

Influence of advanced maternal age on histology of full term human placenta in Basrah

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(Received 20/1/2013, Accepted 9/4/2013)

الخلاصة

تعتبر الأم الحامل متقدمة في العمر عندما يكون عمرها خمس و ثلاثين عاما فما فوق عند وقت الولادة. أهداف هذا البحث تُقرّر تأثيرَ عمر الأم على سُمك المانع المشيمي، ووزن الجنين والمشيمة. الدراسة أجرت على مجموع 25 مشيمة إنسان كاملة بعد الولادة. المشيمات اخذت من النساء الحبلية الصحيحات الولودات من قسم وحدة الطب النسائي والتوليد في ابن غزوان مستشفى في البصرة، النساء المقحوصات فُسمن إلى مجموعتين؛ مجموعة قياسية مُتضمنة من 10 مشيمات من النساء الحبلية بين عُمر 20 - 34 سنة ومجموعة تجريبية شملت 15 مشيمة من النساء الحبلية من عمر 35 عاما فما فوق وتمت دراستها دراسة نسيجية مجسمة .

وقد لوحظت التأثيرات التالية:

1. زيادة في متوسط سُمك المانع المشيمي لمشيمة الأم بعمر 35 سنة فما فوق مقارنة مشيمة المجموعة القياسية.
2. زيادة في الوزن المشيمي الرئيسي لعمر الأمهات بعمر 35 سنة فما فوق بالمقارنة مع المجموعة القياسية.
3. نقصان في متوسط وزن الوليد عند الولادة للامهات بعمر 35 سنة بالمقارنة مع المجموعة القياسية.
4. التغييرات النسيجية الشاملة في المكون الهيكلي للزغابات المشيمية الطرفية حيث لوحظ زيادة في سُمك المانع المشيمي، نقصان الأوعية الدموية في الزغابات الطرفية للمشيمة وزيادة في تليف الزغابات المشيمية في مشيمة الأم أكثر من بعمر 35 سنة بالمقارنة مع المجموعة القياسية.

Abstract

Advanced maternal age defines as age over 35 years at estimated date of delivery .The aims of this research were to determine the impact of maternal age on placental barrier thickness, fetal and placental weight .The study was conducted one total of 25 human full term placentas of multiparous healthy pregnant women obtained from department of Obstetrics and Gynecology unit in Bin Gazwan hospital in Basrah .The examined women were divided into 2 groups ;the control group of consisted of 10 placentas from pregnant women between age of(20 -34) years and experimental group consisted of 15 placenta from pregnant women of 35years old and older .Stereological and histological study were applied to determine the effect of advanced maternal age on placental barrier and fetal and placental weight . The results showed:

1. Increase in the mean of placental barrier thickness of the placenta of mother >35 years than that of placenta of control group (20-34) .
2. Increase in the main placental weight of mothers >35 years in comparison to that of the control .
3. Decrease in mean birth weight of mothers > 35 years in comparison to that of control.
4. Extensive morphological changes in the structural component of terminal villi (capillaries, stroma and trophoblast). The results showed that there is an increase in the thickness of placental barrier of placenta, decrease in vascularization of the terminal villi and increase in stoma and fibrin deposition in the placenta of mothers more than 35 years of age in comparison to the control group .

Introduction

The Placenta is essential for normal fetal development and failure of placenta can result in fetal problems. Normal placental development is dependent upon the differentiation and invasion of the trophoblast⁽¹⁾. During this process of invasion and differentiation the trophoblast cells rapidly divide to form interface between mother and fetus. As a developing organ, the placenta undergoes constant tissue remodeling, which is characterized by the functional loss of trophoblast cells by apoptosis. After proliferation and differentiation into specific cell subtypes, aging trophoblast cells are removed and replaced by younger trophoblastic cells without affecting neighboring cells⁽¹⁾. The main functional units of the placenta are the chorionic villi within which the fetal blood is separated by only three cell layers (placental membrane) from maternal blood in the surrounding intervillous space⁽²⁾. The capillaries are only the content of terminal villi. The exchange of materials between fetus and mother takes place at fetomaternal membrane which separates maternal blood in the intervillous space from fetal circulation⁽¹⁾. The fetomaternal membrane is the most important part of the placenta. It is composed of vascular endothelial cells and their basement membrane, connective tissue of villous, subepithelial basement membrane and its covering of cytotrophoblast and syncytiotrophoblast⁽³⁾. The barrier allows water, O₂, nutritive substances and hormones to pass from mother to fetus and some products of excretion from fetus to mother⁽²⁾. The structure of villi

alters during the pregnancy to satisfy the increase demands of fetus for its growth and development⁽⁴⁾. The changes of the placental membrane have a direct effect on fetomaternal transfusion, fetal growth and development⁽⁵⁾. These changes lead to structural placental changes and affect the course and the outcome of pregnancy. Placental insufficiency may contribute to the intrauterine growth retardation, low birth weight and disturb the development of the fetus⁽⁶⁾. The optimal age of women for pregnancy and delivery is between 20 and 29 years, pregnancies of women older than 35 years are considered at risk⁽⁷⁾. Advanced maternal age is known as a risk factor for various types of obstetric complications including placental dysfunction. The age of the mother has an influence on the placental function during pregnancy and delivery⁽⁸⁾. It has been well documented that the risks for premature delivery and fetal complications are higher in pregnancies of older women⁽⁹⁾. Pregnancy of older women is also associated with many confounding factors including diabetes mellitus, hypertension, placenta previa, premature rupture of membrane, miscarriage risk, preterm delivery, and abruption placenta⁽¹⁰⁾. The placenta is the highly specialized organ of pregnancy that supports the normal growth and development of fetus. Growth and function of placenta are regulated and coordinated to perform the exchange of nutrients and waste products between fetal and maternal circulation⁽²⁾. In this research we assess the thickness of placental barrier in older women and compare them to the young pregnant.

Materials and Methods

The research was performed on a total of 25 term human placentas of multiparous healthy pregnant women. The samples were collected from the department of Obstetrics and Gynecology in Bin Gazwan hospital in Basrah. The

samples consisted of pregnant women divided into two groups according to maternal age at delivery. The control group consisted of 10 women between the age 20-34 and the experimental group consisted of 15 women over 35 years old

. Placental samples are collected. Fetal weight and placental weight were measured. placental tissue sample were taken from various part of placenta .Placental tissues were fixed in 10% formalin for 24 hours ,dehydration was done by using graded concentration of alcohol .Clearing was done by using xylene ,then embedding in paraffin .The sample the cut into thin section 3-5 μ . The section then stained with hematoxylin and eosin ⁽¹¹⁾ .Thickness of

placental barrier of both control and experimental sections were measured by using Reichert Austeria Nr381116 light microscope with screen.

Statistical Analysis:

Data were analyzed statistically, using student (t test) of significant and p value. The test was done between the two groups regarding the birth weight, placental weight and placental barrier thickness.

Results

The main results are detailed in table (1) and figures (1,2,3,4,5,6,7) :

1.Placental barrier thickness :

There is an increase in the mean of placental barrier thickness of the placenta of mothers age >35 years than that of placenta of control group (20-34) years. The difference is significant (P<0.01) as shown in (Table 1) & (Figure 1).

2. Placental weight:The results showed that there is an increase in the main placental weight of mothers' age >35 years in comparison to that of the control (20-34) years. The mean placental weigh is significantly greater in placentas of mother > 35 years than in placentas of control (20-34) years, (P<0.01) as in (table 1) and (figur2).

3.Birth weight :The results showed that there is decrease in mean birth weight of mothers age \square 35 years in comparison to

that of control .The difference between the birth weight of the two groups was not significant ($p>0.05$)as in(table 1) and (figure 3).

4.Morphological changes: The placenta of pregnant mother > 35 years of age showed extensive morphological changes in the structural component of terminal villi (capillaries, stroma and trophoblast). The results showed that there is an increase in the thickness of placental barrier of placenta of mother > than 35 years of age in comparison to the control group as shown in (Figure 4, 5). There is decrease in vascularization of the terminal villi (Figure 5, 6) and increase in stoma and fibrin deposition in the placenta of mother > than 35 years of age in comparison to the control group as shown in (Figure 6,7).

(Table 1) Shows a comparison between placenta of maternal age >35 year of age and the control regarding placental barrier thickness, fetal and placental weight.

Parameters	Maternal age >35 year Mean \pm SD	Maternal age (20-34) years Mean \pm SD	P Value
Mean of placental barrier thickness in m μ	4.44 \pm 0.57	2.30 \pm 0.55	P<0.01
Mean of placental weight in kg.	0.68 \pm 0.012	0.63 \pm 0.021	P<0.01
Mean of birth weight in kg.	3.27 \pm 0.25	3.42 \pm 0.24	P>0.05

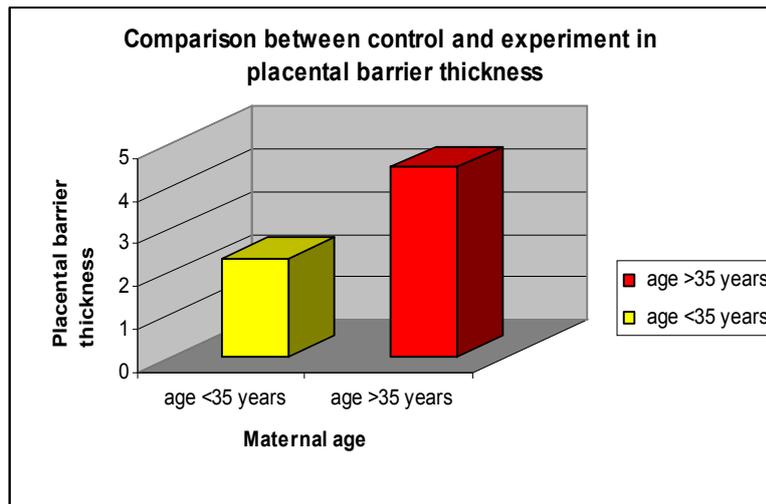


Figure 1 ;Shows a comparison between the mother >35 years of age and the control group in placental barrier thickness.

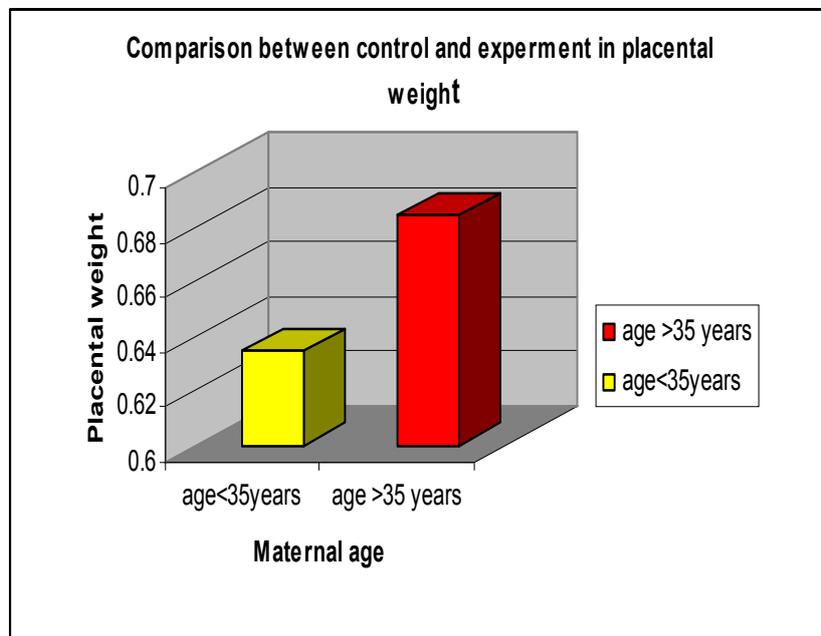


Figure 2 ;Shows a comparison between the mother >35 years of age and the control group in placental weight.

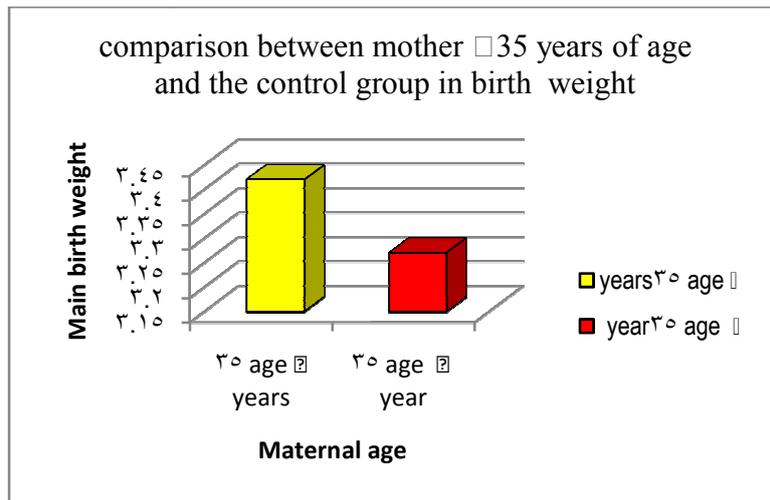


Figure 3 ;Shows a comparison between mother >35 years of age and the control group in fetal weight.

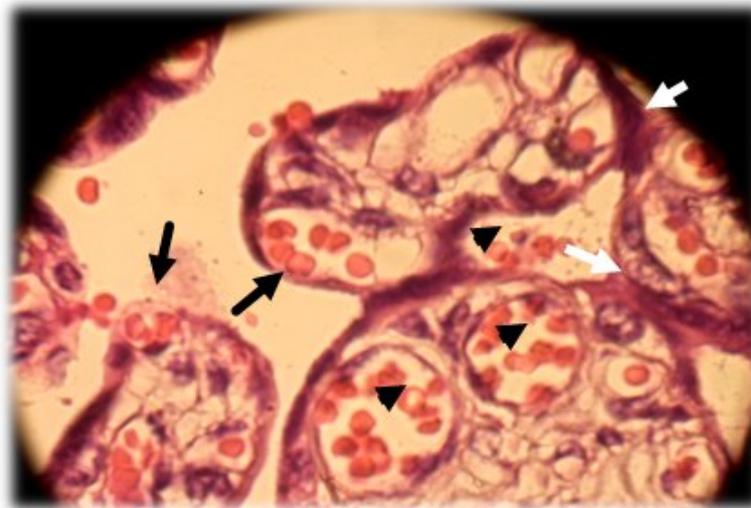


Figure 4 ;Placenta of the control group shows thin placental barrier (black arrows) and synsyrial knots (white arrows) and more villous capillaries (black head arrows) . X1000.

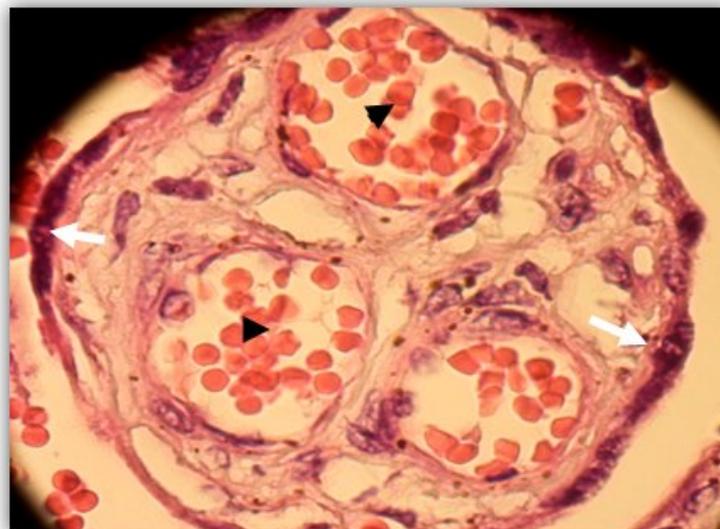


Figure 5 ; Terminal villi of the placenta of the control group shows more villous capillaries (black head arrows) and more synsyrial knot(white arrows).X1000

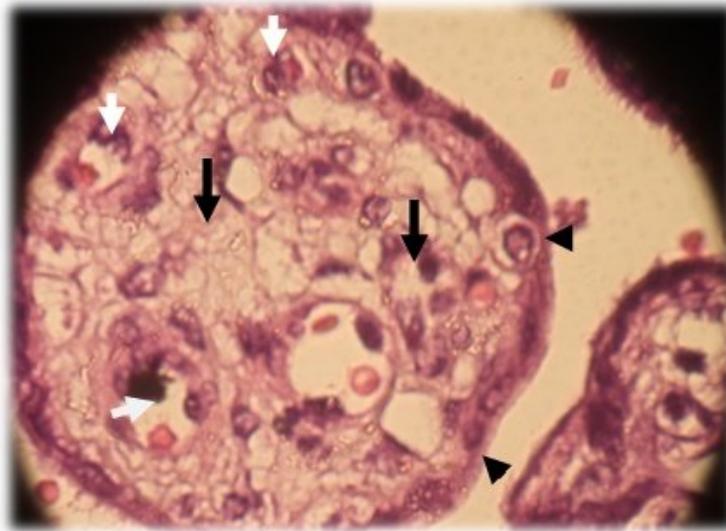


Figure 6; Placenta of maternal age >35 year shows stromal fibrosis (black arrows) , small villous capillaries (white arrows),and thick placental barrier (black head arrows) X1000

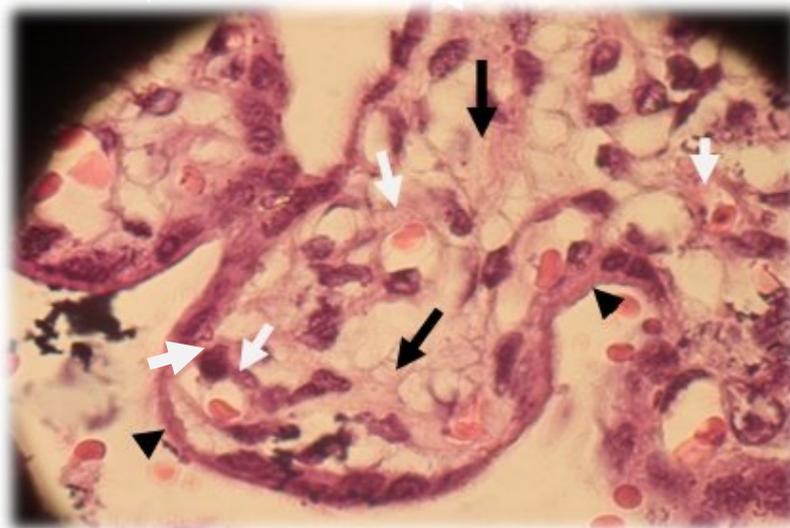


Figure7; Placenta of maternal age >35 year shows stromal fibrosis(black arrows), small villous capillaries (white arrows) and thick placental barrier (black head arrows) X1000

Discussion

Placenta is a complete organ which is very firmly connected to the mother and rather loosely connected to the developing fetus through umbilical cord organ providing interchange between mother and fetus .The life of fetus depend on welfare of the placenta and the life of placenta depends on welfare of the mother to whom it so intimately attached.

This triad mother –placenta –fetus becomes very important in the whole process of development of the fetus .So that one can take care of any problems that arise before and during its development⁽¹²⁾.

The placental basic histological structures undergo considerable changes throughout its lifespan All the

developmental changes need to be in accordance with its function⁽¹⁰⁾. In pregnancy the major physiological changes occur in the morphology of blood vessels in order to meet the demands of developing fetus.

The blood filled terminal villi are the essential for fetomaternal transfer of substances⁽⁸⁾. Maternal age has an effect on the function of placenta during pregnancy and delivery⁽⁸⁾. The risk for several kinds of antenatal, natal and delivery complications are higher in pregnancies of older women⁽⁹⁾. Advanced maternal age defines as the age 35 years and older⁽¹³⁾. The placenta of mother <35 years shows morphological changes which include increase in trophoblastic layer thickness, increase stromal fibrosis, decrease vascularization, more syncytial knots and low incidence of apoptosis. Our findings reveal that there is a significant increase in the thickness of the placental barrier of mother >35 years of age in comparison to the control group ($p < 0.001$) and (figure 1,4). These findings corroborate with the studies of (Zeno Yamada et al 2001)⁽¹⁴⁾. It was noticed that there is an increase proliferative activity of trophoblast layer in the pregnant mother > 35 years in comparison to pregnant mother (20-34) years. Our finding may indicate that increase trophoblastic layer thickness in pregnant mother >35 year occur as a compensatory mechanism to allow the placenta provides nutrition for fetus for its normal growth and development. Our suggestion confirm the reported findings (Hupertz B. et al)⁽¹⁵⁾ that the increase in the proliferative activity occur in older women implies that the transfer of substance across the placenta is facilitated by compensatory mechanism and thus enable the placenta to meet the functional demands of fetus for its normal growth and development⁽¹⁵⁾. Our results support (Zlata et al 2010)⁽¹⁶⁾ findings which show morphological changes of blood filled terminal villi

which are essential for fetomaternal transfer of the substances. It was noticed that there is an increase in the stromal tissue and decrease in the vascularization of the terminal villi in mother > 35 years in comparison to the control (20-34) years. (Grbesaet al 1994)⁽¹⁷⁾ showed in his study that total capillary surface area of placenta in older pregnant mother is significantly lower in comparison to placenta of younger pregnant mother. Ramic S. et al (2002)⁽¹⁸⁾, Ramic S. et al (2006)⁽¹⁹⁾ had observe that the volume density of fibrinoid in older pregnant women compared to younger is significantly increase. These findings are similar to our findings which shows decrease in vascularization of terminal villi and as a result there is increase in the stroma fibrosis of the placenta of the mother > 35 year in comparison to placenta of control group as shown in (Fig 6, 7).

Placental apoptosis which is a normal physiological phenomena is increased significantly as pregnancy progresses, suggesting that it could play a role in normal pregnancy (Smith et al 2000)⁽²⁰⁾. Qumsiyeh et al (2000)⁽²¹⁾ have reported that apoptotic cell are significantly higher in younger age group compared with those from older age group. This finding is similar to our finding which shows more syncytial knot and high incidence of apoptosis in the control group in comparison to older age group as shown in (Fig. 4,5). Toki et al (1999)⁽²²⁾ identify an inverse relationship between Bcl -2 family protein expression in syncytiotrophoblast, apoptosis and maternal age. Our results revealed that there is no significant differences in the mean birth weight of the babies of the two groups ($p > 0.05$) but there is significant increase in the mean placental weight as maternal age increase ($p < 0.01$) as in (Fig. 2,3). Our results are in agreement with finding by Haavaldsen C. et al (2011)⁽²³⁾.

Conclusion

Since we collected the placenta from healthy mother with normal pregnancies and deliveries, we could speculate that the placenta from mother >35 years represent cases where age related hypo function of the placenta have been

overcome by increase proliferative activity of the syncytiotrophoblast and reduce apoptotic signals. So maternal age is an independent risk factor on birth weight unless there is an antenatal maternal disease.

References

1. Shwan L, Starszewski-Chavez, Vikki M, Abrahams a, Gil Mor . The role of apoptosis in regulation (2005). *Endocrine reviews*, doi:10.1210/er
2. Gude N.M., Roberts C.T., Kalionis B., King R.g. growth and function of normal placenta.(2004). *Tromb Res.* :114(5-6):379-407.
3. Vogt Issaksen C. Maternal smoking intrauterine growth retardation and placental apoptosis .(2001) *Pediatr. Dev.Pathol.* ;7(5) 433-462.
4. Hellstorm M. Gerhardt H. Kalen M. Eriksson U. Wollburg H. Betsholtz C. Lack of pericytes leads to endothelial hyperplasia and abnormal vascular morphogenesis (2001) *J.Cell Biol* 1153;543-553.
5. Kingdom I.Hoppertz B. Seaward G. Kaufmann I.(evelopment of the placental villous tree and its consequence fetal growth .(2000) *Eur.*
6. Jaunlaux E. Watson A.I.Hempstock J.BaoY.P.Skepper J.N.Burton G.I Oncet of Maternal arterial blood flow and placental oxidative stress .A possible factor in Human early pregnancy failure .(2000) *Am.J.Pathol.*157;2111-2122
7. Miletic T., Aberel N. Mikulandra F. Prenatal outcome of pregnancies in women aged 40 and over .*Coll.Antropol*(2002) 26:251-258.
8. Hansen,J.P. Older maternal age and pregnancy outcome :a review of the literature .(1986). *Obstetric .GynecolSurv.* ,41, 726-742.
9. Fretts , R.C. ,Schmittiedel ,J., Mclean ,F.H. et al .Increased maternal age and the risk of fetal death (1995) *N.Engl.J.Med.* 333, 953-957
10. Neal D.M., More G.The role of mediated apoptosis in preeclampsia,(2005) *J .Perinat. med* .33(6):471-7
11. Clay EC Practical section cutting and staining (1971) 5th ed., Churchill Livingstone, Edinburgh and London
12. A.H.Nagi.Placenta ;Examination and pathology .2011.*Biomedica* Vol.27,Jan. P 82.
13. Mino Rajae , Sareh Amirzadeh, Fariba Mirblook, Metra Ahmad Soltan The effect of maternal age on pregnancy outcome. (2010) *Asian Journal of medical sciences* 2(3):159-162.
14. Zeno Yamada ,Masanobu Kitagawa Tamiko Takemura , Katsuiku Hirokawa .Effect of maternal age on incidences of apoptotic and proliferative cells in trophoblasts of full term human placenta(2001) *Molecular human reproduction*.Vol.7 No. 12 pp. 1179-1185.
15. Mayhew T.M. Stereological studies on fetal vascular development in human placental villi (2004) . *Placenta* 25(3-5): 226-233.
16. Zlata Z. Sergje M. Durdica G. Suads R. Almir H. Quantitative research of capillaries in terminal villi of mature placentae (2010) *Bosnian of journal of basic medical sciences*.10(2):142-152 .
17. Grebesa D. Durest Zivkovic B .D. Dose the human placenta differentiate structurally during 10th lunar month .(1994) *Acta .Med. Croat.* 48(3) :117-121.
18. Ramic S. Zigic Z. Stereological analysis of chorionic fibrinoids in mature placenta in pregnant women of various ages .(2002) *Med. Arth.* 56 (5-6)255-258.
19. Ramic S. Zigic Z. Grebsa D. Begic L. Morphological research of fibrinoid and intervillous space of human term placenta in relation to age of pregnant women .(2006) *Med. Arth.* 60(5):282-284 .
20. Smith, S.C. Leung ,T.N. To ,E.F. apoptosis is a rear events in first trimester placental tissue. *Am .J. Obst. Gynecol.*,177,57-65.
21. Qumsiyeh, M.B. Kim ,K.R. Ahmad ,M.N. Cytogenetics and mechanisms of spontaneous abortion :increase apoptosis and decreased cell proliferation in chromosomally abnormal villi .(2000) *Cytogenet.Cell . Genet.* 88,230-235
22. Toki,T.,Horiuchi ,A. Ichikawa, N. Inverse relationship between apoptosis and Bcl-2 expression in syncytiotrophoblast and fibrin -type fibrinoid in early gestation (1999). *Mo .Hum. Reprod.*,5,246-251
23. Haavaldsen C, ,SO Samulelsen ,A Esklid . The association of maternal age with placental weight (2011) *BJOG International journal of obstetrics and gynecology* ; DOI:10.1111/J 1471-0528.030.