The Role of Parity on Some Macroscopical and Microscopical Variables in Placentas of Normal and Preeclamptic Women

Lina A. Hussain*, Malak A. Al-Yawer*, Huda M. Al-Khateeb *

ABSTRACT:

BACKGROUND:

The placenta is a dynamic organ, throughout gestation, it continuously undergoes different changes in structure and function to support the prenatal life. The anomalies of the placenta are usually associated with pregnancy complicated diseases which could lead to fetal complications. Hence, a careful examination of placenta in-utero as well as post-partum provides much insight into the prenatal health of the baby and the mother and can give information which could be useful in the management of complications in mother and the newborn, especially in a community like ours, where antenatal mothers still come unbooked to the labour room.

OBJECTIVE:

The aim of the present study was designed to elicit some morphometrical variables of delivered placentas (both gross and microscopic) in normal and preeclamptic pregnancies with regard to the role of parity (birth order) as a physiological change in women's life that may affect placental morphometrical variables.

PATIENTS AND METHODS:

A total of twenty- four placentas were freshly collected. They were grouped into two major groups (normal and preeclamptic) and each group was further subdivided according to parity into primi and multi subgroups (6 placentas for each subgroup). The placentas were grossly examined for (shape, insertion of umbilical cord,diameter and central thickness). Then tissue samples were fixed, processed, sectioned and stained by heamatoxylin and eosin stain to study the following microscopical variables as number of (villi, syncytial knots and fetal capillaries). **RESULT:**

Studying placentas had circular to oval shape. The percentage of central insertion of umbilical cord was increased in control group, mainly in multi one. While marginal insertion was increased mainly in primi preeclamptic. There was a significant reduction in diameter of placentas of preeclamptic group, mainly at primi. The placental thickness was significantly increased in preeclampsia. Statistical analysis for histomorphometrical variables had got an increased in number of villi, syncytial knots and fetal capillaries with preeclampsia and parity. The number of fetal capillaries was significantly increased with preeclampsia (mainly in primi subgroup). **CONCLUSION:**

In our study, the definite changes in macroscopical and microscopical variables in placentas of normal and preeclamptic women could be attributed to placental insufficiency especially in preeclamptic group and this may be a compensatory repair mechanisms to factors like hypoxia in order to provide better fetal growth.

KEY WORDS:placenta, preeclampsia, parity, morphology, histomorphometry.

INTRODUCTION:

Placenta enjoys much attention as an organ of union between mother and fetus. Their histological composition

was from fetal portion which consists of the villi of the chorion frondosum and maternal portion which is formed by the decidua basalis containing the intervillous space ^(1,2). Placenta nearly provides anaccurate record of

intrauterine journey of fetus which may undergo morphological and biological deviation ^(3,4), owing to the needs of fetus growth and in response to

pathological conditions ^(5,6).One such disorder is preeclampsia which is mainly peculiar to human pregnancy and based on a presence of hypertension and proteinuria, occurring after 20 weeks gestation $^{(7,8,9)}$ and affecting 1% to 7% of primiparous women, who have a three times higher risk than multiparous women⁽¹⁰⁾. Placenta has long been recognized as the necessary compenent for the genesis of syndrome. A well described pathological feature in preeclampsia is a shallow fetal trophoblast invasion into spiral arteries during maternal immunological tolerance semiallogenic fetus and placental to а development ⁽¹¹⁾. Roberts (2007) suggested stage model for maternal preeclampsia through proposing that placenta produce material(s) in response to reduce perfusion and mechanical factors upon the mother to bring a clinical finding of preeclampsia ⁽¹²⁾. Therefore, the aim of this study was designed to elicit some morphometrical variables of delivered placentas (both gross and microscopic) in normal and preeclamptic pregnancies with regard to the role of parity (birth order) as a physiological change in women's life.

PATIENTS MATERIALS AND METHOD:

Experimental study was performed on a group of 24 placentas during period (October 2013- April 2014) which were collected from Obstetrical and Gynecological Department of Baghdad Teaching hospital and Al- Yarmouk Teaching hospital. They were collecting from delivered women who were aging between 27-32 years. Placentas were divided

into 12 control and 12 preeclamptic groups then each group further subdivided according to parity into 6 primi and 6 multi. The criteria related to

 $\begin{array}{ll} \mbox{experimental} & \mbox{preclamptic} & \mbox{group} \\ \mbox{were(hypertension} \geq 140/90; \end{array} \right.$

proteinuria \geq 300 mg in GUE). The placentas were grossly examined for the following variables (shape, diameter, thickness and site of insertion of umbilical cord). Tissue samples were taken from six sites of each placenta and they were fixed with 10% neutral buffered formalin for 24 hours to prepare paraffin embedded blocks ⁽¹³⁾ and from each tissue block, 5-6 micron thick ribbons were collected and stained with haematoxylin and eosin (H&E) stain to study the number of the following variables (villi, syncytial knots and fetal capillaries). Six random high power fields were chosen from each tissue section to be studied.

Statistical analysis: Statistical Package for Social Sciences version 20 (SPSS v20) was used for data input and analysis. Continuous variables presented as means with standard deviation (M \pm SD) and discrete variables presented as numbers and percentages. T test for two independent samples was used to test the significance of difference between two means of two independent samples. Fishers' exact test and chi square test of independence was used to test the significance of association between discrete variables.

ANOVA test was used to test the significance of variation of mean of more than two independent samples. Tukey test was used as a Post Hoc test for multiple comparisons of means.

RESULTS:

Gross morphometrical study revealed a higher percentage of circular shaped placentas in multi control and a higher percentage of oval shaped placentas in primi subgroups (mainly preeclamptic one), (fig.1).

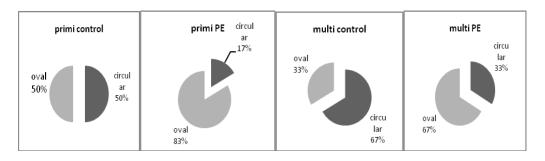


Figure 1: Shows the percentage level for placenta samples' shape in comparable subgroups.

The umbilical cord was 33.3% (centrally, marginally and paracentrally) inserted in primi control subgroup. 50% of multi control

subgroup exhibited a central insertion of cord. In preeclamptic (PE) groups, 50% of primi PE revealed a marginal insertion and 50% of multi PE revealed a paracentral insertion(table 1).

Umbilical Insertion; n(%)	Primi control	Multi control	Primi PE	Multi PE
Central	(33.3)	(50.0)	(16.7)	(16.7)
Marginal	(33.3)	(16.7)	(50.0)	(33.3)
• Para-central	(33.3)	(33.3)	(33.3)	(50.0)

Table 1: Shows the percentage level for umbilical cord insertion.

Statistical analysis showed that the diameter of placenta was ranged from 19.5cm (primi) to 20.5 cm (multi) in control group. It was significantly decreased in preeclampsia (p < 0.001) and it was ranged from 16.2cm (primi) to 16.8cm (multi), (table 2). The diameter of placenta was negatively correlated with placental thickness and with the number of fetal capillaries (table 4). Additionally, placental thickness was significantly increased in preeclampsia (p < 0.001) and it was ranged from 2cm (control) to

3cm (preeclamptic subgroups),(table 2), which was positively correlated with some microscopical variables (numbers of syncytial knots and fetal capillaries),(table 4).

Microscopical study of placentas disclosed an increased in number of villi, syncytial knots and fetal capillaries with parity and preeclampsia. The number of fetal capillaries was significantly increased with preeclampsia (mainly in primi subgroup), (p= 0.003), (tables 2,3).

 Table 2: Shows macroscopical and microscopical characteristics of studying placentas in control and preeclamptic (PE) groups.

		Primi contro l	Multi control	Primi PE	Multi PE		
		M±SD	M±SD	M±SD	M±SD	P Value	
	Placenta Diameter (cm)	19.5± 0.5	20.5±0.5	16.2±2.2	16.8±0 .4	< 0.001	
Macroscopic Variables	Placenta Thickness (cm)	2.0±0. 0	2.2±0.4	3.0±0.0	3.0±0. 0	< 0.001	
Microscopic Variables	Number of Villi(n)	12.2± 2.7	14.6±4.4	14.1±3.2	15.4±2 .5	0.404	
	Syncytial Knots (n)	11.4± 2.3	14.2±4.4	15. 3±4.3	19.2±5 .2	0.034	
	Fetal Capillarie s (n)	5.0±0. 3	4.9±0.5	5.9±0.5	5.4±0. 4	0.003	

• Bold data means that $p \le 0.05$

-		P value for variables				
		Numbers of some macroscopic and microscopic features of placenta				
Index Group	Compariso n Group	Placenta Diameter (cm)	Placenta Thickness (cm)	Villi	Syncyti al Knots	Fetal Capillarie s
Primiparous PE	Primi no PE	0.001	0.000	0.739	0.394	0.010
	Multi PE	0.771	1.000	0.908	0.409	0.247
	Multi no PE	0.000	0.000	0.996	0.964	0.004
Multiparous PE	Primi PE	0.771	1.000	0.908	0.409	0.247
	Primi no PE	0.005	0.000	0.355	0.022	0.402
	Multi no PE	0.000	0.000	0.969	0.200	0.199
Primiparous no PE	Primi PE	0.001	0.000	0.739	0.394	0.010
	Multi PE	0.005	0.000	0.355	0.022	0.402
	Multi no PE	0.486	0.505	0.609	0.672	0.966
Multiparous no PE	Primi PE	0.000	0.000	0.996	0.964	0.004
	Primi no PE	0.486	0.505	0.609	0.672	0.966
	Multi PE	0.000	0.000	0.969	0.200	0.199

Table 3: Shows P values for multiple comparison (among different study subgroups) of some macroscopic and microscopic features of placenta.

Table 4: Shows correlations between microscopic and macroscopic variables.

Variables		Villi	Syncyti al Knots	Fetal Capillaries	Placenta Diameter(cm)	Placenta Thickness (cm
Villi	r		0.399	-0.101	-0.205	0.280
	Р		0.054	0.640	0.337	0.185
Syncytial	r	0.399		0.153	-0.358	0.558
Knots	Р	0.054		0.474	0.086	0.005
Fetal	r	-0.101	0.153		-0.766	0.577
Capillaries	Р	0.640	0.474		< 0.001	0.003
Placenta	r	-0.205	-0.358	-0.766		-0.764
Diameter(cm	Р	0.337	0.086	< 0.001		0.000
Placenta	r	0.280	0.558	0.577	-0.764	
Thickness(c m)	Р	0.185	0.005	0.003	0.000	

• Bold data means that $p \le 0.05$

DISCUSSION:

Gross examination study revealed a higher percentage of circular shaped placentas in multi para which could be due to the fact that the trophoblast invasion , in multipara, is mostly robust in the center of placenta and less is moving towards the periphery in which peripheral villous necrosis is increased and this correlated to appearance of a placenta as circular disc. This result was agreed with Kalifa (2011) ⁽¹⁴⁾ and archana et al (2013) ⁽¹⁶⁾ who found that circular to oval placentas were the predominant human placental form in normal and well controlled metabolic diseases, including preeclampsia and any shaped deviation was determined by

implantation, apoptosis and abnormal maternal environments. Our different

percentage levels of insertion sites of umbilical cord in each subgroups may agreed with Kalifa and Becker opinions ^(14,17) in that the insertion of cord may be influenced by intrauterine position of placenta . Generally, umbilical cord insertion is structurally impressive but functionally unimportant variable.

In our study, the significant decrease in placental diameter in preeclampsia(mainly in primi) was parallel with Raghunathan et al (2011) (15) and archana et al(2013) ⁽¹⁶⁾ who found that the diameter of placenta was one of variables which was directly proportional to diffusion rate in order to provide a better diffusion in preeclampsia. This may contribute to the severity and pathphysiology of preeclampsia under hypoxic condition which was mostly occurred with first birth. The significant increase in placental thickness in preeclampsia found in this study was positively correlated with syncytial knots and fetal capillaries .Our result was agreed with previous studies which were proposed that the length of stem villi were more in multipara and in preeclampsia as a response to mechanical & metabolic effects that result from increased damaging to floating villi by high velocity of blood flow from untransformed spiral arteries under oxidative stress (18,19).

Microscopical variables of studying placentas may be agreed with previous studies who found that fetal villi are a part of the border between maternal and fetal blood which were at term become more smaller with less stroma containing 4-6 fetal capillaries per section, covering with syncytiotrophoblast having nucleus tend to accumulate and shed as syncytial knots with 10% - 30% in normal term pregnancies ^(20,21). Our histological finding showed an increased number of placental villi with parity and preeclampsia. This result was in coincidence with previous opinions that proposed a longitudinal growth and coiling of fetal capillaries that bulged inside villous surface, making grape-like branches called terminal villi in order to provide more favorable conditions for fetal growth ⁽¹⁶⁾. In addition to the role of factors like hypoxia in preeclampsia that induced accelerated villous branching ⁽²²⁾. Our study manifested a significant increase in number of syncytial knots with parity and preeclampsia. This result parallels previous studies (23,24,25) which their authors, remarked an increased accumulation of syncytial nuclei as knots through intervillous space in preeclamptic placentas as a structural expression of decreased

placental perfusion with advanced gestational aged and or structural expression of hypoxia for inducing syncytiotophoblast membrane modification . Present study revealed a significant increase of fetal capillaries in preeclampsia as compared to controls, mainly in primi subgroups and they were directly correlated with placental thickness. This result was agreed with previous studies who proposed that non branching angiogenesis in placenta which was expressed through third trimester of pregnancy while hypoxia role in preeclampsia may induce upregulation of proangiogenic factors, that altered angiogenesis model to branching nest (multiple sprouting of microvessels producing multiply branched capillaries webs),^(26,27)

CONCLUSION:

In our study, the definite changes in macroscopical and microscopical variables in placentas of normal and preeclamptic women could be attributed to placental insufficiency especially in preeclamptic group and this may be a compensatory repair mechanisms to factors like hypoxia in order to provide better fetal growth.

REFERENCES:

- 1. Gray, Henry.. *Anatomy of the Human Body*: Philadelphia Lea & Febiger; Bartleby.com, 20th ed., thoroughly rev. and re-edited by Warren H. Lewis 2000:4-25.
- Drake P.M.; Gunn M.D.; Charo I.F.; Tsou C.L.; Zhou Y.; <u>et al.</u> . Human placental cytotrophoblasts attract monocytes and CD56(bright) natural killer cells via the actions of monocyte inflammatory protein 1alpha.; J. Exp. Med.; 2001; 193:1199–212.
- **3.** Standring s. Gray's Anatomy. The anatomical Basis of Clinical Practice, 40th edition, London, UK; Church Liugstone: J. Elsevier; 2008;176-77, 1302.(IVSL).
- **4.** Brosens I.; Pijnenborg R.;Vercruysse L.; Romero R.. The "Great Obstetrical Syndromes" are associated with disorders of deep placentation. American journal of obstetrics and gynecology; 2011;204:193-201. (IVSL).
- 5. Archana M. ;Hatti S. S.; Imran , A.H. Effect of birth order on placental morphology and its ratio to birth weight . J.Int Biol Med Res.2013;4:2765-71.
- 6. Moore K.L. and Persaud TVN. The Developing Human , Clinically Oriented Embryology. 8th edn. Philadelphia Pennsylvania; Saunders 2009;116-117-23.

- 7. Turner J. A.. Diagnosis and management of pre-eclampsia. International journal of women's health 2010; 2:327.
- **8.** ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. Obstetrics and gynecology 2002;99:159-67.
- **9.** Roberts JM, Gammill HS. Preeclampsia: recent insights. Hypertension. 2005; 46:1243–49. [PubMed: 16230510]
- Sibai B.M.;Gordon T.;Thom E.; Caritis S.N., <u>et al.</u>. Risk factors for preeclampsia in healthy nulliparous women. American journal of obstetrics and gynecology 1995;172:642-48.
- **11.** Lain K.Y.; Roberts J.M. Contemporary concepts of the pathogenesis and management of preeclampsia. J. American Medical Association; 2002;287: 3183-86 [Pup med: 12076198].
- 12. Roberts J.. Pre-eclampsia a two-stage disorder: what is the linkage? Are there directed fetal placental signals?. In: FL; MB, editors. Pre-eclampsia: Etiology and Clinical Practice. New York: Cambridge University Press: pp. 183-94. Turner J. A. (2010). Diagnosis and management of pre-eclampsia. International journal of women's health; 2007;2:327.
- **13.** Luna L.G. Manual of histologic staining methods of the armed forces institute of pathology 3rd ed. 1998:17-18.
- 14. Kalifa N.F. A Comparable macroscopical & microscopical study of the placenta & umbilical cord in normal , diabetes, preeclampsia & diabetes with preeclamptic pregnancies.. Thesis Submitted to the College of Medicine and the Committee of Post Graduate Studies of Baghdad University in Partial Fulfillment of the Requirements for the Degree of Master of Science in Anatomy 2011.
- **15.** Raghunathan G.; Vijayalakshmi, Varshashenoy. A study on the Morphology and Morphometry of the Human Placenta and its clinical Relevance in a population in Tamilnadu. J. of Clinical and Diagnostic Research. 2011;5:282-86.
- **16.** Archana. M. ; Hatti S. S. ; Imran ; Ashwini H.. Effect of birth order on placental morphology and its ratio to birth weight. J of Biol Med Res. 2013;4: 2765-71.
- Becker V.. Placenta, In pathologie der plazenta und des Abortes.V. Becker and G. Röckelein, eds. Springer-Verlag, Berlin 1989;23:1-155.

- **18.** Moore, L.K..The developing human. 3rded; philadelphia;W.B. Saunders . 1983;65-66:111-18.
- **19.** James M.R..; Escudero C.. The placenta in preeclampsia: J Pregnancy Hypertens. 2012;2:72–83.
- **20.** Woodruff N.. Gynecologic and obstetric pathology 8th edition .Philadelphia: W.B. Saunders 1979:594-29.
- **21.** Ellery P.M. ; Cindrova-Davies T.; Jauniaux E.; Ferguson-Smith A.C.; Burton G.J.. Evidence for transcriptional activity in the syncytiotrophoblast of the human placenta.J of Placenta; 2009;30: : 329–34.
- **22.** Anteby E.Y. Natanson-Yaron S.; Hamani Y.; Sciaki Y.; Goldman-Wohl D.; <u>et al.</u>. Fibroblast growth factor-10 and fibroblast growth factor receptors 1-4: expression and peptide localization in human decidua and placenta. Eur J Obstet Gynecol Reprod Biol. 2005;119:27-35.
- **23.** Boyd J.D.& Hamilton W.J..The human placenta 2nd.ed Huffer and sons,Cambridge. 1970:709-12.
- **24.** Sohlberg S.;Lindgren P.; Lutvica A.;Olovsson M.; *et al.*. 'Placental perfusion in normal pregnancy and in early and late preeclampsia'. Pregnancy Hypertension: 2013;3:63.
- **25.** James M. ; Roberts A.; Escudero C.. The placenta in preeclampsia: J Pregnancy Hypertens. 2012;2:72–83.
- **26.** Ancar B.; Chardonnens D.. Main regulators of angiogenesis and their role in preeclampsia and intrauterine growth restriction.J .MOLECULAR MEDICINE 2012;6:23-27.
- 27. Li H.; Gu B.; Zhang Y.; Lewis D.F.; Wang Y. Hypoxia-induced increase in soluble Flt-1 production correlates with enhanced oxidative stress in trophoblast cells from the human placenta.Placenta. 2005;26:210-17.

THE IRAQI POSTGRADUATE MEDICAL JOURNAL 583