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STUDY OF SOME PHYSIOLOGICAL ASPECTS OF BLOOD RHEOLOGY IN FETUSES BY INTRAUTERINE UMBILICAL CORD VENEPUNCTURES. RELATIONSHIPS WITH HEMODYNAMIC MEASUREMENTS

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ABSTRACT

This study was carried on in order to describe intrauterine fetal blood rheology, and to try to correlate these measurements with hemodynamic data obtained by doppler. Fetuses underwent cordocentesis in utero during pregnancy with a method allowing an ambulatory sampling with no premedication. Pathologic cases (malformations, fetal distress) were excluded from the study. Finally, a group of 80 'normal' fetuses was constituted, covering the period between 25 and 30 week's gestation. When compared to mothers studied at the same time, have significantly lower blood viscosity, lower plasma viscosity, lower RBC flexibility (measured by filterability) and higher hematocrit/viscosity ratio. Measurement of RBC rigidity by viscometry gave no significant differences. Fetal RBC aggregation was studied in 52 samples and was very low when compared to mothers with 'M' values equal to zero before 30 wks. The following parameters are linearly related to time : blood viscosity, hematocrit, hemoglobin count, RBC count, WBC count, eosinophil count, RBC aggregation index 'M'. A correlation between umbilical artery resistance index and both whole blood viscosity and hematocrit is also found and requires confirmation on a larger sample.

key words: fetal blood, cordocentesis, hemorheology, erythrocyte deformability, blood viscosity, erythrocyte aggregation, vascular resistance

INTRODUCTION

The hemorheological profile of the normal fetus has been the object of several studies (1-6). The fetus has, compared to pregnant or nonpregnant adult women, a significantly raised hematocrit (5,6), and reduced erythrocyte filterability (6), such a pattern resulting in an elevation of whole blood viscosity (1-4, 5). Fetuses have also reduced erythrocyte aggregation and lowered plasma viscosity (7). This pattern has been suggested to play a physiological role in maintaining a sufficient O_2 supply to fetal tissues, since it reduces the tendency to increase viscosity despite increased RBC rigidity (7). In addition it has been postulated that fetal circulation is rather poorly situated to cope with any increase in blood viscosity, so that hyperviscosity may markedly influence blood flow in umbilical circulation (8). However, the physiology of hemorheological parameters in fetuses as currently described was inferred from studies on cord blood at birth. In a previous paper, we reported preliminary data of blood rheology in fetuses measured during intrauterine venepunctures (9-10) suggesting that the previous assumptions of authors working in this field were accurate. However, this first paper concerned only a small sample of fetuses and needed further confirmation. Thus, this study was carried on in order to confirm these preliminary conclusions, to describe intrauterine fetal blood rheology, and to try to correlate these measurements with hemodynamic data obtained by doppler just before the puncture.

MATERIAL AND METHODS

Patients

All fetuses included in this study underwent the cord puncture for the detection of genetic abnormalities and/or recent infection by rubella or toxoplasmosis. Cordocentesis was performed in utero during pregnancy as previously reported (11). The method allowed an ambulatory sampling during a hospital visit performed in an operating room with surgical preparation of the abdomen. No premedication (e.g. maternal sedation) was administered. Bladder filling was unnecessary. The ultrasound device was a 3.5 MHz sectorial transducer (Combison Kretz 320) manipulated through a sterile bag. After local anesthesia (1 per cent xylocaïne), a 22.5 gauge needle fixed on a syringe was introduced in the plane of the ultrasound section through the abdominal wall, the uterine wall, the membranes, into the amniotic cavity, and finally into the umbilical cord. The 22.5 gauge needle was chosen in order to reduce cord bleeding when the needle was withdrawn. Fetal blood was aspirated after changing the syringe in order to avoid contamination of samples with maternal blood or amniotic fluid. The duration of funicular bleeding was noted at the withdrawal of the needle. Two hours after sampling, patients were again examined ultrasonographically. Preventive antibiotic treatment consisting of 2g of cefotaxime daily was administered for 5 days, as well as an injection of anti-D gamma globulin if the mother was Rh-negative and fetus Rh-positive. Two methods were used for verifying purity of blood samples: the Kleihauer test and the measurement of the mean corpuscular volume on a Coulter Counter S Plus II. During the study period, samplings were performed by the same obstetrician and ultrasound guidance was performed by the same specialist.

Pathologic cases (malformations, fetal distress) were excluded from the study. Finally, a group of 80 'normal' fetuses was constituted. Fetuses were

studied between 25 and 30 week's gestation. At the same time, maternal blood was also drawn (just before the cord puncture).

Doppler measurements

Arterial resistance index of Pourcelot (12) was calculated from Doppler waveform analysis as the difference between systolic and diastolic velocity index divided by the systolic index. This index was calculated in this study in the umbilical artery and in uterine maternal artery, just before the puncture.

TABLE I

Hemorheological parameters measured on fetal versus maternal blood. μb: apparent blood viscosity at native hematocrit (mPa.s); μpl: plasma viscosity (mPa.s); h: hematocrit (%); 'Tk' and 'k': RBC rigidity index obtained by viscometry at high shear rate (dimensionless); μ45: blood viscosity at corrected hematocrit 45%; h/μ: hematocrit/viscosity ratio ($mPa^{-1}s^{-1}$); μfr: RBC rigidity index measured by the hemorheometre (dimensionless). M and M1 : indices of RBC aggregation measured with the Myrenne Aggregometer. Comparison: Wilcoxon test for paired data..

Parameter	fetus	mother	comparison
μb	2.59 ± 0.05	2.95 ± 0.04	p<0.01
μpl	1.22 ± 0.018	1.38 ± 0.009	p<0.01
h	35.27 ± 0.73	34.62 ± 0.46	n.s.
'Tk'	0.489 ± 0.02	0.514 ± 0.01	n.s.
'k'	1.21 ± 0.03	1.270 ± 0.03	n.s.
μ45	3.08 ± 0.07	3.52 ± 0.07	p<0.01
h/μ	0.237 ± 0.005	0.198 ± 0.003	p<0.01
μfr	0.22 ± 0.11	0.46 ± 0.23	p<0.01
M	0.1 ± 0.03	10.39 ± 0.549	p<0.01
M1	2.83 ± 0.366	12.16 ± 0.492	p<0.01

Hemorheological measurements

Blood was collected into potassium EDTA. In fetuses, this amount was reduced to 2 or 3 ml (quantity defined by the clinical conditions, since fetal heart rate was monitored during cordocentesis). In mothers 7 ml were drawn. Measurements were performed within two hours after venepuncture. Hematocrit (packed cell volume) was measured by microcentrifugation. Blood viscosity and plasma viscosity were measured at very high shear rate (1000 s^{-1}) with the MT90 falling ball viscometer (Medica-test, 37 rue de l'Ermitage F-86280 Saint Benoit) (13, 14). The coefficient of variation of this method ranges between 0.6 and 0.8 % (10 repetitive measurement of the same sample). The results of viscometric measurements were expressed as apparent viscosity at native hematocrit μb, viscosity for corrected hematocrit 45% μ45, and RBC rigidity index 'Tk'. Correction of blood viscosity for hematocrit was calculated according to Quemada's equation (15):

$$\mu b = \mu pl \, (1-1/2 \; k.h)^{-2}$$

where μpl is plasma viscosity, h hematocrit, and k a structural parameter of blood viscosity which depends at high shear rate on RBC flexibility. A

viscometric index 'Tk' of red cell rigidity (as reflected by shear-induced erythrocyte elongation) was calculated from this viscometric measurement according to Dintenfass (16). 'Tk' is given by the following equation:

$$Tk = (\mu r^{0.4}-1)/(\mu r^{0.4}. h)$$

where μr is relative blood viscosity (i.e. μb/μpl). The 'k' index of RBC rigidity was also calculated according to Quemada (15):

$$k=2.(1-\mu r^{-0.5}).h^{-1}$$

Quality control of the measurements performed with the MT90 falling ball viscometer was regularly made with the Carrimed rheometer (17) which allows a precise measurement of blood viscosity over a wide variety of shear rates (from less than 0.1 up to 2000 s^{-1}). This latter device was not used in the study because it needs more blood sample volume than available from fetuses.

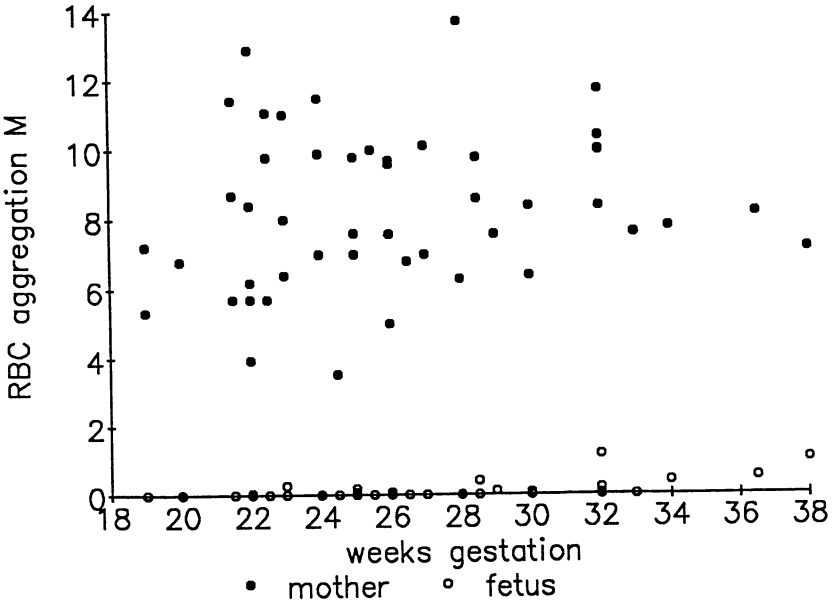

FIG 1

RBC aggregation M during pregnancy in fetus and mother.

Erythrocyte rigidity was measured by filtration of red cells resuspended at 8% hematocrit in Tris-Albumin buffer, with the Hemorheometre MK-1 (from IMH, 2, allee du Jardin de la Cure, 95470 Saint Witz, France). This apparatus measures the the initial flow rate of a suspension of red cells (18) through 5 μm Nuclepore sieves. Results were expressed as a relative viscosity of filtration (μfr) and corrected by hematocrit:

$$\mu fr = (ts/tb)/h$$

where ts is the time of passage of the suspension of red cells at 8% hematocrit, tb the time of passage of the buffer alone, and h the packed cell volume (%).

TABLE II
Regression of fetal hemorheologic parameters against week's gestation.

Blood viscosity	r=0.256	p<0.05
Hematocrit	r=0.263	p<0.05
Hemoglobin count	r=0.441	p<0.05
RBC count	r= 0.423	p<0.05
WBC count	r=0.676	p<0.001
Eosinophils	r=0.581	p<0.01
RBC aggregation M	r=0.560	p<0.01
RBC aggregation M1	r=0.270	ns
plasma viscosity	r=0.095	ns
RBC rigidity (Tk)	r=0.055	ns
RBC rigidity (k)	r=0.060	ns
RBC rigidity (μfr)	r=0.339	ns
Hb charge (pg/RBC)	r=-0.254	ns
Hb concentration (g/100)	r=0.393	ns
MCV (fl/RBC)	r=-0.339	ns
platelet count	r=-0.082	ns

Hematocrit viscosity ratio (h/μ) was calculated according to Stoltz (19), as an index of the contribution of blood rheology to O_2 supply to tissues.

Statistics

Correlations were tested by linear regression analysis. Results are presented as mean $\pm$ the SE of the mean. A value of $p<0.05$ was considered as significant. Correlations were performed using the method of least squares. Variables in the two groups were compared using the two tailed nonparametric test of Mann-Whitney for unpaired data. Significance was defined as $p<0.05$. The choice of nonparametric tests was done in order to adhere the guidelines of J. Stuart 20) and the ICSH expert pannel for blood rheology (21), since hemorheological parameters usually appear to exhibit a nonnormal distribution.

RESULTS

Table I shows that fetuses, when they are compared to their mothers studied at the same time, have significantly lower blood viscosity at both native ($p<0.01$) and corrected ($p<0.000000001$) hematocrit. When looking at the different factors of blood viscosity, it appears that they had lower plasma viscosity ($p<0.0001$), lower RBC flexibility (measured by filterability on the hemorheometre) ($p<0.01$) and higher hematocrit/viscosity ratio ($p<0.01$) than their mothers. The measurement of RBC rigidity by viscometric procedures (i.e. Dintenfass' 'Tk' and Quemada's 'k' indices) gave no significant differences. The difference between mothers and fetuses concerning hematocrit was not found, in this study, to be significant, although a tendency was observed (fetuses having higher hematocrit). RBC aggregation was studied in 52 samples and was very low ($p<0.000000001$ when compared to mothers with both M and M1 indices).

TABLE III

Correlation between the measurement of the Pourcelot index (resistance index) in maternal uterine artery and blood rheological parameters measured in the mother (n=24 mothers).

Weeks gestation	r= 0.447	p<0.05
h/μ	r= 0.006	ns
μ45	r= 0.104	ns
Tk	r= 0.129	ns
M1	r= -0.215	ns
M	r= 0.210	ns
μpl	r= 0.14	ns
H	r=0.240	ns
μb	r= -0.005	ns

TABLE IV

Correlations between fetal blood rheology and umbilical artery resistance index (n=14 fetuses).

weeks gestation	r=-0.274	ns
μb	r=0.476	p<0.05
Ht	r=0.683	p<0.01
μpl	r=-0.02	ns
M	r=-0.183	ns
M1	r=-0.175	ns
Tk	r=0.08	ns
μ45	r=-0.15	ns
h/μ	r=0.558	p<0.01

The period studied by these cordocenteses allows to describe a physiological evolution of hemorheological parameters during late pregnancy (19 to 40 week's gestation). Table II gives the regression coefficients of rheologic parameters plotted against time. The following parameters are linearly related to time : blood viscosity, hematocrit, hemoglobin count, RBC count, WBC count, eosinophil count, RBC aggregation index 'M'. In 22 subjects fibrinogen was assayed. It was not linearly correlated with time (r=0.374 nonsignificant tendency) but the regression became significant when an exponential relationship was tested (r=0.479 p<0.05). Albumin was measured in 27 subjects and was linearly correlated with time (r=0.494 p<0.01). The albumin/fibrinogen ratio (17 subjects) and the total fetal plasma protein concentration (22 subjects) were not significantly related to time (respectively r= 0.322 and r=0.273).

Fig. 1 and 2 shows the compared evolution of fetal and maternal RBC aggregation index between 19 and 38 wk gestation.

Preliminary results of our study on resistance indices measured by doppler are shown on table III and table IV. A correlation between umbilical artery resistance index and both whole blood viscosity and hematocrit is found. Fig. 3 and 4 show these correlations.

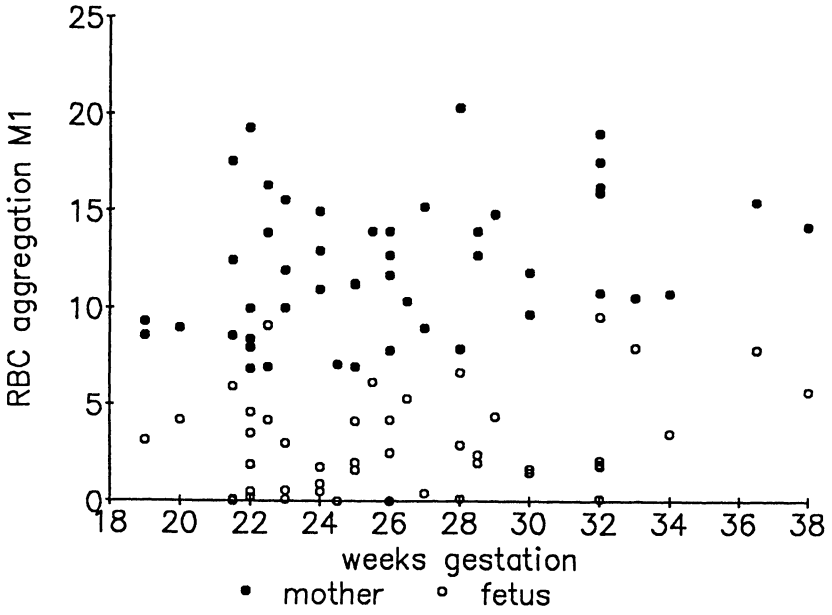

FIG 2
RBC aggregation M1 during pregnancy in fetus and mother.

DISCUSSION

Methodological aspects

It is difficult, for obvious ethical reasons, to measure fetal blood rheology without medical reasons for performing a cordocentesis. Therefore, our sample of fetuses is not a 'physiological' one and is selected after the fetal pathologies have been ruled out: this represents an important cause of methodological bias which seems difficult to overcome. However, we think that this approach provides a more direct evaluation of what happens in utero than the previous studies using cord blood at birth. In our preliminary report on 29 fetuses (9,10) we postulated that the study of cord blood of prematures at birth was a good model for evaluating fetal rheology. Our present findings are in agreement with these previous statements. However, two major possibilities of artifacts exist for this method: (a) prematures are not 'normal' newborns and could be expected to have diseases which modify blood rheology; (b) labor and delivery are very stressful events which induce in the mother drammatic increases in blood viscosity (22-23). Moreover, for many physiological reasons, the newborn can no longer be considered as a fetus.

Concerning methodology, a slight difference between the values presented here and our preceding ones (9-10) in preliminary papers should be pointed out. The introduction of a quality control with the Carri-Med rheometer helped us to correct our results obtained with the falling ball viscometer by a proportionnality factor. We think that the values given in this paper are more

consistent with what would give classical Couette viscometry at the same shear rate (14).

Particularities of fetal blood

This study confirms that fetuses exhibit a peculiar hemorheologic pattern: lower plasma viscosity, lower blood viscosity, more rigid RBCs, higher hematocrit/viscosity ratio. RBC aggregation which could not be measured in our preceding preliminary reports (9-10) is very low (M index equal to zero before 20 wks). This latter finding is in agreement with the reports of the team of MW Rampling (7, 24). These authors interprete the increase in rouleaux formations in fetal blood at the end of pregnancy as a consequence of increases in concentrations of fibrinogen, a2 macroglobulin, IgG and a reduction in the degree of sialination of fibrinogen. In addition cellular factors which are not overcome by resuspension of fetal RBCs in adult plasma are probably involved also (25). Our finding that hematocrit/viscosity ratio is higher in fetuses than in their mothers is of interest, since this parameter is believed to evaluate the contribution of blood rheology to O_2 supply to tissues (19). In maternal organisms, vasodilatation is an important factor of increased blood distribution (26-28), despite lower hematocrit and slowly increased viscosity. In fetus, O_2 content of blood is relatively low (28), as well as systemic blood pressure (27). Thus, a low h/μ ratio is probably important for maintaining a good O_2 distribution to fetal tissues. In our study, this parameter remains constant with no tendency to increase during intrauterine life, as a result of a combination of the various changes observed during this period.

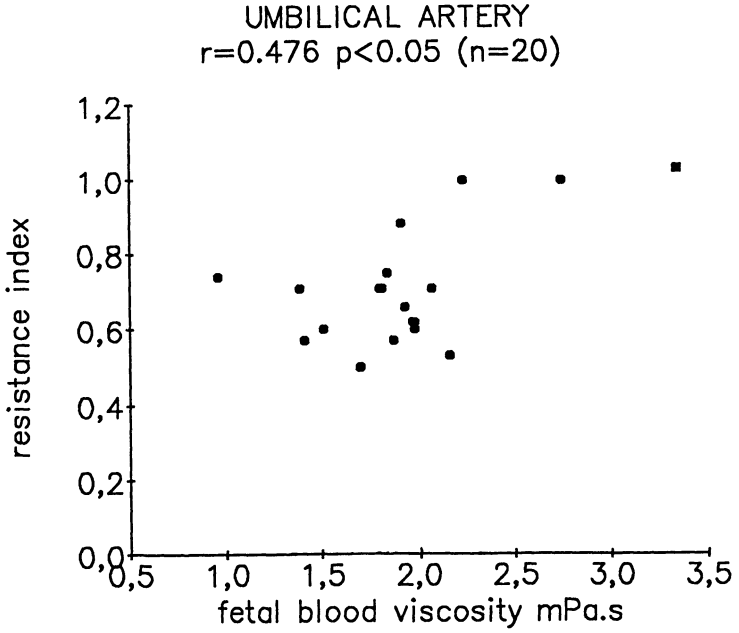

FIG 3

Correlation between fetal whole blood viscosity at high shear rate (measured by intrauterine cord blood sampling) and umbilical artery resistance index measured by doppler just before the puncture.

Natural history

As shown on table II, the following parameters are linearly related to time : blood viscosity, hematocrit, hemoglobin count, RBC count, WBC count, eosinophil count, RBC aggregation index 'M'. Compared to our previous report on 29 women we confirm no change in plasma viscosity and viscometric indices of RBC rigidity. The increase in hematocrit which was non significant ($r=0.152$ ns) in our previous report becomes significant here ($r=0.263$ $p<0.05$). In this paper we did not further investigate RBC filterability which seemed to exhibit a 'U shaped curve' in our previous report. This aspect remains to be investigated. However, Colin and coworkers (29) have reported preliminary data concerning RBC filterability and RBC membrane lipids in 40 fetuses and they pointed out that RBC deformability was lower in term fetuses (37-40 wks) than in earlier fetuses (18-24 yr). Thus, RBC rigidity seems to undergo modifications during the intrauterine life, and these modifications remain to be described with more detail. The viscometric approach used in this paper was unable to detect them. However, filtration studies in fetuses should carefully avoid artifacts related to MCV changes throughout the intrauterine life.

All these aspects of intrauterine evolution of the rheologic properties of blood show a progressive modification of them, from a very peculiar 'fetal' pattern towards a more 'adult-like' one which is found in the newborn. Especially, the physiological meaning of a lack of RBC aggregation in the youngest fetuses remains unclear. As previously indicated (30) these aspects are important for therapeutic purposes, since transfusion of adult blood (with more viscous plasma and much more aggregable RBCs) may result in dangerous hyperviscosity states.

Relations to hemodynamics

As shown on tables II and IV, we tried to correlate blood rheology and hemodynamics in the mother and the foetus. Generally, such studies give rather poor results since modifications of blood viscosity are easily compensated by minor modifications of the vascular tone. However, the pregnant woman as well as the fetus have special hemodynamic conditions which can result in a more pronounced effect of blood viscosity on circulation (26-28). Results of this study are available in a little number of subjects and should be confirmed by a larger study group. Nonetheless, a correlation between resistance index in the uterine artery and blood viscosity is shown on fig. 2. This resistance index is also correlated to fetal hematocrit (fig. 3) and this latter correlation probably explains most of the correlation with blood viscosity. Accordingly, if blood viscosity is corrected for hematocrit, this correlation is not found (table IV). While this preliminary finding requires further confirmation, it can be compared with the report of Jouppila and coworkers (8) who found a significant negative correlation between the umbilical blood viscosity (measured in cord blood at birth) and umbilical vein blood flow evaluated by doppler in 64 pregnant women. In this case also, hematocrit seemed to be an important factor explaining the correlation and the authors concluded that hemoconcentration was responsible foer hyperviscosity which impaired fetal circulation. Since the paper of Jouppila is related to venous blood flow, it will be interesting to confirm a possible influence of blood viscosity on resistance in the umbilical artery.

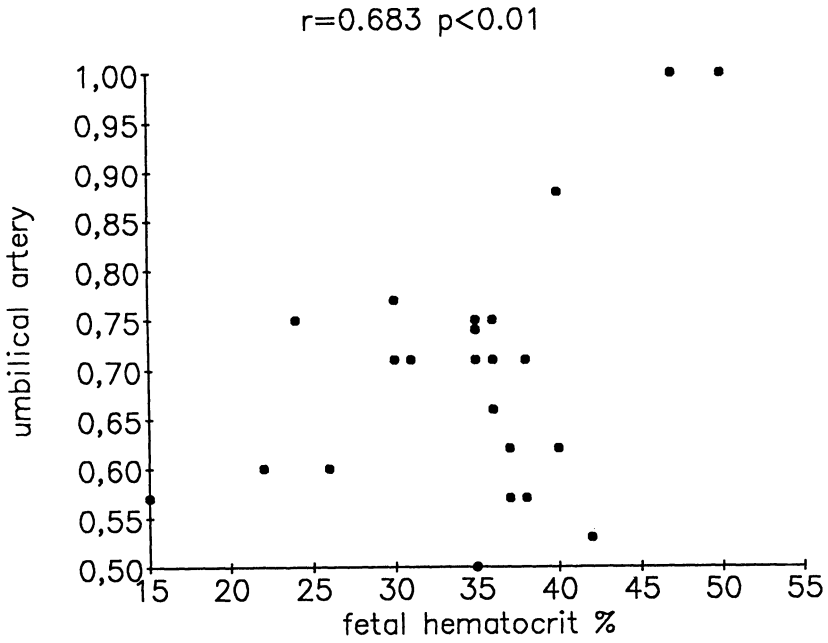

FIG 4
Correlation between fetal hematocrit (measured by intrauterine cord blood sampling) and umbilical artery resistance index measured by doppler just before the puncture.

In conclusion, we think that the physiology of blood rheology in fetus, which remains uncompletely known until now, appears to be interesting to study for three reasons. First, it can help us to improve the accuracy of intrauterine fetal therapeutics (e.g. transfusion). Then, for the hemorheologist, our preliminary findings suggest that the fetus may be a model for studying the interactions of blood rheology with circulation because vascular reactivity is immature (and presumably unable to overcome marked changes in blood viscosity increasing vascular resistances). Finally, some pathophysiological disorders of the fetoplacental unit may involve rheologic abnormalities, with possible hemorheologic treatment.

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REFERENCES

1. LINDERKAMP O, SENGESPEIK HC, McKAY CB, MEISELMAN HJ. Rheological properties of blood in preterm and full-term neonates. In: Heilmann L, Buchan PC (Eds). Hemorheological disorders in obstetrics and neonatalogy. Schattauer, 1984, 83-91.

2. GAEHTGENS P, SCHICKENDANTZ S. Rheologic properties of maternal and neonatal blood. Bibl Anat 13, 107-108, 1975.

3. FOLEY ME, ISHERWOOD DM, McNICOL GP. Viscosity, haematocrit, fibrinogen and plasma proteins in maternal and cord blood. Br J Obstet

Gynaecol 85, 500-504, 1978.

4. FOLEY ME, COLLINS R, McDONALD D. Whole blood viscosity in umbilical cord blood, adult pregnant and non-pregnant blood: the influence of plasma factors. Clin Hemorheol 3, 285, 1983.

5. BUCHAN PC. Evaluation and modification of whole blood filtration in the measurement of erythrocyte deformability in pregnancy and the newborn. Br J Haematol 45, 97-105, 1980.

6. BUCHAN PC. Maternal and fetal blood viscosity throughout normal pregnancy. Br J Obstet Gynaecol 4, 343, 1984.

7. RAMPLING MW, ANWAR MA, WELCH R, BIGNALL S, RIVERS RPA. Gestational age related changes in haemorheology determined from blood of the newborn premature infant and from in utero sampling. 7th Europeran Conference on Clinical Haemorheology, 16th-19th July 1991, Southampton. Abstract book p. 54.

8. JOUPPILA P, KIRKINEN P, PUUKKA R. Correlation between umbilical vein blood flow and umbilical blood viscosity in normal and complicated pregnancies. Arch Gynecol 237, 191-197, 1986.

9. BOULOT P, BRUN JF, FONS C, EL BOUHMADI A, HEDON MN, VIALA JL, ORSETTI A. The haemorheology of foetus studied by umbilical cord venepunctures in utero. Rev Port Hemorreol 5, 111-117, 1991.

10. BOULOT P, BRUN JF, FONS C, EL BOUHMADI A, HEDON MN, VIALA JL, ORSETTI A. Caractéristiques du sang foetal prélevé in utero par cordocentèse. Rev Franç Gynécol Obstet 86, 164-157, 1991.

11. BOULOT P, DESCHAMPS F, LEFORT G, SARDA P, MARES P, HEDON B, LAFFARGUE F, VIALA JL. Pure fetal blood samples obtained by cordocentesis: technical aspect of 322 cases. Prenatal diagnosis 10, 93-100, 1990.

12. POURCELOT L, ARBEILLE P. Evolution de la circulation foeto-placentaire au cours de la grossesse normale et pathologique. Soir Echog Gynecol Obstet 30, 23-29, 1982.

13. DOFFIN J, PERRAULT R, GARNAUD G. Blood viscosity measurements in both extensional and shear flow by a falling ball viscometer. Biorheology, suppl.1 , 89-93, 1984.

14. FONS C, BRUN JF, SUPPARO I, MALLARD C, BARDET L, ORSETTI A. Measurement of blood viscosity at high shear rate with a falling ball viscometer. 7th Europeran Conference on Clinical Haemorheology, 16th-19th July 1991, Southampton. Abstract book p.133.

15. QUEMADA D, Rheology of concentrated disperse systems. II. A model of non newtonian shear viscosity in steady flows. Rheol Acta 17, 632-642, 1978.

16. DINTENFASS L. Red cell rigidity, "Tk", and filtration. Clin Hemorheol 5, 241-244, 1985.

17. BOUTON J, ANSERMIN M. Rhéomètre Carrimed CS. Appareil à contrainte imposée pour mesure de fluides viscoélastiques et de fluides à seuil. Stoltz JF, Donner M, Puchelle E: Techniques en biorhéologie. Séminaire INSERM Vol. 143, 1986, 121-124.

18. HANSS M. Erythrocyte filterability measurement by the initial flow rate method. Biorheology 20, 199-211, 1983.

19. STOLTZ JF, DONNER M, MULLER S. Syndromes d'hyperviscosité et transport d'oxygène: notion de profil hémorhéologique. 7e Réunion Conjointe de la Société d'Hémorhéologie de l'Ouest et de la Société de Biorhéologie de Langue Française, Rennes (France), May 18th, 1990 (proceedings in press).

20. STUART J. Design principles for clinical and laboratory studies of erythrocyte deformability. Clin Hemorheol 5, 159-169, 1985.

21. ICSH expert panel on blood rheology. Guidelines for measurement of blood viscosity and erythrocyte deformability. Clin Hemorheol 6, 439-453, 1986.

22. BRUN JF, BOULOT P, HEDON MN, VIALA JL, ORSETTI A. Modifications physiologiques de la rhéologie sanguine au cours de la grossesse et de l'accouchement: résultats préliminaires. Artères et Veines 9, 552-557, 1989.

23. BRUN JF, BOULOT P, FONS C, HEDON MN, VIALA JL, ORSETTI A. Paramètres hémorhéologiques pendant l'accouchement normal et la contraction utérine. Rev Franç Gynécol Obstet 86, 148-153, 1991.

24. ANWAR MA, RAMPLING MW, BIGNALL S, RIVERS RPA, WELCH R. Six ages of man (a comparative study). 7th Europeran Conference on Clinical Haemorheology, 16th-19th July 1991, Southampton. Abstract book p. 141.

25. WITTINGSTALL P, MEISELMAN HJ. Aggregation behavior of neonatal red blood cells. 7th Europeran Conference on Clinical Haemorheology, 16th-19th July 1991, Southampton. Abstract book p. 53.

26. LONGO LD, RENEAU DD. Fetal and newborn cardiovascular physiology. Vol. 2: Fetal and newborn circulation. Garland, editor. STPM press, New York, 1979.

27. TCHOBROUTSKY C. Circulation placentaire, maternelle, ombilicale et foetale. In: Tournaire M, editor. Physiologie de la Grossesse. Masson, Paris, 1986, 125-133.

28. GOODLIN RC. Care of the fetus. Masson Ed, New York, 1979.

29. COLIN F, MENEZ JF, CHABAUD JJ, BLANC MJ, VICARIOT M, LE ROUX AM. Hemorheological properties of fetal blood. Correlation with erythrocyte membrane lipid content. Clinical Hemorheology 7, 403, 1987 (abstract).

30. WELCH CR, RAMPLING MW, RODECK CH. The effect of donor blood hematocrit on fetal blood rheology after in utero transfusion. 7th Europeran Conference on Clinical Haemorheology, 16th-19th July 1991, Southampton. Abstract book p. 53.