

Macroscopic Examination of Placental Vascularization with a Corrosive Agent in Pregnant Women Diagnosed with Thrombophilia

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The normal development of the placenta is a major factor in the fetus's growth and development, whilst the maternal-fetal placental vasculature is essential in this regard. During placentation, there is an ongoing process, which combines angiogenesis with vasculogenesis, as demonstrated by numerous studies, which reveal important roles of various known angiogenic factors, while other studies show the roles of different classes of factors in vascular morphogenesis nonspecific to the placenta. The method used in the case of our study is a standardized method of the Laboratory of Anatomy and Embryology, Victor Babes University of Medicine and Pharmacy, Timisoara, for over 50 years. The making of corrosion concoction followed the recipe of the laboratory using type AGO II plastic substances, differently colored and then subjected to the corrosive action of hydrochloric acid. During the routine check outs all the pregnant woman's were diagnosed with thrombophilia. The examination of the placental parameters - shape, weight, thickness - is important as a preliminary stage for the study of the placental architecture. The normal placental development remains a major factor in the growth and development of the fetus, and the maternal-fetal placental vasculature is essential in this regard. Placental angiogenesis has a different local component of angiogenesis, found in other anatomical regions.

Keywords: maternal-fetal placental vasculature, corrosive agent, thrombophilia

Thrombophilias are hereditary or acquired haematological disorders, creating a predisposition towards thrombo-occlusive events or thromboembolic disease, caused by molecular abnormalities of the haemostasis.

Thrombophilias are associated with an increased risk of fetal loss in most case studies. The risk is increased during pregnancy, but may be even higher in the second and third trimesters of pregnancy. As a frequency, thrombophilias can be found in approximately 5-10% of the European population. Thrombophilia may be congenital or acquired and is related to changes in hemostatic mechanisms, characterized by an increased tendency for the blood to clot and a consequent risk of thromboembolism [1,2].

The normal development of the placenta is a major factor in the fetus's growth and development, whilst the maternal-fetal placental vasculature is essential in this regard. During placentation, there is an ongoing process, which combines angiogenesis with vasculogenesis, as demonstrated by numerous studies, which reveal important roles of various known angiogenic factors, while other studies show the roles of different classes of factors in vascular morphogenesis nonspecific to the placenta.

Placentation includes extensive angiogenesis in maternal and fetal placental tissues, accompanied by a marked increase in uterine and umbilical blood flows [3-7].

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Experimental part

Material and methods

We studied 20 human placentas collected immediately after naturally performed births in the *Bega* Clinic of Obstetrics and Gynecology, Emergency County Hospital, Timisoara, Romania, from 2015 to 2016. After the macroscopic evaluation and weighing of the placentas, they were processed in the Laboratory of Anatomy and Embryology, Victor Babes University of Medicine and Pharmacy, Timisoara.

The examination of the placentas was made soon after delivery, after a protocol of a quick description of the placenta and the associated structures. Then, the placentas were transported to the Laboratory of Anatomy and Embryology, Victor Babes University of Medicine and Pharmacy, Timisoara, to obtain the corrosion concoction.

Study of the corrosion concoction

The method used in the case of our study is a standardized method of the Laboratory of Anatomy and Embryology, Victor Babes University of Medicine and Pharmacy, Timisoara, for over 50 years. The making of corrosion concoction followed the recipe of the laboratory using type AGO II plastic substances, differently colored and then subjected to the corrosive action of hydrochloric acid. This technique has been published and reported in the

Authors with equal contributions.

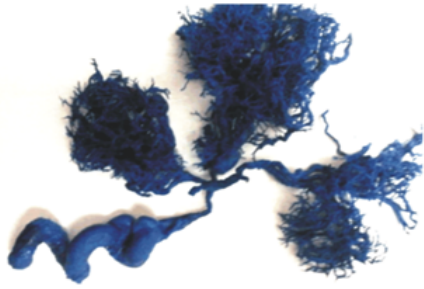


Fig. 1. Placenta - fetal face - corrosive agent. It can be noticed an umbilical vein that splits into three primary trunks and a branch for an accessory lobe; in pregnant women diagnosed with thrombophilia

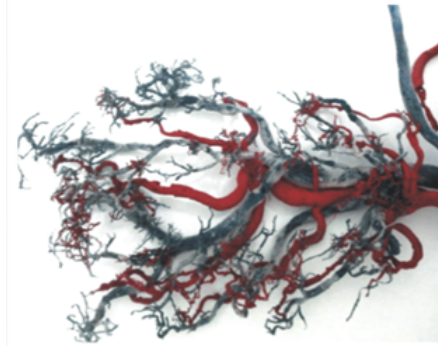


Fig. 2. Placenta at 32 weeks - fetal face- corrosive agent. It can be noticed a single umbilical artery, with a caliber higher than the usual, which branches in all placental territory, giving four primary branches of approximately equal caliber; in pregnant women diagnosed with thrombophilia

national and international anatomical press, under the signature of Prof. Gheorghe Corondan and Lecturer Leonida Bejan in 1956, and was later improved by Ciobanu (1960), Diaconescu (1962), Radu (1968), Kuhn (1961), Rottenberg (1969). This technique produces corrosive agents, which are the mold vessels in the organ studied - in our case - the placenta. These preparates provide a 3D image that is very close to real, thus allowing the study of vascular arborization.

The statistical analysis was computed using the following programs Microsoft Excel,

EpilInfo v7 and SPSS v17. For the Person coefficients, the determination coefficients and the associated p - values we used the Regression Model. For computing the p value in order to see if the habit of smoking can influence the fetuses weight we used a Mann - Whitney test.

Results and discussion

We present a follow up study, which was conducted for two years, the data were collected from 2015 (30 patients) and 2016 (42 patients). During the routine check outs all the pregnant woman's were diagnosed with thrombophilia. The examination of the placental parameters - shape, weight, thickness- is important as a preliminary stage for the study of the placental architecture.

The examination of the placental surfaces provided data on the possible placental pathologies. We have not demonstrated the presence of shape placental abnormalities in our study.

The statistical parameters	The values obtained
<i>Results for the gestational period (presented in weeks) compared to the Apgar score</i>	
r (Pearson coefficient)	0.95
R^2	0.89
p value	p<0.001
<i>Results for fetus weight compared to the Apgar score</i>	
r (Pearson coefficient)	0.89
R^2	0.80
p value	p<0.001
<i>Results for the placenta's weight compared to the placenta's thickness</i>	
r (Pearson coefficient)	0.85
R^2	0.71
p value	p<0.001
<i>Results for the fetus weight compared to the placenta's weight</i>	
r (Pearson coefficient)	0.99
R^2	0.99
p value	p<0.001
<i>Results for the gestational period compared to the placenta's weight</i>	
r (Pearson coefficient)	0.92
R^2	0.85
p value	p<0.001
<i>Results for the gestational period compared to the fetus length</i>	
r (Pearson coefficient)	0.94
R^2	0.88
p value	p<0.001
<i>Results for the gestational period compared to the fetus weight</i>	
r (Pearson coefficient)	0.92
R^2	0.85
p value	p<0.001
<i>Results for the mother's age compared to the gestational period</i>	
r (Pearson coefficient)	0.12
R^2	0.01
p value	p=0.32

Table 1

The aim of this study is to observe the evolution of pregnancy for a patient who has thrombophilia. So, in the first part for all our patients (N=72) we wanted to see if there is any association between the gestational period (presented in weeks) and the Apgar score that the baby received at birth; between the fetus weight and the Apgar

score; between the placenta's weight and the placenta's thickness; between the fetus weight and the placenta's weight, respectively the fetuses length and weight; between the mother's age and the gestational period. We obtained a strong positive correlation, extremely significant

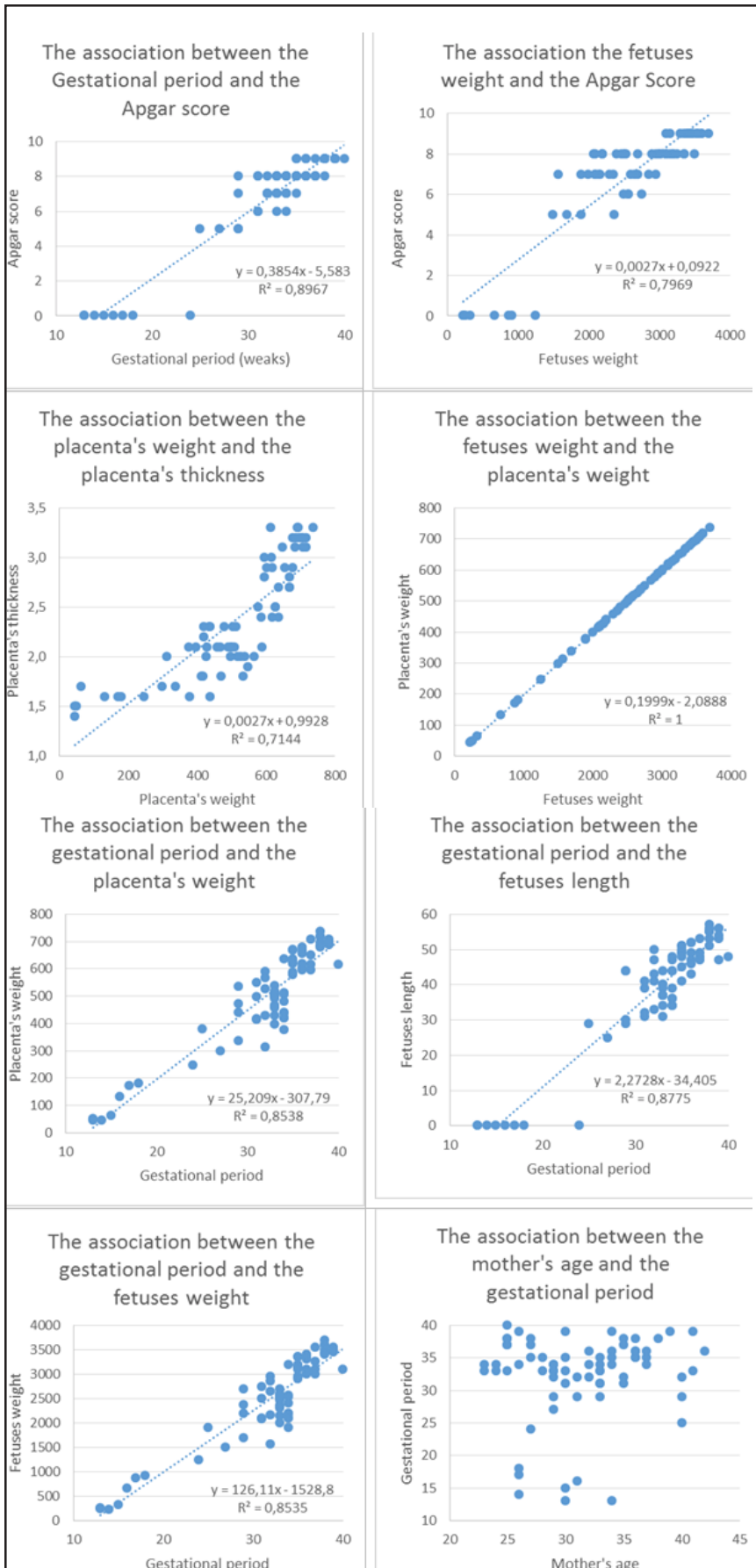


Table 2
IN THIS TABLE WE PLOTTED ALL THE REGRESSION MODELS PRESENTED ABOVE

for all our cases except for the last association, which was between the mother's age and the pregnancy period. All the results are presented in table 1 and table 2.

In the second part of our study we wanted to see if there is any statistical differences between the smoker and non-smoker mothers regarding the fetuses weight. We have 48.6% patients (N1=35) who are smokers and 51.4% patients (N2=37) who are non-smokers. After computing a Kolmogorov-Smirnov normality test on the variable fetuses weight we obtained that we don't have a normal distribution in our data, so we applied a Mann-Whitney test and we determined that the fetuses who have smoker mothers are significantly smaller than the other fetuses ($p < 0.001$). So, smoking during pregnancy can influence a fetus evolution negatively.

The smoking future mother is more predisposed to have complication during pregnancy, complications such as the premature peeling of the placenta - placenta praevia. Smoking increases the risk of thrombosis [8] thrombosis and the occurrence of premature labor with repercussions on the fetus, with varying degrees of prematurity and increased risk of infection [9 - 12].

In table 1 we computed the regression model in order to see if we have an association between the gestational period (presented in weeks) and the Apgar score; between the fetus weight and the Apgar score; between the placenta's weight and the placenta's thickness; between the fetus weight and the placenta's weight; between the gestational period and the placenta's weight, respectively the fetuses length and weight; between the mother's age and the gestational period.

Conclusions

The normal placental development remains a major factor in the growth and development of the fetus, and the maternal-fetal placental vasculature is essential in this regard. Placental angiogenesis has a different local component of angiogenesis, found in other anatomical regions. The placental development is a complex process; the villous vasculature is in, and its dysfunction may lead to a placental insufficiency.

Preliminary data suggest, however, that the administration of anticoagulant-based prophylaxis may improve the chances of taking a pregnancy to term in thrombophilic women with unexplained recurrent fetal loss. We must not forget that treatment during pregnancy is individualized.

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