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 off (20 - 34) years and experimental group consisted of 15 placenta from pregnant women of 35 years 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 cells layers (placental membrane) from maternal blood in the surround intervillous space (2). The capillaries are only the content of terminal villi. The exchange of materials between fetus and mother takes place at feto-maternal membrane which separates material blood in the intervillous space from fetal circulation (1). The feto-maternal membrane is the most important part of the placenta. It is composed of vascular endothelial cells and their basement membrane, connective tissue of villous, sub epithelial basement membrane and its covering of cyto and syncytiotrophoblast (3). The barrier allows water, O₂, nutritive substances and hormones to pass from mother to fetus and same 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 feto-maternal 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 brevia, premature rupture membrane, miscarriage risk, preterm delivery, and abruption placenta (10). The placenta is the highly specialized organ of pregnancy that support 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 placenta of multiparous healthy pregnant women. The samples were collected from the department of Obstetrics and Gynecology in Bin Gazwan hospital in Basrah. The samples are 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 3-5µ. 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 (figure2).

3. **Birth weight :**The results showed that there is decrease in mean birth weight of mothers age □ 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.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Maternal age &gt;35 year Mean ± SD</th>
<th>Maternal age (20-34) years Mean ±SD</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean of placental barrier thickness in µm</td>
<td>4.44±0.57</td>
<td>2.30±0.55</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>Mean of placental weight in kg.</td>
<td>0.68±0.012</td>
<td>0.63±0.021</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>Mean of birth weight in kg.</td>
<td>3.27± 0.25</td>
<td>3.42± 0.24</td>
<td>P&gt;0.05</td>
</tr>
</tbody>
</table>
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 birth weight.

Figure 4; Placenta of the control group shows thin placental barrier (black arrows) and symsytial 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 symsytial knot( white 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 feto-maternal 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 synsytial 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 (ZenoYamada 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 feto-maternal 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. (Grbesa et 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 synsytial 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