Original Article

Histomorphometrical Analysis of the Umbilical Cord and Placenta in Human Fetuses with Macrosomia

Lina A. Salih

ABSTRACT

Objective: To evaluate the histomorphometrical changes in the umbilical cords and placenta associated with excessive fetal growth.

Study Design: Comparative cross-sectional study

Place and Duration of Study: This study was conducted at the College Science, University of Baghdad, Baghdad, Iraq from 1st September 2025 to 28th February 2026.

Methods: A total of 160 Iraqi pregnant women at 3rd trimester of pregnancy with their neonates under vaginal or caesarean delivery were enrolled.

Results: No significant differences (P≥0.05) observed in maternal age between groups, the mean maternal age with normal fetus weight was 24.21±20.5 years, women carrying macrosomic fetus was 25.11±18.5 years. The pregnant with macrosomic fetus showed significantly (p≤0.01) shorter gestational age and higher maternal and neonatal weights 32.10±1.2, 94±3.2 kg, 4.8±2.5 kg than control group 36.1±1.5, 80±10.5 kg, 2.5±0.4 kg respectively. The macroscopic examination showed significant differences in placental and umbilical cords between groups(P≤ 0.05) the placental weight and length were lower in the macrosomic infants (319.5±10.03g, 16.43±1.04 cm) while in the non-macrosomic infants (509.17±11.42 g,19.15±2.05 cm)while umbilical cords length and diameter were significantlyincreased (72±0.06, 55±3.05 cm) compared to control 3.44±2.15, 1.82±0.06cm) .The morphometric analysis demonstrated reduced placenta surface area 190±20.5cm, diameter 15.33±10.5cm^2, and the placental thickness 1.32±1.5 cm compared to the non-macrosomic infants 210.2±18.5 cm, 18.3±1.4 cm^2, 1.72±1.2 cm respectively. The placental villiin macrosomic infants appeared increased surface area and villous diameter (1.38 ± 0.1 mm2,, 0.14 ± 0.02mm) while blood vessel diameter was reduced in the macrosomic infants 0.03 ± 0.02 mm.

Conclusion: Placental morphometrical index is associated with fetal macrosomia and understanding gestational complications.

Key Words: Macrosomia, Histomorphometrical, Fetal growth, Placenta

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INTRODUCTION

Fetal macrosomia is a major obstetric problem commonly defined as birth weight 4,000-4,500 g or more, regardless of the gestational age.[1] It's associated with increased maternal and fetal complications during pregnancy and delivery.[2] Several factors are involved in fetal overweight like maternal diabetes, pre-gestational diabetes, maternal overweight, many births, the advanced age of the mother, in addition to genetic factors.[3]

Department of Biology, College Science, University of Baghdad, Baghdad, Iraq.

Correspondence: Lina A. Salih, Department of Biology, College Science, University of Baghdad, Baghdad, Iraq.
Contact No: +9647713444139
Email: lina.abdmatalb@sc.uobaghdad.edu.iq

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Increased glucose to the placenta stimulates fetal insulin, adipose tissue deposition and faster growth of the fetus.[4]

The placenta is a main factor in regulating fetal development, the changes in the size of the placenta, and weight may cause structural immaturation of some chorionic villi and abnormal circulation in placenta.[5] The structural changes in umbilical cord effect on blood flow.[6] These histological changes are clinical important for understand of the mechanisms of foetal development, and may provide better chances to develop more effective strategies in managing pregnancy.[7]

METHODS

This comparative cross-sectional study was conducted at College Science, University of Baghdad, Baghdad, Iraq from 1st September 2025 to 28th February 2026 vide letter No. 2111B/BU/Approval/JSDJNEHU Dated August 25, 2025. A total of 160 Iraqi pregnant women at 3rd trimester of pregnancy with their neonates under vaginal or caesarean delivery, they divided into two

groups; group1 the mothers who had macrosomic infants, (fetuses with weight ≥4000 g) group 2 the mothers delivered fetus with birth weight (<4 kg). The mothers who had twins or previous abortion, any genetic or autoimmune diseases, and pregnancy age ≤37 weeks of gestation were excluded. Fifty placentae with membranes and umbilical cord were collected within 1 h after delivery. Fresh tissue samples were placed in 10% buffered neutral formalin solution until time of histological procedure.[8] Hematoxylin and Eosin (H&E) was used.[9] All sections selected located close to the midline of the blocks, used about 10-20 sections(5-6µm. thick). Digital pictures of the serial histological sections were measured by using the software programs 2015 Motic Image Plus version 2.0.

RESULTS

Table 1 indicated no significant alterations (P≥0.05) in the maternal age between groups, the maternal age in the pregnant women with normal fetus weight was 24.21±20.5 years, while mother with macrosomic fetus was 25.11±18.5 years. The gestational age, was short significantly (P≤0.01), (32.10±1.2 w) compared to the control group (36.1±1.5 w), maternal weight in the pregnant women with macrosomic fetus was increase highly significant (P≤0.01) (94±3.2 kg) compared to other group (80±10.5 kg) the weight of the neonates in the macrosomic group was increase significantly (P≤0.05) (4.8±2.5 kg) compared to control (2.5±0.4 kg)

The histological examination of the placenta showed in figures 1,2, immature placental villus with few blood vessels and visible deposition of fibrin in villus , the histological sections appeared crowding of the villi with reduced intervillous space while in the non-macrosomic placenta the histological texture appeared normal mature villi with obvious blood vessels without fibrosis. In the figure 3, the sections showed normal appearance of differentiated mature villus containing blood vessels, cytotrophoblasts, cyncytiotrophoblast and few syncytial knot, while the macrosomic villus showed less development and with peri-villous edema, with fibrosis and increased syncytial knotting.

The histological examination of the umbilical cords showed in figure 4, normal appearance of umbilical with normal section in artery a layer of normal texture. Wharton's jelly with normal distribution of mesenchymal cells (A&B), at 100x, the Wharton's jelly in the macrosomia distinguished with much fat droplet deposition when compared to the non-macrosomia (C&D)

The median placental weight was 319.5±10.03gm in the macrosomic infants, while in the non-macrosomic infants 509.17±11.42 gm considered significant statistically (P≤0.05), the length of the placenta showed significant differences (P≤0.05) between the studied groups; the length of placental was shorter in the macrosomic infants compared to the non-macrosomic infants 16.43±1.04, 19.15±2.05 cm (Table 2). The gross measurements of the umbilical cords proved highly significant differences (P≤0.01) between the two groups; the umbilical cords length was increased in the macrosomic fetus compared to the non-macrosomic infants 72±0.06, 55±3.05 cm respectively, the umbilical cords diameter was increased in the macrosomic infants 3.44±2.15 cm compared to the non-macrosomic 1.82±0.06 cm.

The placental morphometric results appeared decreased statistically ; the surface area of the placenta was 190±20.5cm, diameter of the placenta was 15.33±10.5cm^2, and the placental thickness was 1.32±1.5 cm compared to the non-macrosomic infants (210.2±18.5 cm, 18.3±1.4 cm^2, 1.72±1.2 cm) respectively (Table 3).

The placental villus surface area and diameter had higher measurements significantly (P≤0.01) in the macrosomic infants (1.38±0.1 mm^2, 0.14±0.02mm) compared to the non-macrosomic infants (0.58±0.5 mm^2, 0.07±0.09 mm) respectively. The blood vessel diameter results appeared low significant measurements in the macrosomic infants compared to the non-macrosomic infants (0.03±0.02, 0.05±0.16) mm respectively (Table 4).

Table No. 1: Parameters of maternal and neonates

Parameters	Non-macrosomic infants (n=80)	Macrosomic fetus (n=80)	P-value
Maternal age (years)	24.21±20.5	25.11±18.5	0.0610 NS
Gestational age (weight)	36.1±1.5	32.10±1.2	0.0001**
Maternal weight (kg)	80±10.5	94±3.2	0.0180*
Neonatal weight (kg)	2.5±0.4	4.8±2.5	0.01*

*significant (P≤0.05), **highly significant (P≤0.01) NS = non- significant P≥0.05

Table No. 2: The mean differences of macroscopic gross of placenta in the studied groups

Variable	Non-macrosomic infants (n=80)	Macrosomic fetus (n=80)	P-value
Placental weight (g)	509.17±11.42	319.5±10.03	0.03*
Placental length (cm)	19.15±2.05	16.43±1.04	0.01*
Umbilical cords length (cm)	55±3.05	72±0.06	0.001**
Umbilical cords diameter (cm)	1.82±0.06	3.44±2.15	0.001**

*Ssignificant (P≤0.05) **Highly significant (P≤0.01)

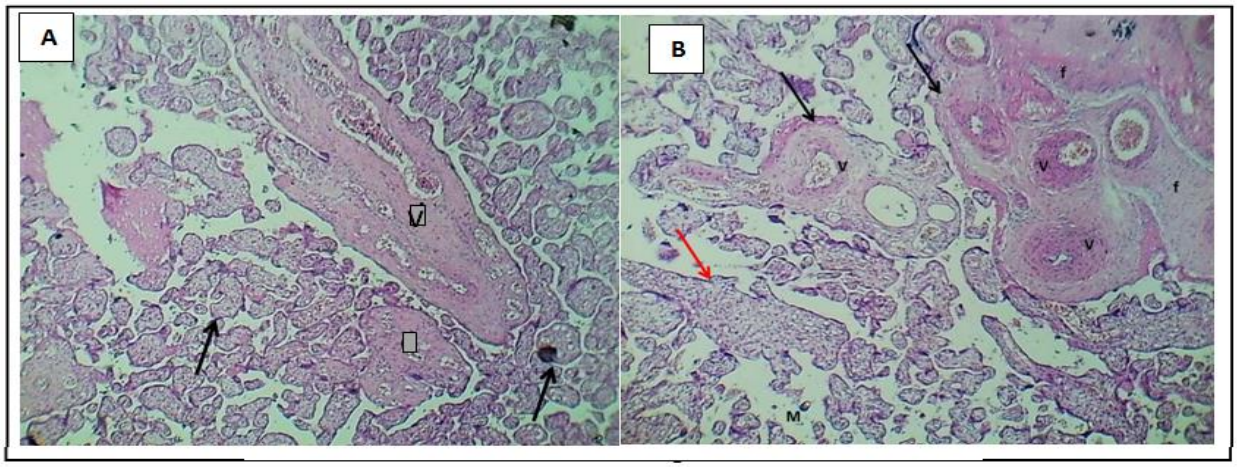

Figure No. 1: CS of normal placenta, normal appearance of differentiated stem villus (Black arrows) containing blood vessels (v) surrounded by progressive fibrosing (f) & differentiated mature intermediate villus (Red arrows) maternal blood space (m). A:40x.B:100x

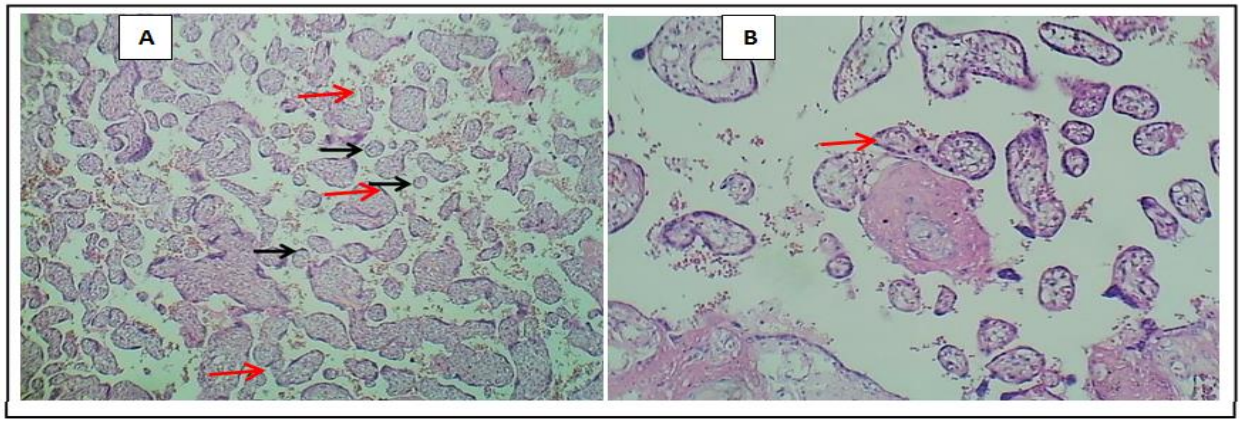

Figure No. 2: CS of section of macrosomic placenta show hypoplasia of immature villus (black arrows) with few blood vessels, atrophy of stem villus some peri-villous edema (red arrows) A:40x. B:100x

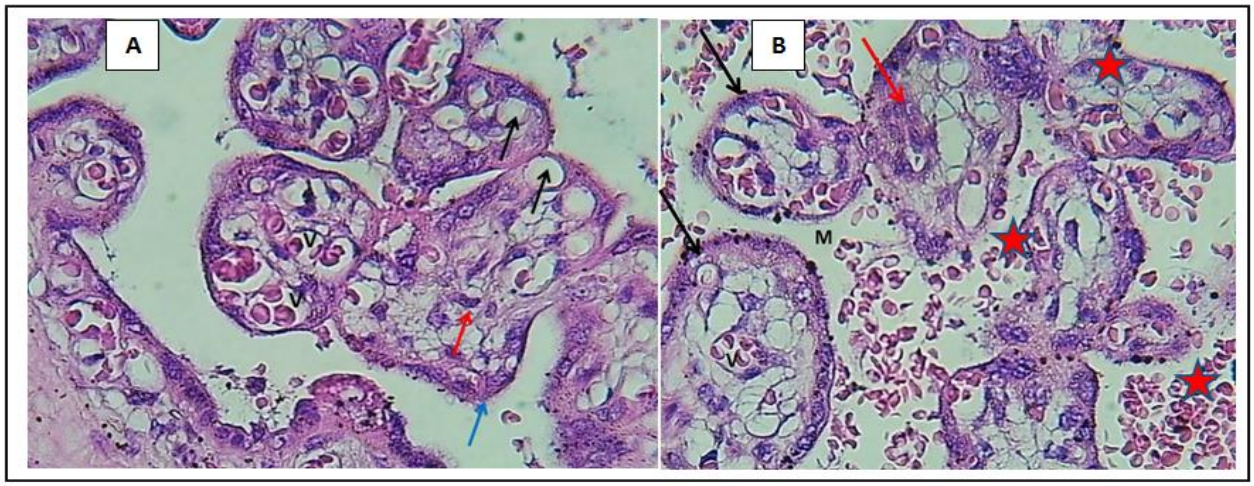

Figure No. 3: CS of section of macrosomic placenta shows A: normal appearance of differentiated maturevillus containing blood vessels (v) cytotrophoblasts (red arrow) & cyncytiotrophoblast (blue arrow). B: macrosomic mature villus with several syncytial knot(red star)H&E.400x

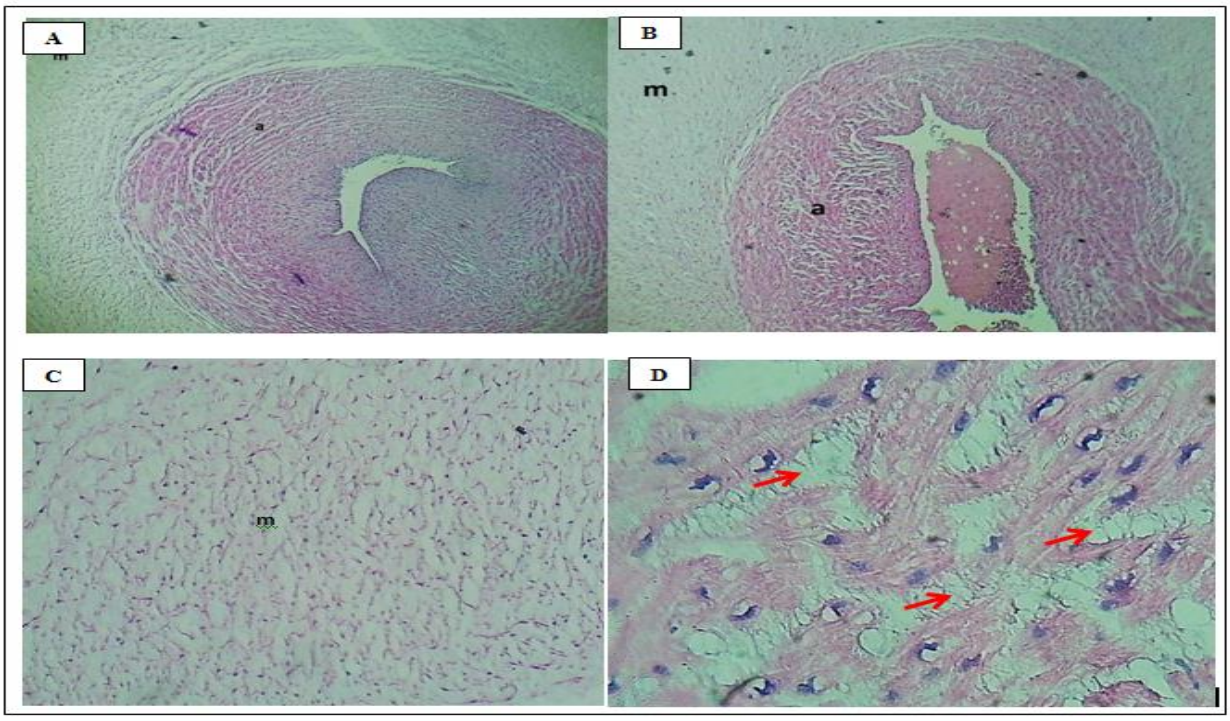

Figure No. 4: CS in the umbilical cords, A&B normal appearance of umbilical artery (a) & layer of Wharton's jelly (m). H&E 40x. C: normal texture of Wharton's jelly with mesenchymal cells, D: shows fat droplet deposition. (red arrows) H&E.100x A, C: non-macrosomia B, D: macrosomia

Table No. 3: Placental morphometric parameters

Variable	Non-macrosomic infants (n=80)	Macrosomic fetus (n=80)	P-value
Placental Surface area (cm)	210.2±18.5	190±20.5	0.0001**
Placental diameter (cm2)	18.3±1.4	15.33±10.5	0.0001**
Placental thickness (cm)	1.72±1.2	1.32±1.5	0.0200*

*Significant (P≤0.05) **Highly significant (P≤0.01)

Table No. 4: Placental villus histomorphometrical parameters

Type of villus	Non-macrosomic infants (n=80)	Macrosomic fetus (n=80)	P-value
Villus surface area (mm^2)	0.58±0.5	1.38±0.1	0.0001**
Villus diameter (mm)	0.07±0.09	0.14±0.02	0.0001**
Blood vessel diameter (mm)	0.05±0.16	0.03±0.02	0.0001**

**Highly significant (P≤0.01)

DISCUSSION

Macrosomia is one of the risk results of the maternal complications lead sometimes to fetal death during delivery or cause many metabolic syndromes during life.[10] The maternal age did not have direct effect, because the range of the ages wasn't much different, according to the random selection of subjects, as previous studies proved that maternal age is not a primary factor in the risk of macrosomia.[11]

Many previous studies proved direct correlation of increased maternal weight with development of fetal overgrowth in the early pregnancy and later incidence of macrosomia[12], this agree with the present study showed the increased maternal weight involved in the macrosomic group. Maternal obesity frequently leads to macrosomia by various mechanisms, such as increased body fat levels, then cause insulin resistance later , this can occur even in women without diabetes, leading to elevated pass of glucose to fetus, placental lipases break down triglycerides in the maternal bloodstream, facilitating the transfer of excess free fatty acids to the developing fetus.[13] The study by Sweeting et al[9] showed that the risk of fetal macrosomia is more closely associated with maternal obesity than gestational diabetes alone

The availability and quantifiably of umbilical cord and placenta make them organs for expecting birth weight in a short time.[14] Some results find a strong relation between placental growth in the second trimester and birth weight.[15] The weight and length of the placenta in

macrosomic infants appeared lower than the normal infants' weight significantly; this explained the effect of the insufficient development of placenta meaning a decrease in placental index (i.e. weight and length). These results might be showing the rate of the fetal growth unequal to placental growth. The placental index is influenced by various factors, including the nutritional status of the mother, her metabolic activity, and the presence of some diseases like, gestational hypertension or gestational diabetic.[16]

These previous findings documented the abnormal syncytial knots, on the surface of terminal villi in the placenta, potentially indicating significant stress on the placenta, such as oxidative stress or hypoxia this explains the placental insufficiency.[17]

The mass of the umbilical cord depends on the amount and content of the Wharton's jelly present which surround the cords; Wharton's jelly, a mucous connective tissue rich in proteoglycans, give physical protection and stability.[18] The connection between thickness of the umbilical cord and neonate's weight.[19] The length and diameter of the umbilical cord in macrosomic fetuses were greater than in the non-macrosomic group, supporting numerous earlier studies.[20]

Previous studies suggest that irregularities in placental shape frequently serve as a compensatory mechanism to meet the heightened metabolic demands linked to macrosomia.[21] Redman et al[22] verified high weight, thickness, and diameter of placenta in macrosomic fetuses, supporting findings maternal complications stimulates placental hypertrophy. This growth is realized as an adaptation manner to get the higher nutritional and oxygen stresses of the overgrowth of the fetus.

A small sized placenta in a macrosomic pregnancy often indicates that the placenta is functioning under high stress to support a large fetus, resulting in a low fetal-to-placental weight ratio cause the fetus to grow large, but the placenta itself does not grow proportionally or may even experience structural, inefficient, or fibrotic changes, leading to decreased transport efficiency.[23]

The data of the current study has been proven surface area and diameter of the placental villus increased macrosomia. The average surface area of the placenta in mothers with diabetes is larger than that the control group, the placenta exhibits a significantly higher amount of parenchymal and villous tissues, which results in an increase in tissue mass rather than surface area measurements.[24]

Carrasco-Wong et al[25] examined the harmonic thickness of the villous membrane was found in the macrosomic group compared to the controls. The fall in the specific diffusing capacity of the villous membrane may donate to the fetal hypoxia and increased chance of Stillbirths.[26]

The volume of blood flow in the umbilical vessels shows a positive correlation with fetal weight and growth, and birth weight, it has been previously noted that resistance to blood flow in the uterine and umbilical arteries can result in a decreased volume of blood reaching the fetus in pregnancies complicated by fetal macrosomia.[27] Breaks and erosion in the endothelial layer lining of the umbilical arteries, leading to increased permeability and bleeding and leakage of plasma proteins into the interstitial spaces of Wharton's jelly.[28]

CONCLUSION

The maternal gestational complications may contribute in the overgrowth of the fetus; macrosomia, this leads to increased risk of cases during delivery; shoulder dystocia, birth injuries or many long-term complications later in life. Therefore the quantitative assessment obtained from this article involved in the histological, morphometric investigation about placenta and umbilical cords may add better understand the relationship between placental index and its influence on maternal and neonatal outcome.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Lina A. Salih
Drafting or Revising Critically:	Lina A. Salih
Final Approval of version:	The above author
Agreement to accountable for all aspects of work:	The above author

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