

REFERENCE

1) Bartholomew R. A., Colvin E. D., Grimes W. H., Fish J. S., Lester W. M., Galloway W. H.: "Criteria by which toxemia of pregnancy may be diagnosed from unlabeled formalin-fixed placenta". *Am. J. Obst. Gyn., 82,* 277, 1961
2) Borruto F., Menestrina F.: "Placental black holes". In Foetal Ultrasonography, edited by Borruto F., Hansmann M., Wladimiroff. J. Wiley & Sons., 1981.
3) Bernirschke K., Driscoll S. G.: "The pathology of the human placenta". Springer Verlag, 1967.
4) Bracero L. A., Beneck D., Kirshenbaum N., Pfeiffer M., Stalter P., Schulman H.: "Doppler velocimetry and placental diseases". *Am. J. Obst. Gyn., 161,* 388, 1989.
5) Brosens J., Dixon H. G., Robertson W. B.: "Fetal growth retardation and the arteries of the placental bed". *Br. J. Obst. Gyn., 84,* 656, 1977.
6) Campbell S., Pearce M. F., Hackett G., Cohen-Overbeek T., Hernander C.: "Qualitative assessment of utero-placental blood flow: early screening for high-risk pregnancy". *Obst. Gyn., 68,* 649, 1986.
7) Dawes G. S.: "Fetal and neonatal physiology". Year Book Ed., 1968.
8) Dawes G. S., Redman C. W. G., Smith J. H.: "Improvement in the registration and analysis of fetal heart rate records at the bedside". *Br. J. Obst. Gyn., 92,* 317, 1985.
9) Dawes G. S., Zacutti A., Borruto F., Zacutti A. Jr.: "Fetal autonomy and adaptation". Wiley Ed., 1990.
10) Fisher C. C., Garret W., Kossof G.: "Placental aging monitored by grey scale echography". *Am. J. Obst. Gyn., 1,* 483, 1976.
11) Fleischer A., Schulman H., Farmakides G. *et al.:* "Umbilical artery velocity waveforms and intrauterine growth retardation". *Am. J. Obst. Gyn., 151,* 502, 1985.
12) Fox H.: "Pathology of placenta". Saunder, Ed., 1978.
13) Giles W. B., Trudinger B. J., Baird P. J.: "Fetal umbilical artery flow velocity waveforms and placental resistance: pathological correlation". *Br. J. Obst. Gyn., 92,* 31, 1985.
14) Grannum P. A. T., Berkowitz R. L., Hobbis J. C.: "The ultrasonic changes in the maturing placenta". *Am. J. Obst. Gyn., 133,* 915, 1979.
15) Haney A. F., Trought W. S.: "The sonolucent placenta in highrisk obstetrics". *Obst. Gyn., 55,* 38, 1980.
16) Hellman L. M., Kobayashi M., Tolles W. *et al.:* "Ultrasonic studies on the volumetric growth of the human placenta". *Am. J. Obst. Gyn., 108,* 740, 1970.
17) Hills D., Irwin G. A. L., Tuck S., Baim R.: "Distribution of placental grades in high-risk gravidas". *Am. J. Obst. Gyn., 143,* 1011, 1984.
18) Jaurniaux E., Campbell S.: "Fetal growth retardation with abnormal blood flows and

placental sonographic lesions". *J. Clinical, Ultrasound, 18,* 210, 1990.
19) Jaurniaux E., Campbell S.: "Ultrasonographic assessment of placental abnormalities". *Am. J. Obst. Gyn., 163,* 1650, 1990.
20) Kurjak A.: "Measurements of fetal blood flow". CIC Ed., 1984.
21) McCowan L. M., Mullen B. M., Ritchie K.: "Umbilical artery flow velocity waveforms and the placental vascular bed". *Am. J. Obst. Gyn., 157,* 900, 1987.
22) Morris D. T.: "An evaluation of the use of texture measurements for the tissue characterisation of ultrasonic images of in vivo human placenta". *Ultrasound in Med. & Biol., 14,* 387, 1988.
23) Nessmann C., Huten Y., Uzan M.: "Placental correlations of abnormal umbilical Doppler index". *Trophoblast Res., 3,* 309, 1988.
24) Onnis A.: "Istochimica del villo coriale umano. B glicogeno del villo coriale nella gravidanza normale e patologica". *Attualità Ost. Gyn., 9,* 51, 1963.
25) Proud J., Grant A. M.: "Third trimester placental grading by ultrasonography as a test of fetal wellbeing". *Br. Med. J., 294,* 1641, 1987.
26) Quinlau R. W., Cruz A. C., Buhi W. C., Martini M.: "Changes in placental ultrasonic appearance: pathologic significance of grade III placental changes". *Am. J. Obst. Gyn., 144,* 471, 1982.
27) Rochelson B., Schulman H., Farmakides G. *et al.:* "The significance of absent end-diastolic velocity waveforms". *Am. J. Obst. Gyn., 156,* 1213, 1987.
28) Shepard M. J., *et al.:* "An evaluation of two equations for predicting fetal weight by ultrasound". *Am. J. Obst. Gyn., 147,* 47, 1982.
29) Vermenlein R. C. W., Lambalk N. B., Exalto N., Arts N. F. T.: "Anatomic basis for ultrasound images of the human placenta". *Am. J. Obst. Gyn., 153,* 806, 1985.
30) Villee C. A.: "The placenta and fetal membranes". Williams & Wilkins Co., 1960.
31) Wilkin P.: "Pathologie du placenta". Masson Ed., 1965.
32) Zacutti A., Landini L., Bernardi E., Ballarini A.: "Quantitative assessment of blood flow in fetal vessels by pulse doppler techniques". *J. Nucl. Biol. Med., 26,* 2, 1981.
33) Zacutti A., Bottacci G., Elena G., Landini L., Zacutti A. Jr.: "Le metodiche doppler nello studio del flusso fetoplacentare". *Giornale It. di Ost. e Gin., 8,* 664, 1985.
34) Zacutti A., Landini L., Elena G., Bottacci G., Zacutti A. Jr.: "Il significato clinico della forma d'onda doppler dell'arteria ombelicale". *Riv. di Ost. Gin. Pratica e Med. Perinatale, 1,* 65, 1986.
35) Zacutti A., Bottacci B., Elena G. *et al.:* "Valutazione computerizzata del tracciato cardiocografico antepartale". Aggiornamenti in Ostetricia e Ginecologia. CIC Ed., 1990.

A. ZACUTTI
Div. Ostetrico - Ginecologica
Ospedale Civile "S. Andrea"
19100 La Spezia, Italy