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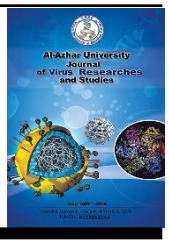

Ultrasonic and Histopathological Changes of Umbilical Cord in Pregestational Diabetic Pregnant Women

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Abstract

To explore morphological and structural effects of pregestational diabetes on the umbilical vein to provide a theoretical basis for fetal development in comparison to normal pregnancy. A prospective case–control observational study was done on 100 pregnant women who visited Al-Zahraa University Hospital. Their gestational ages varied from 28 to 40 weeks, while their ages ranged from 20 to 40. During the period from January 2021to December 2021. The chosen topics were split into two groups: Group I [control group] (n=50) consisted of 50 healthy pregnant women without any complication or any medical disorders. [Study group] Group II (n=50): This group consisted of 50 pregestational diabetic pregnant women (Type 1 and Type 2). Sonography was used to determine the diameter of the umbilical cord and the diameters of the umbilical veins, as well as the surface area of Wharton's jelly. A total of 100 formalin-fixed and paraffin-embedded specimens were gathered and prepared. In this research, there was a greatly statistically relevant variance in umbilical cord diameter (p=0.000), umbilical artery diameter (p = 0.000), umbilical vein diameter (p= 0.000), and Wharton's jelly between the two groups (p 0.000). Microscopic study of diabetic UC samples showed considerable Wharton's Jelly bleeding next to a vein, perivascular and intraparietal hemorrhage with wall dissection. The UC vein of diabetic samples showed dilatation and hemorrhage compared to that of control group. Measurements of umbilical cord, umbilical vein and umbilical arteries diameter and Wharton's jelly surface area can be used as an additional sonographic tool for assessing maternal and fetal health.

Keywords: Umbilical cord diameter, Umbilical artery diameter, Umbilical vein diameter, Wharton's jelly, Normal Pregnancy, Pregestational diabetes mellitus.

1. Introduction

The most prevalent medical issue during pregnancy is diabetes. Women may be divided into two groups: those who had diabetes before to pregnancy (pregestational) or throughout pregnancy (overt), and those who were diagnosed during pregnancy (gestational). According to Martin et al., [1] about 179,898

American women had pregnancies complicated by diabetes in 2006, accounting for 4.2 percent of all live births. Maternal problems such as persistent hypertension impact 6 to 8% of pregnant women with pregestational diabetes mellitus [2], and nephropathy affects 2% to 5% of pregnancies in women with pregestational diabetes mellitus [3]. Preeclampsia is more common in women with pregestational diabetes [4], retinopathy may deteriorate in pregnancy [5], and diabetic ketoacidosis affects 5% to 10% of women with type 1 diabetes [6]. Diabetes mellitus at pregnancy is linked to a high incidence of fetal and neonatal morbidity and death. Congenital abnormalities, aberrant fetal development, fetal loss, birth damage, neonatal hypoglycemia, and hyperbilirubinemia are all known problems [8]. Preterm birth and its accompanying neonatal hazards are much more common in women with PDM [9]. In the third week of embryonic development, the umbilical cord starts to expand. The umbilical cord length is 50-60 cm long at term. The umbilical cord is generally wrapped with Wharton's Jelly, which includes vessels, two arteries, and one vein [10]. Wharton's Jelly levels are lower in the first and early second trimesters than in the third trimester. In intrauterine life, the umbilical cord plays a critical function. The morphological and morphometric characteristics of the umbilical cord have been researched for decades and have been shown to connect with fetal weight and neonatal outcome retrospectively [11]. Umbilical cord features may be investigated using sonographic imaging methods throughout fetal life, and it has been shown that a changed cord structure is linked to pathologic diseases (i.e., preeclampsia, fetal growth restriction, diabetes, fetal demise) [12]. Pathological umbilical cords presented mainly several types of lesions namely: perivascular and/or intraparietal hemorrhages with wall dissections, parietal recent thrombosis and focal moderate or extensive Wharton's jelly hemorrhages [13]. The goal of this research is to look at the morphological and structural consequences of pregestational diabetes on the umbilical vein in order to give a theoretical foundation for fetal development in contrast to a normal pregnancy.

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2. Patients and Methods

Between January 2021 and December 2021, a prospective case–control research was done on 100 pregnant women who visited Al-Zahraa University Hospital. Their gestational ages varied from 28 to 40 weeks, while their ages ranged from 20 to 40 split into two groups: Group I [control group] (n=50) consisted of 50 healthy pregnant women without any complication or any medical disorders. [Study group] Group II (n=50): This group consisted of 50 pregestational diabetic pregnant women (Type 1 and Type 2).

2.1. Inclusion criteria of the participants

Pregnant females with the following criteria: A singleton pregnancy, primigravidae or multiparas, age: 20 – 40 years old and gestational ages were between (28-40) weeks calculated according to the date of last menstrual cycle.

2.2. Exclusion Criteria

Previous history of hypertension, thyroid disease, blood disease, renal disease, hepatic disease, any associated disorders like urinary tract infections.

2.3. Ethical Approval

The quality Education Assurance Unit, Al-Azhar University faculty of medicine for girls, Egypt, approved the ethics committee No (RHDIRB202008351). Before participating in this research, all patients and controls gave their verbal agreement. All women participate in the study were fully informed about the nature and purpose of the research. Any patient who took part in the trial had the option to withdraw without affecting the medical care she got.

2.4. Methodology

Informed consent from all patients was taken, full history talking, complete general and obstetric examinations were done. Investigations including Complete blood count, HbA1C, complete urine analysis and random blood sugar (RBS) were done.

2.5. Ultrasound Examination

Fetal viability, fetal biometry (BPD, FL, AC, HC) and Amniotic fluid Index. Umbilical cord diameter measurement and umbilical vessel diameter measurement (Measurements of the umbilical cord and vessels acquired following magnification for each measurement from the long-axis perspective.) The vessels were measured from inside to inside, whereas the umbilical cord was measured from outside to outside. The surface area of Wharton's jelly was determined by subtracting the areas of the umbilical vein and two arteries from the cross-sectional area of the cord.

2.6. Tissue Specimens

Formalin-fixed and paraffin-embedded (100) specimens were collected and prepared. Specimens included (50) cases of umbilical cords from normal pregnancy and (50) cases of umbilical cords with pregestational diabetic patients. For histological analysis, several five-micron sections were cut and stained with Hematoxylin and Eosin.

2.7. Method of Data management and statistical analysis

In the present study, statistical analyses of data were carried out using SPSS version 20. Shapiro –Wilks test was used to test normal distribution of variables.

3. Results

Table .1 shows there is high statistical for BMI between the two groups. Table .2 shows there is a high substantial variation in RBS between the two groups, and a significant relation in HbA1C between the two groups. Table .3 shows there is a high statistically substantial distinction in terms of the AC and AF Index, and a significant correlation between groups in terms of FL. Table .4 shows there is a highly significant variance in umbilical cord diameter, umbilical artery diameter, umbilical vein diameter, and Wharton's jelly surface area between the control and study groups. Table .5 shows there is a highly substantial distinction in fetal outcome between the control and study groups, as well as a statistically significant variance in Apgar scores at 1 and 5 minutes. Table .6 shows there is a highly substantial distinction in Pathological finding between control and study groups.

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Table (1): Comparing the control and study groups in terms of demographic data.

	Control Group (n=50)	**Study Group (n=50)**	**Paired t test.**		
	Median ± SD	Median ± SD	t	**P-value**	**Sig**
Age (years)	28.64±5.884	31.20±4.187	0.623	0.501	NS
Gestational age (weeks)	36.46±2.154	35.28±1.995	0.133	0.055	NS
BMI	26.64±1.947	31.46±3.144	-10.06	0.000	HS

Table (2): Comparing the control and study groups in terms of RBS (random blood sugar) and HbA1C.

	Control Group (n=50)	**Study Group (n=50)**	**Paired t test.**		
	Median ± SD	Median ± SD	t	**P-value**	**Sig.**
RBS (mg/dl)	92.600±13.124	179.28±50.994	11.9	0.00	HS
HbA1C (mmol/mol)	4.64±0.237	7.46±0.928	1.82	0.032	S

Table (3): Comparing the control and study groups as regarding fetal biometry and AFI.

	Control Group (n=50)	**Study Group (n=50)**	**Paired t test.**		
	Median ± SD	Median ± SD	t	**P-value**	**Sig.**
BPD (weeks)	35.290±2.083	36.481±2.120	1.843	0.082	NS
FL (weeks)	35.610±2.000	36.460±1.992	2.662	0.012	S
AC (weeks)	36.160±2.401	37.53±2.289	3.286	0.001	HS
HC (weeks)	33.261±2.061	32.922±1.981	-1.049	0.299	NS
AFI	13.644±0.988	15.845±2.284	6.322	0.000	HS

BPD (Biparital diameter), FL (Femur length), AC (Abdominal circumference), HC (Head circumference), AFI (Amniotic fluid Index).

Table (4): Comparing the control and study groups in terms of Umbilical Cord diameter, Umbilical artery diameter, Umbilical vein diameter and Wharton's Jelly surface area.

	Control Group (n=50)	**Study Group (n=50)**	**Paired t test.**		
	Median ± SD	**Median ± SD**	**t**	**P-value**	**Sig.**
Umbilical cord diameter /mm	14.7±0.824	18.18±0.889	-9.435	0.000	HS
Umbilical Artery diameter/mm	3.2±0.238	4.5±0.298	6.862	0.000	HS
Umbilical Vein diameter /mm	6.4±0.261	8.5±0.399	4.828	0.000	HS
Wharton's Jelly /mm^2	33.1±0.111	56.8±0.962	-16.495	0.000	HS

Table (5): Comparing the control and study groups in terms of Fetal out- come and Apgar score.

Fetal outcome	Control Group (n=50)		Study Group (n=50)		Paired *t* test.		
	N	%	N	%	t	P-value	Sig.
No NICU admission	49	98%	32	64%	4.52	0.000	HS
NICU	1	2%	17	34%			
NICU + Death	0	0%	1	2%			
Fetal weight (g)	2984.5±292.33		3444.5±434.70		-5.8	0.000	HS
Apgar score at 1 minute	4.65±0.683		4.25±0.686		3.646	0.002	S
Apgar score at 5 minutes	8.68±0.866		8.15±0.864		1.98	0.052	S

Table (6): Comparing the control and study groups in terms of Pathological finding in umbilical Cord.

Pathological finding	Control Group (n=50)		Study Group (n=50)		Paired *t* test.		
	N	%	N	%	t	P-value	Sig.
No Pathological changes	50	100%	0	0%	4.52	0.000	HS
Perivascular, intraparietal hemorrhage	0	0%	25	50%			
Wharton's Jelly hemorrhage	0	0%	15	30%			
Umbilical vein, dilated arterial hemorrhage	0	0%	10	20%			

3.1. Cases Presentation

3.1.1 Ultrasonographic Finding: Group I (Control Group)

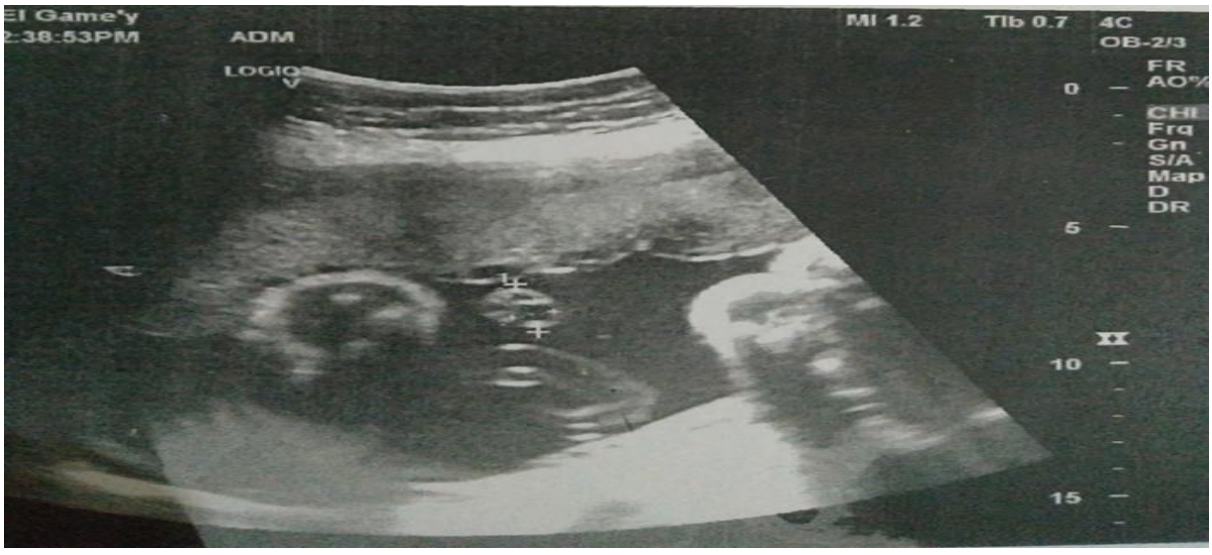

Figure (1): Shows 14 mm diameter of umbilical cord 3.2 mm diameter of the umbilical artery. 6.4 mm diameter of the umbilical vein.

3.1.1 Ultrasonographic Finding: Group II (Study Group)

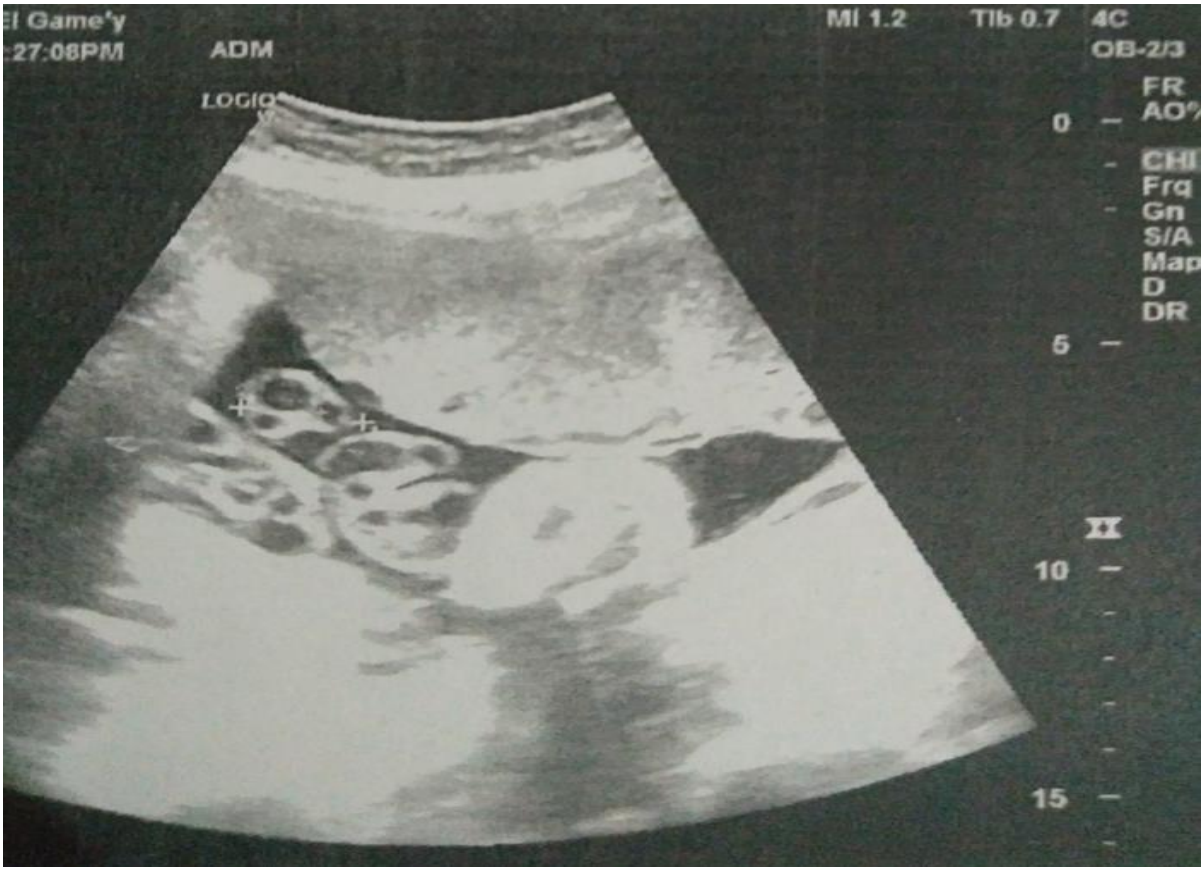

Figure (2): Shows Diameter of umbilical cord: 20 mm, Diameter of the umbilical artery: 4.5 mm and Diameter of umbilical vein: 9 mm

3.1.2 Pathological Finding: Group I (Control Group)

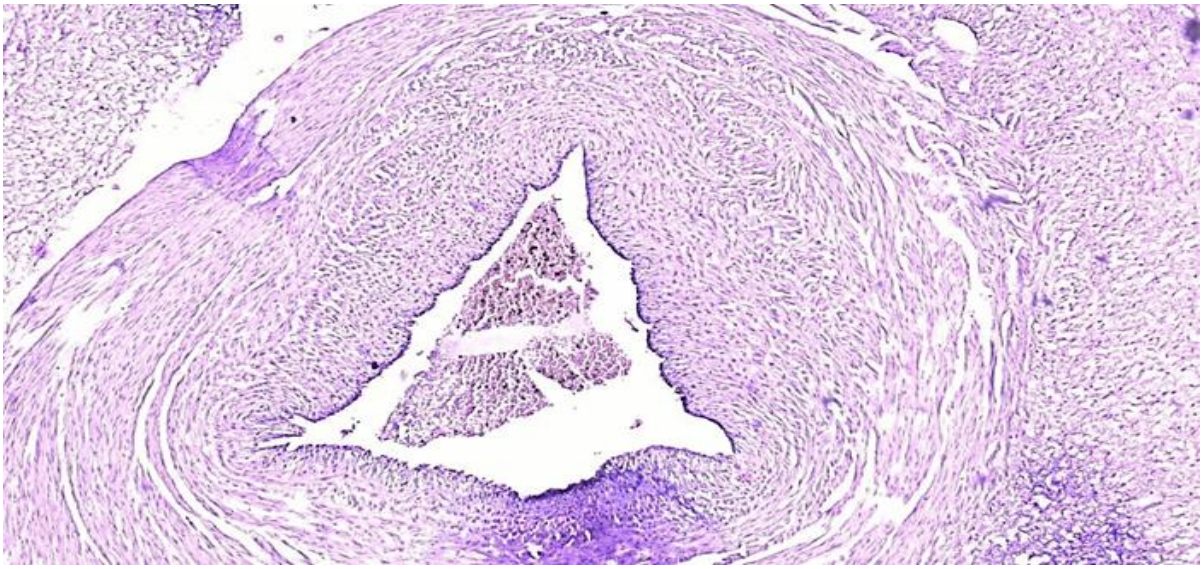

Figure (3): The umbilical vein (H&E 200X) has a star-shaped lumen and is composed of tunica intima, media, and adventitia; the intima is composed of endothelium and a very little endothelial space. Smooth muscle makes up the tunica media. The tunica adventitia is a connective tissue composed of collagen and elastic fibers.

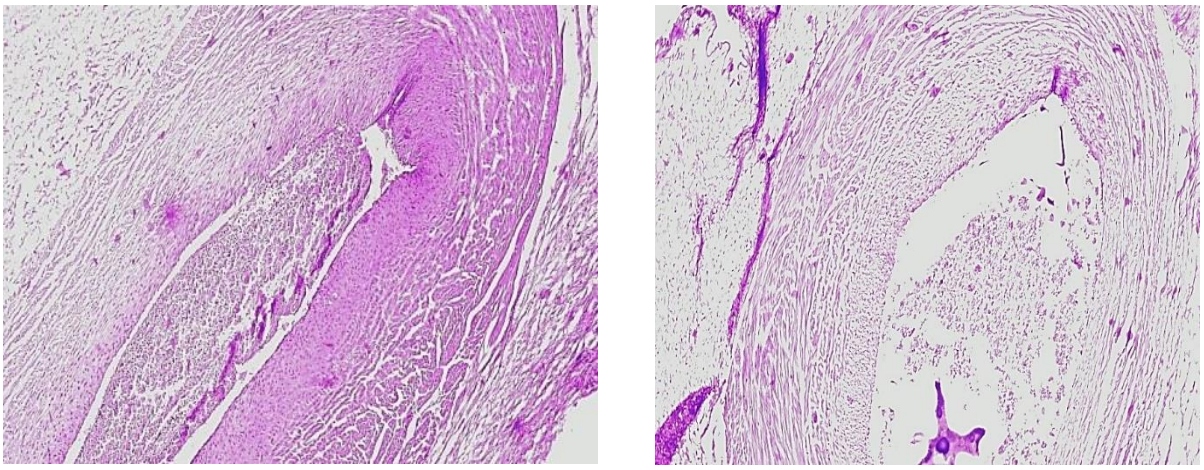

Figure (4): (H&E 200X) The tunica intima of the umbilical artery was constituted of simple squamous epithelium and a tiny endothelial gap. Double-layered muscular smooth muscle bundles made up the tunica media. Collagen, smooth muscle, and elastic fibers make up the tunica adventitia.

3.1.2 **Pathological Finding:** Group II (Study Group)

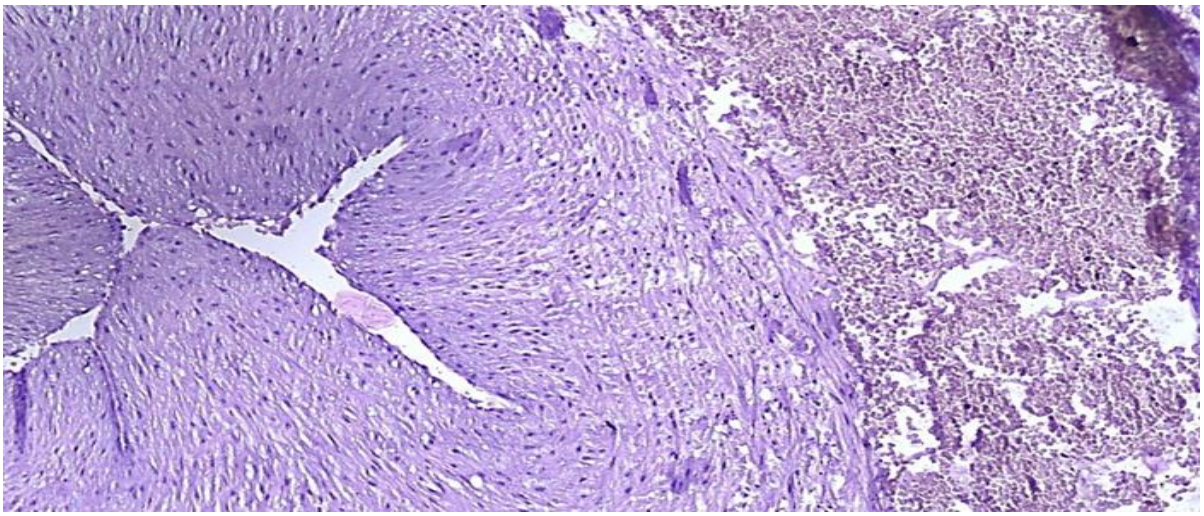

Figure (5): The diabetic umbilical cord (H&E 200X) showed considerable Wharton's Jelly bleeding next to a vein.

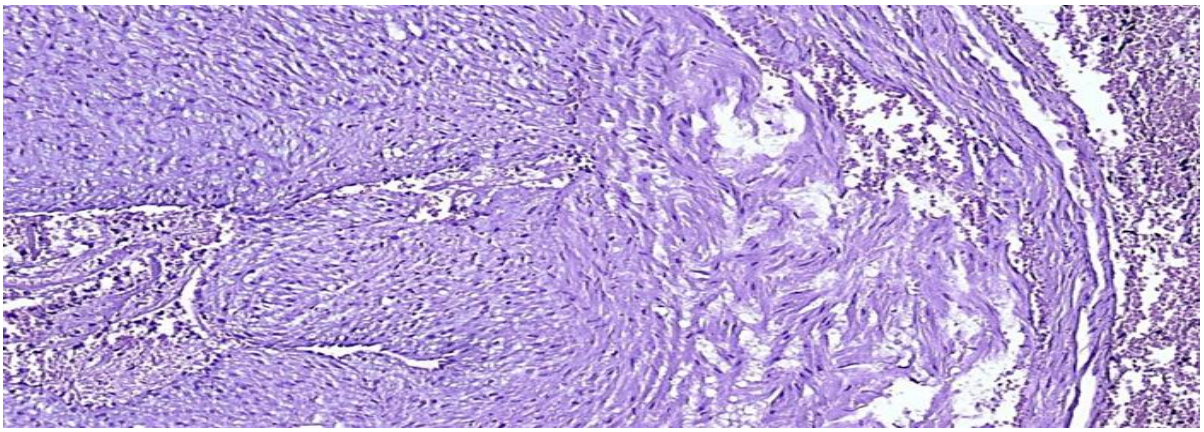

Figure (6): (H&E 200X) showed perivascular and intraparietal hemorrhage with wall dissection.

4. Discussion

The diabetic pregnancy is characterized by numerous disturbances in pregnant mother herself as well as in the fetus and in the placenta. The fetal growth and development show various abnormalities as fetal macrosomia, congenital malformations, intrauterine growth retardation, spontaneous abortions, hypoxia and polycythemia with neonatal jaundice which are commonly seen in poorly- controlled diabetes [14]. Cardiovascular consequences of Pregestational diabetes mellitus include persistent high blood pressure, pregnancy-induced hypertension, and, in rare cases, atherosclerotic cardiovascular disease, as well as nephropathy and retinopathy. Because the umbilical cord serves as a conduit between the uterine and fetal vasculature, any disorder that causes a change in the uteroplacental vascular tree, such as gestational diabetes mellitus, should include an impact on the umbilical vessels and fetal well-being [15]. The umbilical cord (UC) connects the fetus to the mother and runs from the fetal umbilicus to the fetal surface of the placenta. It protects the veins that pass between the baby and the placenta, allowing gas and nutrition exchange, during pregnancy [16]. The current research's demographic data indicated that there was no substantial distinction in age or gestational age between the control and study groups. In terms of BMI, however, the difference between the two study groups was highly relevant. Teliga-Czajkowska et al., (2019) [17] agreed with the results of the present study as regards gestational age and BMI, but Radhia et al., (2013) [18] disagreed as regards maternal age, they found significant difference in maternal age in diabetic group in comparison to non-diabetic group. In terms of Random Blood Sugar (RBS) and HbA1C, there was a highly statistically significant variation between the control and study groups. This was in line with Mohamed et AL (2018) finding's [19]. In terms of BPD and HC, there was no statistical correlation between the control and study groups. This was in contrast to the findings of Fattah (2017) [20], who discovered that fetal growth markers in DM had significantly high values. In terms of AC and AFI, there was a highly statistically relevant variance between the two groups, as well as a significant variation in FL. This agreed with the study of Eltahir (2015) [21]. In terms of umbilical cord diameter, umbilical artery diameter, umbilical vein diameter, and Wharton's jelly, The difference between the control and study groups was highly relevant. Karaca et al., (2020) [22] and Stanirowski et al., (2021) [23] reported the same results. However , Alam et al., (2014) [24] disagreed with our study they found that no significant association between pregestational diabetes and umbilical cord diameter. As regards admission to NICU and fetal weight a high significant variance was found between the two groups and significant difference of Apgar scores. This was consistent with the study of Abdelrahman and Salama (2018) [25], but this was contradictory with the study of Yeagle et al., (2018) [26] they found that The PGDM group and controls had no significant variations in 1-minute and 5-minute Apgar scores. The current investigation discovered pathological changes in the umbilical cord, umbilical artery, umbilical vein, and Wharton's jelly in the study group including perivascular, intraparietal hemorrhage with wall dissection and extensive hemorrhage of Wharton’s jelly adjacent to a vein. This was consistent with the study of Chakraborty and Banu (2013) [27] but this was contradictory with the study of Rafah (2013) [28] they found that the PGDM group and controls had no significant pathological changes in the umbilical cord.

5 .Conclusion

- The umbilical cord diameter can help in determination of normal growth of fetus in second and third trimester, so it can be used as an additional sonographic tool for assessing maternal and fetal health.

- Complications from the PGDM have an impact on mother and fetal health, as well as child health. Fetus who had mother with pregestational diabetes mellitus have a significant high risk to develop complications such as caesarean delivery, macrosomia and NICU admission.

- Pregestational diabetes has a number of negative impacts on the umbilical cord's histological structure.

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