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Research Article

Maternal Hematological Aspects in Correlation to Placental and Pathological Findings in Gestations with Growth Restrictive Issues

Walid M Elnagar[1]*, Maha Abdelhamid Amin[2], Mai M Abdelwahab[3] and Samia Hussein[4]

[1]*Department of Obstetrics and Gynecology, Zagazig University, Egypt*

[2]*Department of Physiology, Zagazig University, Egypt*

[3]*Department of Pathology, Zagazig University, Egypt*

[4]*Department of Medical Biochemistry and Molecular Biology, Zagazig University, Egypt*

***Corresponding author:** Walid M Elnagar, Department of Obstetrics and Gynecology, Zagazig University, Egypt

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Abstract

Background: The placental circulation and microvasculature is a highly sensitive system particularly during development. A growing research interest all over the globe is to utilize the biomarkers in diagnosis of common clinical case scenario to enhance the level of medical care.

Aim: To assess and evaluate the placental and umbilical cord histopathological findings in cases of intrauterine growth restriction and their correlation to second gestational trimester maternal hematological indices.

Methodology: A prospective case-control clinical research trial conducted study between January 2016 and December 2018 at Zagazig university. Hospital research data have been gathered from the medical records; blood indices have been obtained within second gestational trimester. Study subjects have been categorized as IUGR when the expected fetal weight on the 20th gestational week of gestation was under the 10th centile as corresponding gender, and gestational age.

Results: Umbilical cord and placental pathological findings among both research groups in which there was no statistical significant difference between IUGR and control research groups as regards Vena umbilicalis vessel wall thickness, Vena umbilical is lumen area, arteria umbilicalis vessel wall thickness, ratio of star-shaped arteries, umbilical cord diameter, longest placental diameter, placental thickness (p values = 0.130, 0.672, 0.398, 0.061, 0.221, 0.087, 0.276, 0.269 consecutively) however arteria umbilicalis lumen area, number of placental pathologies present, native placental volume, placental volume after formalin fixation, placental weight after formalin fixation, shortest placental diameter, placental coefficient are statistically significant difference (p values<0.001).

Conclusions: The current study elucidates the importance of histopathological evaluation of the placentas of growth restricted fetuses in order to understand the histopathological development of this disease in an effort to innovatively develop an effective management line for this common obstetric clinical case scenario.

Keywords: Hematological aspects, Histopathological findings, Intrauterine growth restriction

Introduction

Intra uterine growth restriction (IUGR) is a common clinical scenario that is presented in every day obstetric practice raising morbidity and mortality issues at both maternal and neonatal levels particularly in the presence of comorbid medical diseases with pregnancies [1-3]. The placental circulation and microvasculature are a highly sensitive system particularly during development. A growing research interest all over the globe is to utilize the biomarkers in diagnosis of common clinical case scenarios to enhance the level of medical care, however the issues of sensitivity and sensitivity of various maternal biomarkers is a great area of research efforts. Maternal hematological changes during pregnancy could have a great impact on the placental development and maturity [4-7].

Researchers are gaining interest to reveal and display any correlation between placental histopathological finding between maternal hematological indices in various obstetric clinical scenarios such as chorioamnionitis condition, however as complex issue of intrauterine growth restriction still there is requirements to put more investigative efforts to elucidate the value and linkage between maternal hematological indices and placental histopathology issues in cases with IUGR [8-11].

An interesting fact to mention is that the placental size, weight, and shape have a wide range of normal values besides placental size and integrity at cellular, physiological levels is crucial for fetal nutritive and respiratory functions. Furthermore, the placenta is a complex organ that have endocrinal and enzymatic activity that could be easily affected by maternal hematological issues [12-15]. Researchers in prior research studies have revealed that placentas of neonates affected by intrauterine restrictive issues are shown to be smaller in diameters and reduced in overall weight and volume in comparison to normal-weight neonates [16,17]. Furthermore, placental vascular pathological issues such as calcification, decreased cyto trophoblastic proliferation and perivillous fibrin deposits are correlated and linked in previous research studies to intrauterine growth restrictive issues whether symmetrical or asymmetrical [18,19].

Aim of the Work

To assess and evaluate the placental and umbilical cord histopathological findings in cases of intrauterine growth restriction and their correlation to second gestational trimester maternal hematological indices.

Methodology

A prospective case-control clinical research trial conducted study between January 2016 and December 2018 at Zagazig university hospital research data have been gathered from the medical records, blood indices have been obtained within second gestational trimester study subjects have been categorized as IUGR (10 cases) when the expected fetal weight on the 20th gestational week of gestation was under the 10th centile as corresponding gender and gestational age.

Exclusive research criteria were as follows cases having twin gestations, preterm deliveries, congenital anomalies, hypertension with pregnancy, DM whether gestational or pregestational smokers and cases with history of substance abuse cases recruited for the research study didn't have immunological, cardiovascular, gastrointestinal, or pulmonary illnesses.

Sonographic assessment has been conducted by the same sonographer to prevent interobserver variability issues. Gestational age has been calculated according to the first day of the last menstrual period and sonographic biometry indices (CRL and BPD) between the 9th and 11th gestational weeks. At the 20th-24th gestational weeks, obtained fetal biometric indices were implemented to evaluate expected fetal weight using Hadlock formulas after delivery, the neonatal weight and placental volume have been measured.

Umbilical cord and placental sample assessment after around 3-7 days of fixation by formalin, placental weight and volume had been measured with histopathological gross examination and the umbilical cord was executed by an experienced pathologist. The obtained placenta has been cut along the longest diameter in 1cm thick strips and the thickness of the tissue was measured at the site of umbilical cord insertion. Umbilical cord samples were taken from the placental end and divided into transverse slices measuring 4mm, in a perpendicular manner to the umbilical cord. Histological slices have been dehydrated in graded ethanol series, cleaned in xylene, and embedded in paraffin. After hematoxylin/eosin (HE) staining process, histological samples have been examined microscopically.

Statistical analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when parametric and median with inter-quartile range (IQR) when nonparametric. Also, qualitative variables were presented as number and percentages. The comparison between groups regarding qualitative data was done by using Chi-square test and/or Fisher exact test when the expected count in any cell found less than 5. The comparison between two independent groups with quantitative data and parametric distribution was done by using Independent t-test while with nonparametric data were done by using Mann-Whitney test. Spearman correlation coefficients were used to assess the correlation between quantitative parameters. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant at the level of < 0.05.

Results

Table 1 reveals and displays that there was no statistically significant difference between IUGR and control research groups as regards the MCV, RBC count, Hb, Hct, platelet count, MPV, prothrombin time, INR, APTT, (p values=0.123, 0.571, 0.538, 0.526, 0.132, 0.492, 0.136, 0.314, 0.281 consecutively); however concerning umbilical artery S/D ratio was statistically significantly higher among IUGR research group, on the other hand there was no statistically significant difference between IUGR and control research groups as regards maternal age and BMI, parity with p values 0.122, 0.342, 0.623, consecutively. Statistical significant difference existed concerning birth weight of neonates being higher in control research group (p value<0.001), although APGAR score at 1 min was statically significantly higher among control research group (p value=0.042); the APGAR score at 5 and 10 min wasn't statically significantly different between both research groups (p values = 0.119, 0.321 consecutively), finally gestational age and gender among both research groups wasn't statistically significantly different (p values =0.061,0.603 consecutively) (Table 1).

Table 2 and Figure 1 reveals and displays the placental histopathological findings among both IUGR and control research groups in which there was no statistical significant difference as regards focal calcification, amnion nodosum, villitis, hematoma

(p values=0.080, 0.681, 0.681, 0.469 consecutively) whereas Villous hypo vascularization, Villous hypoplasia, Intervillous fibrin deposition, Syncytial node, Non-conversion of maternal vessels were statistically significantly more frequent among IUGR research group (p values <0.001, 0.010, 0.022, <0.001, 0.022 consecutively) (Table 1) (Figures 1-4).

Table 1: Clinical research data of the mothers and newborns.

	IUGR (n = 10)	Control (n = 60)	Test value	P-value	Sig.
MCV (fL)	83.95 ± 0.83	84.65 ± 1.37	1.563•	0.123	NS
RBC (T/L)	4.21 ± 0.18	4.18 ± 0.15	0.569•	0.571	NS
Hgb (g/L)	12.65 ± 2.45	12.24 ± 1.85	0.619•	0.538	NS
Hct (L/L)	0.38 ± 0.10	0.37 ± 0.03	0.638•	0.526	NS
PLT (x109/L)	224.8 ± 18.38	213.5 ± 22.17	1.524•	0.132	NS
MPV (fL)	11.72 ± 1.12	11.95 ± 0.95	0.691•	0.492	NS
Prothrombin time (s)	11.98 ± 0.21	12.12 ± 0.28	1.508•	0.136	NS
INR	0.93 ± 0.02	0.94 ± 0.03	1.014•	0.314	NS
APTT (s)	32.84 ± 0.36	33.07 ± 0.65	1.087•	0.281	NS
Umbilical artery (S/D)	3.65 ± 0.28	2.35 ± 0.18	19.400•	<0.001	HS
Maternal age (years)	31.17 ± 2.3	29.32 ± 3.6	1.567•	0.122	NS
Maternal BMI (kg/m^2)	27.65 ± 3.17	26.85 ± 2.32	0.956•	0.342	NS
Parity	1 (0-3)	1 (0-2)	0.617*	0.623	NS
Birth weight (g)	2350.1 ± 215.6	3415.3 ± 314.9	10.271•	<0.001	HS
Gestational age (weeks)	38.95 ± 0.92	39.4 ± 0.65	1.904•	0.061	NS
Apgar score 1-min	7 (7-8)	8 (8-9)	2.107*	0.042	S
Apgar score 5-min	8 (7-9)	9 (8-9)	1.201*	0.119	NS
Apgar score 10-min	9 (8-9)	9 (8-9)	0.912*	0.321	NS
Gender [no. (%)]			0.270≠	0.603	NS
Males	6 (60.0%)	41 (68.3%)			
Females	4 (40.0%)	19 (31.7%)			

*: Data were presented as median with (IQR) and compared using Mann-Whitney test

•: Data were presented as mean with SD and compared using Independent t-test

≠: Data were presented as numbers and percentages and compared using chi-square test

Table 2: Placental histopathologic alterations.

	IUGR n = 10	Control n = 60	Test value	P-value	Sig.
Focal calcification	3 (30.0%)	6 (10.0%)	3.06	0.08	NS
Villous hypovascularization	6 (60.0%)	2 (3.3%)	27.191	<0.001	HS
Villous hypoplasia	5 (50.0%)	9 (15.0%)	6.563	0.01	S
Intervillous fibrin deposition	4 (40.0%)	7 (11.7%)	5.195	0.022	S
Syncytial node	4 (40.0%)	1 (1.7%)	18.99	<0.001	HS
Amnion nodosum	0 (0.0%)	1 (1.7%)	0.169	0.681	NS
Villitis	0 (0.0%)	1 (1.7%)	0.169	0.681	NS
Hematoma	0 (0.0%)	3 (5.0%)	0.522	0.469	NS
Non-conversion of maternal vessels	3 (30.0%)	4 (6.7%)	5.185	0.022	S

Data were presented as numbers and percentages and compared using Chi-square test and or Fisher exact test

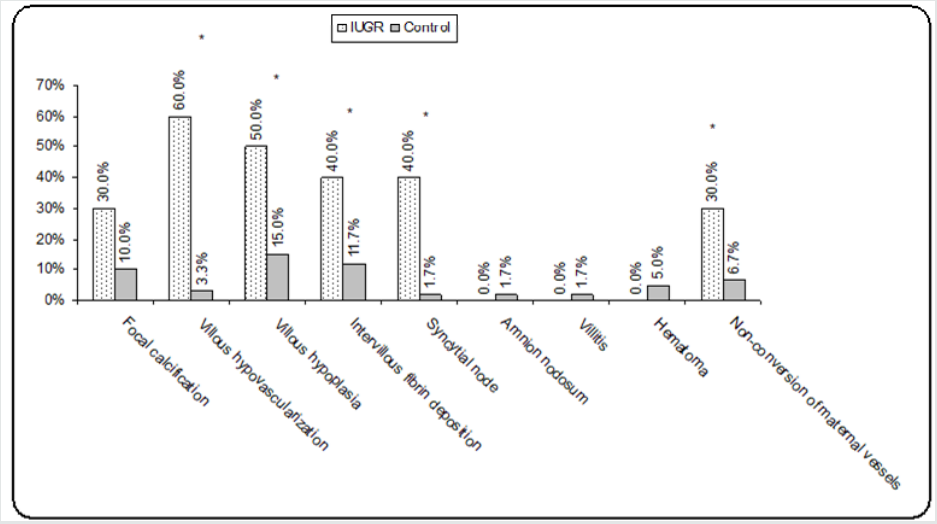

Figure 1: Placental histopathologic findings among the two research groups (*) indicate statistically significant difference among most findings investigated.

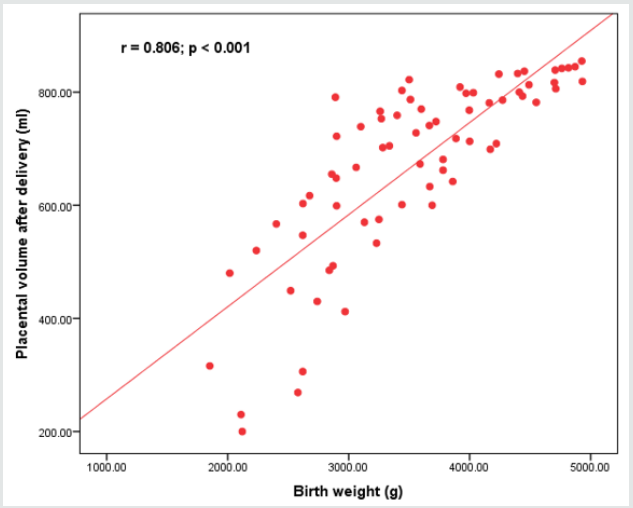

Figure 2: Placental morphometry; placental volume measured after delivery shows the strongest correlation with birth weight, not the placental volume.

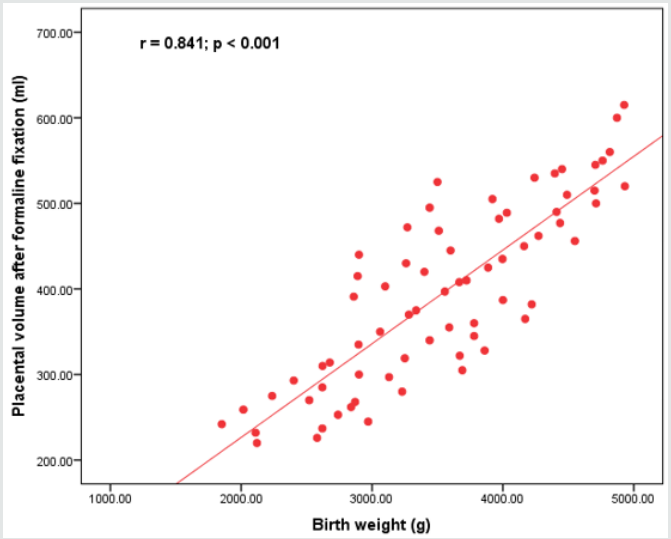

Figure 3: Placental morphometry; placental volume measured after delivery or weight.

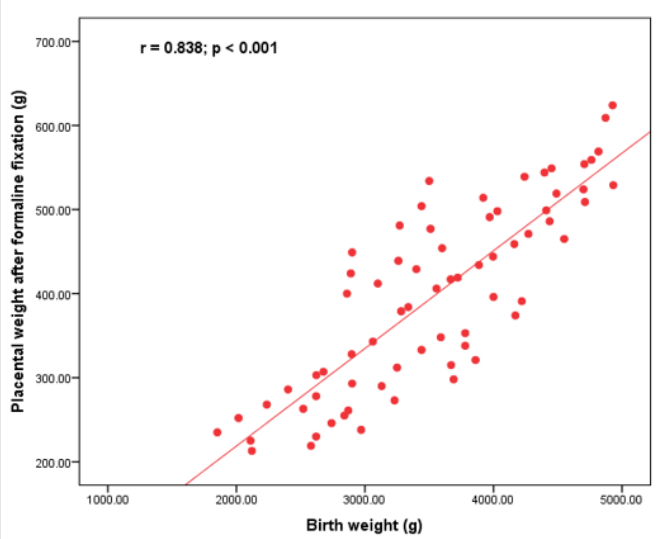

Figure 4: Placental morphometry; placental volume measured after delivery after formalin fixation.

Table 3 reveals and displays umbilical cord and placental pathological findings among both research groups in which there was no statistical significant difference between IUGR and control research group as regards vena umbilicalis vessel wall thickness, vena umbilicalis lumen area, Arteria umbilicalis vessel wall thickness, Ratio of star-shaped arteries, Umbilical cord diameter, Longest placental diameter, placental thickness (p values =0.130, 0.672, 0.398, 0.061, 0.221, 0.087, 0.276, 0.269 consecutively) however Arteria umbilicalis lumen area, number of placental pathologies present, Native placental volume, placental volume after formalin fixation, Placental weight after formalin fixation, Shortest placental diameter, placental coefficient are statistically significant difference (p values<0.001) (Table 3).

Table 3: Umbilical cord and placental pathological findings.

	IUGR (n = 10)	Control (n = 60)	Test value•	P-value	Sig.
Vena umbilicalis vessel wall thickness, µm	647.32 ± 58.14	623.9 ± 42.31	1.533	0.13	NS
Vena umbilicalis lumen area, µm2	1437000 ± 516320	1664021 ± 614325	0.426	0.672	NS
Arteria umbilicalis vessel wall thickness, µm	652.31 ± 52.13	662.85 ± 33.25	0.85	0.398	NS
Arteria umbilicalis lumen area, µm2	152314.9 ± 11327.3	489365.7 ± 57964.5	18.223	<0.001	HS
Ratio of star-shaped arteries	0.69 ± 0.18	0.83 ± 0.22	1.905	0.061	NS
UCI	1.19 ± 0.31	1.31 ± 0.28	1.236	0.221	NS
Umbilical cord diameter, mm	101.41 ± 11.85	109.37 ± 13.65	1.736	0.087	NS
Number of placental pathologies present	2.5 ± 0.63	0.91 ± 0.21	15.449	<0.001	HS
Native placental volume, mL	287.85 ± 35.14	485.13 ± 28.19	19.777	<0.001	HS
Placental volume after formalin fixation, mL	349.61 ± 28.69	462.74 ± 14.95	19.032	<0.001	HS
Placental weight after formalin fixation, g	398.45 ± 19.27	456.98 ± 14.88	11.032	<0.001	HS
Longest placental diameter, cm	15.32 ± 1.04	15.73 ± 1.10	1.099	0.276	NS
Shortest placental diameter, cm	13.28 ± 0.36	14.05 ± 0.43	5.35	<0.001	HS
Placental thickness, cm	2.66 ± 0.19	2.71 ± 0.12	1.114	0.269	NS
Placental coefficient	1.21 ± 0.02	0.16 ± 0.01	260.081	<0.001	HS

•: Data were presented as mean with SD and compared using Independent t-test

Discussion

Placental development and integrity are a cornerstone process for normal fetal growth pattern and development, however histopathological findings of placentas even in cases with no medical disorder with pregnancy reveal that intrauterine growth restriction could be associated and correlated to considerable placental abnormal histopathological findings [20,21]. Research studies similar to the current research in approach and methodology had revealed that the linkage between total placental volume and neonatal birth weight is more statistically significant than the correlation between neonatal birth weight and placental weight [22,23].

Furthermore, prior research efforts in harmony with the current research study findings the umbilical artery lumen area

was statistically significantly reduced in intrauterine growth restrictive gestations. Those research findings in harmony and great similarity to the current study findings could be justified by the basic physiological fact that the placental normal vascularity is of cornerstone importance in maintenance and integrity of the fetal growth and development process and any affection of the vascular performance of the placenta is associated with reduced fetal growth potential [1,4,7,9].

Interestingly prior investigators have revealed and displayed that from the maternal peripheral venous blood indices, only the platelet count is statistically correlated to growth restrictive issues observed clinical findings [10,14,17]. Clinical scenarios of preeclampsia are associated with raised maternal mononuclear cells and elevated cytokines level that could probably cause endothelial dysfunction and consequently intrauterine growth restrictive issues [19,23].

As regards the reliable maternal blood indices that could be implemented in detectability of growth restrictive issues only the platelet count reveals a statistically significant correlation as shown in the current study findings [2,8,17]. Another prior research team of investigators have shown among their research study findings that the placental volume indices obtained after delivery have a more powerful correlation to neonatal birth weight more than placental weight indices in correlation to neonatal birth weight [4,9,15].

In distinctive manner placentas in intrauterine restrictive gestations have tendency to be more oval in shape and thicker than placentas of healthy fetuses, prior histopathological studies of fetal growth restricted gestations pregnancies have shown that calcification and reduced villous vascularity are a common characteristic finding of placentas in those pregnancies [13,15,22].

Conclusion

The current study elucidates the importance of histopathological evaluation of the placentas of growth restricted fetuses in order to understand the histopathological development of this condition in an effort to innovatively develop an effective management line for this common obstetric clinical case scenario. This is only a small pilot study and further research is needed.

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