Histopathological Lesions of Placenta in Mild and Severe Pre-Eclampsia in a Population of Egyptian Women

Samir A. Nassar[*1], Mahmoud Rabeh[2], Ashraf N. Refaay[3] and Ghada A. Amer[4]

1,2,4: Zoology Department, Faculty of Science, Zagazig University, Zagazig, Egypt

3: Obstetrics & Gynaecology Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt

Corresponding author: Samir A. Nassar

E-mail: sam59nas@gmail.com

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Abstract

Background: Pre-eclampsia (PE) results in adverse maternal and foetal outcomes in our setting. The pathophysiology is strongly linked to placental development. We aimed to study placental lesions associated with two stages of PE mild (MPE) and severe (SPE) in a population of Egyptian women. **Materials and methods**: We conducted a cross sectional, analytical study in Zagazig University Hospital. The experimental period of the current study started from March 2019 till completing the sample size. The study included 30 participants; 20 pre-eclamptic women and 10 women with clinically-normal pregnancy as control group. **Results**: placental sections of MPE revealed diverse placental affection including blood vessel covered by thick fibrinoid, hemorrhage in widened intervillous space, incidence of syncytial knots with thickness of vasculo-syncytial membrane and hyalinization of fetal capillaries. However, placental sections of SPE revealed chorionic plate with congested blood vessels and different types of distorted and atrophied villi enclosing highly widened intervillous space, increased thickness and incidence of syncytial knots and villi with disrupted fetal capillaries and calcification at a part of the maternal surface as compared to the placental histology of normal women. **Conclusion**: PE-associated placental lesions in our study are multiple and diverse especially in its severe stage, and these may be develop due to maternal vascular malperfusion.

Keywords: Preeclampsia, Placental Lesions, Histological Aspects, Egyptian population.

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Introduction

Pre-eclampsia is a global leading cause of maternal and fetal mortality, affecting 5-10% of all pregnancies (**Cunningham** *et al.*, **2018**). The development and wellbeing of the fetal life is

provided by the materno-fetal unit; umbilical cord and placenta (**Kadivar** *et al.,* **2020**). Disturbed placental histology and morphology in complicated pregnancies by preeclampsia (PE) leads to placental impaired function, which finally accounts for fetal and neonatal problems (**Ojha** *et al.,* **2018**). Pre-eclampsia denotes the development of hypertension and proteinuria or hypertension and ends in placental dysfunction, with or without proteinuria after 20 weeks of gestation, or in the postpartum period in a previously normotensive woman **(Anonymous, 2020).** The WHO estimates that 16% of maternal deaths are due to hypertensive disorders and over 100,00 women die from pre-eclampsia globally, with a higher incidence in developing countries (2.8%) than developed countries (0.4%)(**Khan** *et al.,* **2006**; **Osanyin** *et al.,* **2018**).

Subjects and methods:

Selection of cases

The study included 30 pregnant women classified equally into 3 groups; mild preeclampsia (MPE), severe preeclampsia (SPE) and a clinically normal pregnancy as a control group (NC). They were recruited in the 3rd trimester pregnancy from Obstetrics and Gynaecology Department, Zagazig University Hospital. Written informed consents were obtained from all participants and the following exclusion criteria were fulfilled (**Li** *et al.*, **2020**; **Alam** *et al.,* **2017**):

• Mother age less than 20 or more than 35 years.

• Multiple gestations.

• Duration of pregnancy less than 30 weeks.

• History of smoking or alcohol intake.

• Intake of any medications.

• Diabetes mellitus or gestational diabetes.

• Intrahepatic cholestasis of pregnancy.

• Major fetal anomalies.

• Co-existing or preconceptional maternal conditions like polycystic ovary syndrome, autoimmune disease, thrombophilic conditions, renal, thyroid, cardiovascular or liver diseases.

Grouping

Group I: 10 pregnant females suffering from mild preeclampsia.

Group II: 10 pregnant females suffering from severe preeclampsia.

Group III: 10 females with normal pregnancy as control group.

Inclusion criteria

***Cases of preeclampsia are diagnosed by*:** Systolic blood pressure ≥140 mmHg, ddiastolic blood pressure ≥90 mm and Proteinuria >150 mg/24h urine collection and gestational age is from 36 to 38 weeks.

Mild preeclampsia is diagnosed by: Systolic blood pressure ≥140 mmHg, while diastolic blood pressure ≥ 90 mmHg, proteinuria in 24h collected urine is > 0.3 gm/day. There are no other signs of problems with either the mother or the foetus.

***Severe preeclampsia is diagnosed by*:** Systolyic blood pressure ≥160 mmHg, diastolic blood pressure ≥110 mmHg, proteinuria > 2g/24h urine collection, Symptoms as headache, blurring of vision, epigastric pain and other complications.

Duration of the study: The experimental period of the current study started from March 2019 till completing the sample size.

Ethical and Administrative Considerations:

Our study was carried out in accordance to the national guidelines in Egypt. Ethical approval to conduct this study was obtained from the ethical and institutional committee of the Faculty of Medicine, University of Zagazig and biological samples were obtained after informed consent from all participants. Participation was strictly voluntary, with no restrictions if the participant decided to withdraw from the study.

Operational design:

Methods:

1. **Detailed history** (personal, obstetric, menstrual, past and family history) will be obtained from the recorded data in patient's official files **2. Histological Study**

Placental specimens were taken after delivery nearly 3 cm from the cord insertion; halfway between the basal and chorionic plates to be away from areas containing infarction or gross fibrin deposition. Specimens were fixed in formalin then embedded in paraffin. Serial sections of 5µm thickness were subjected to: Hematoxylin & eosin staining (**Keirnan, 2015).**

Results:

Histological results

Group I: Mild pre-eclampsia (MPE)

The light microscopic examination of placental sections of group II (MPE) revealed diverse placental affection. Changes mainly appeared in the chorionic plates and villi including embryonic mesoderm enclosing fibroblasts, blood vessel (bv) covered by thick fibrinoid towards chorionic

villi. Different types of villi were seen; stem villi and terminal villi. Hemorrhage in widened intervillous space could be seen. An incidence of syncytial knots was also seen in addition to hemorrhage in the intervillous space (Fig. 1). In another fields with high magnification, the placental tissue of MPE women exhibited distorted villi; stem villi, intermediate villi with decreased number of fetal capillaries. Also, hyalinization of fetal capillaries was well recognized. An increased incidence of syncytial knots and thickness of vasculo-syncytial membrane could be demonstrated (Fig.2).

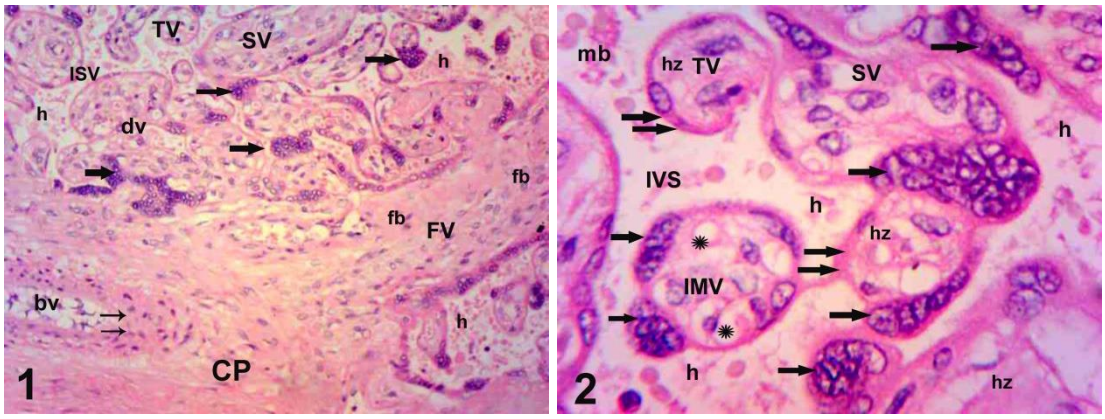

Fig. 1: Photomicrographs of placental sections from group II (mild pre-eclampsia , MPE) stained with H&E(X400) showing chorionic plate (CP) giving floating villi (FV) and containing embryonic mesoderm enclosing fibroblasts (fb), blood vessel (bv) covered by thick fibrinoid (double arrow) towards chorionic villi. Different types of villi are seen; stem villous (SV), and terminal villi (TV). Hemorrhage (h) in widened intervillous space (IVS) is seen. Notice, an incidence of syncytial knots (thick black arrow) was also seen. Fig. 2: Photomicrographs of placental sections from group II (mild pre-eclampsia , MPE) stained with H&E(x1000) showing cross sections of different types of distorted villi; stem villi (SV), intermediate villi (IMV) with decreased number of fetal capillaries (*). Hyalinization of fetal capillaries (hz). An increased incidence of syncytial knots (thick black arrow) and thickness of vasculosyncytial membrane (double arrows) are demonstrated.

Group II: Severe pre-eclampsia(SPE)

The light microscopic examination of placental sections of group III (SPE) revealed chorionic plate (CP) containing congested blood vessels and cross sections of different types of distorted and atrophied villi enclosing highly widened intervillous space (Fig. 3). High magnification of other fields from placenta of SPE women showed increased thickness and incidence of syncytial knots and villi with disrupted fetal capillaries together with increased intervillous space (Fig. 4). Also, placental sections of severe pre-eclampsia exhibiting some sort of calcification at a part of the maternal surface (Fig. 5).

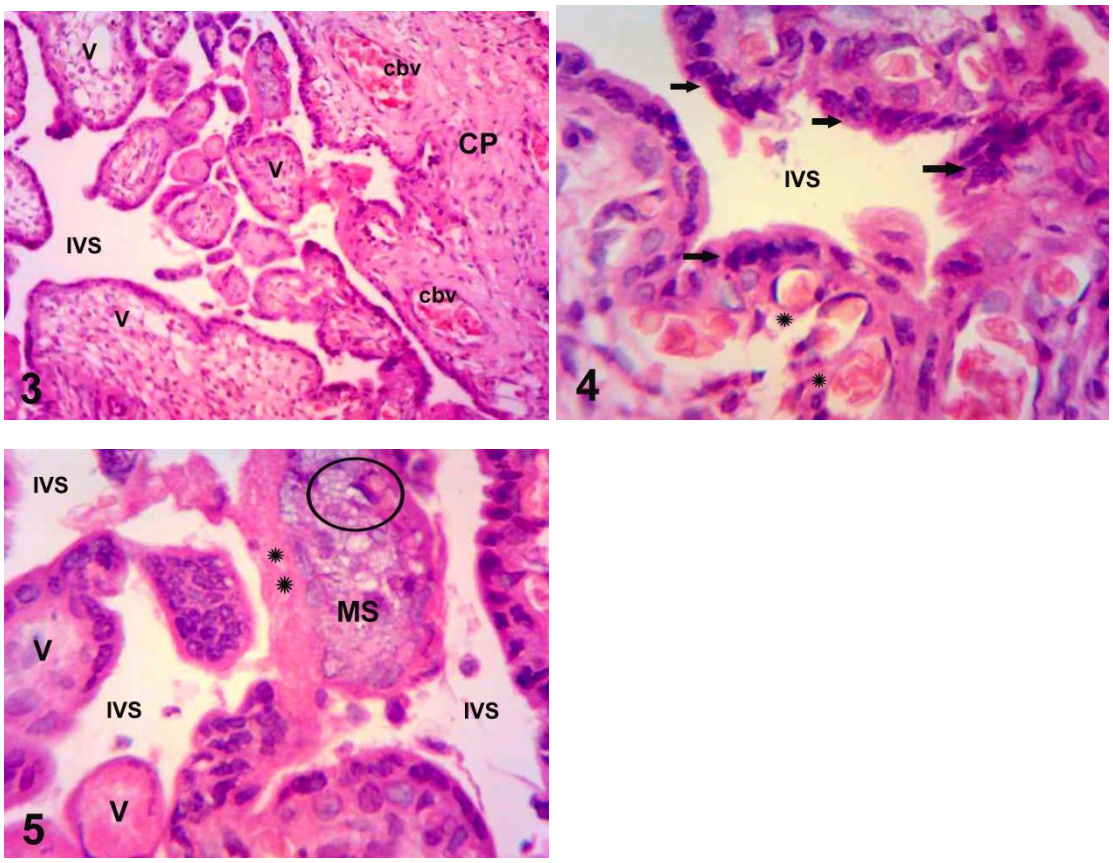

Fig. 3: Photomicrographs of placental sections from group III (severe pre-eclampsia , SPE) stained with H&E(X400) showing chorionic plate (CP) containing congested blood vessels (cbv) and cross secstions of different types of distorted and atrophied villi (V) enclosing highly widened intervillous space (IVS).Fig. 4: Photomicsrographs of placental sections from group III (severe pre-eclampsia , SPE) stained with H&E(X1000) showing increased thickness and incidence of syncytial knots (thick black arrow) and villi with disrupted fetal capillaries (*) together with increased intervillous space (IVS). Fig. 5: Photomicrographs of placental sections from group III (severe pre-eclampsia , SPE) stained with H&E(X1000) showing part of the maternal surface exhibiting calcification, different types of distorted and atrophied villi (V) and highly widened intervillous spaces (IVS) inbetween.

Group III: Normal control group

Placental sections from the control group illustrated the chorionic plate (fetal side); the chorionic mesoderm containing fibroblasts and blood vessels and lined by STB at the surface facing the maternal blood. Different types of villi were present; they are overcrowded with minimal intervillous space (IVS); stem villi the largest ones with with fibrinoid deposition at its periphery, mature intermediate villi had loose stroma with numerous capillaries, terminal villi had the smallest diameter. Each villous was lined by STB and few cytotrophoblasts and had a core of mesenchymal connective tissue containing fetal capillaries lined by flat endothelium. The villi were separated from each other by intervillous space filled with maternal blood (Fig. 6). In magnified fields,

placenta of normal control women exhibited the incidence of fibroblasts inside the embryonic mesoderm (Fig.7) and revealing cross section of villi containing fetal capillaris lined with flattened epithelia, reminants of cytotrophpblasts (rct). Intervillous space containing maternal blood. Alow incidence of syncytial knots, a feature of mature placenta, were seen as clusters of syncytiotrophoblast nuclei are seen at the periphery of villi (Fig. 8).

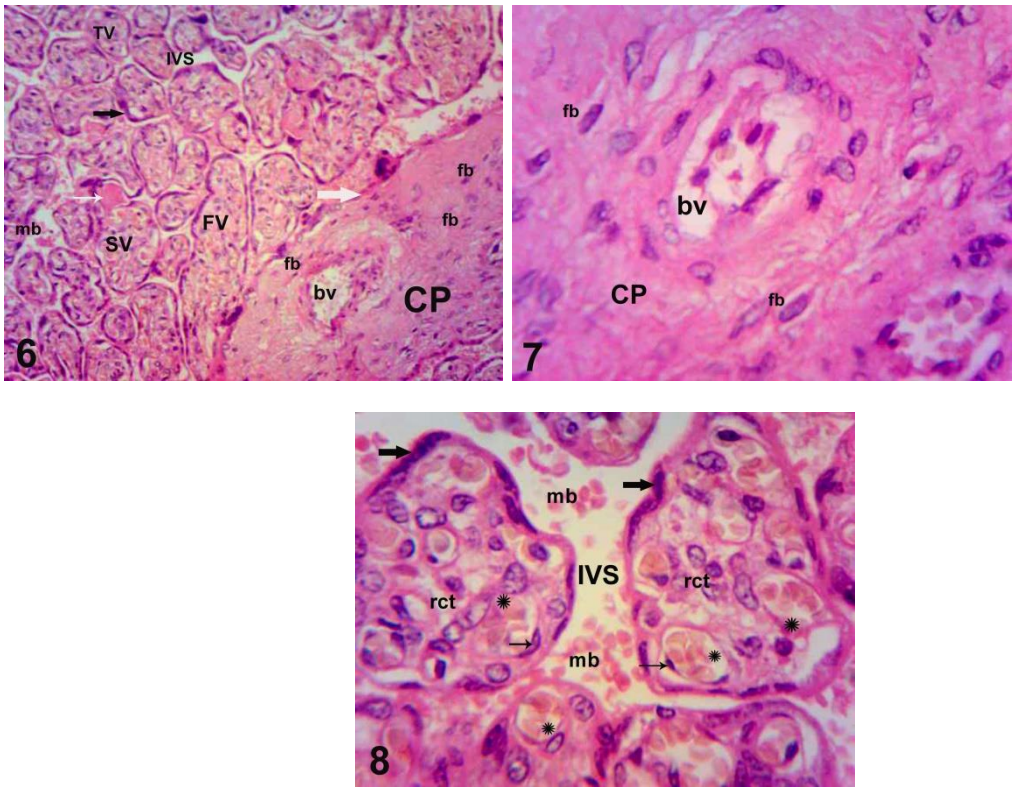

Fig. 6: Photomicrographs of placental sections from control group stained with H&E. X400) Chorionic plate (CP) at the fetal side facing chorionic villi (V) and consists of extraembryonic mesoderm containing fibroblasts (fb) and blood vessels (bv) and covered by STB (thick white arrows). Different types of villi with narrow intervillous space (IVS) are seen; floating villi (FV), stem villi (SV) with fibrinoid deposition at its periphery (thin white arrow) and terminal villi (TV) could be detected .IVS appeared containing maternal blood (mb). A low incidence of syncytial knots was also seen (thick black arrows). **Fig. 7:** Photomicrographs of placental sections from control group stained with H&E. X1000) illustrating a magnified portion revealing the chorionic plate (CP) containing blood vessel (bv) and the incidence of fibroblasts (fb) inside the embryonic mesoderm**. Fig. 8:** Photomicrographs of placental sections from control group stained with H&E. X1000) illustrating a magnified portion revealing cross section of villi containing fetal capillaris (*) lined with flattened epithelia (arrow), remnants of cytotrophoblasts (rct). Intervillous space (IVS) containing maternal blood (mb**).** Syncytial knots (thick black arrow) are seen at the periphery of villi.

Discussion

In the current study, we investigated histological placental lesions in pre-eclamptic Egyptian women and tried to evaluate whether these lesions were correlated to disease severity.

In this study, cases of MPE exhibited different histological changes including blood vessels covered by thick fibrinoid, hemorrhage inside intervillous spaces, incidence of syncytial knots, distorted villi, intermediate villi with decreased number of fetal capillaries. Also, hyalinization of fetal capillaries was well-recognized. The authors attributed these alterations to the placental malperfusion. This is in agreement with observations of various investigators**; Youssef** *et al.* **(2020**) who recorded diverse placental affection in pre-eclamptic women including chorionic plate covered by thickened Langhan's layer of fibrinoid and losing syncytiotrophoblast, numerous syncytial knots and distorted villi and hemorrhage in the intervillous space. **Clemente Castejon** (**2018**) recorded intervillous hemorrhage in sections from PE group and attributed it to placental abruption due to high blood pressure. He added, severe hypertension can directly damage the vessels with concomitant hemorrhage in intervillous space. Hyalinization of villi and fetal blood vessels was observed in placental tissue of PE group by **Ojha** *et al.* (**2018**), which comes in line with our results. Also**, Essiben** *et al.* **(2022**) recorded PE-related histopathological placental lesions in a previous study which were multiple and diverse especially in severe disease, and these arise as a result of defective maternal vascular perfusion.

Concerning SPE in our study; congested blood vessels, distorted and atrophied villi enclosing highly widened intervillous space, increased incidence and thickness of syncytial knots and villi with disrupted fetal capillaries together with some sort of calcification at a part of the maternal surface could be detected. These results come in line with those of **Roberts (2022**) who recorded histopathological findings that correlated to poor maternal vascular perfusion comprising increased syncytial nodes and reduced number of intermediate villi due to atrophy resulting in increased inter-villous space. The author also added that chronic malperfusion finally leads to placental infarctions, when these infarcts on the maternal side of placenta being severe and ends in calcifications. Placental lesions of pre-eclampsia (due to defective maternal vascular perfusion, infarction, large syncytial nodes) were significantly present in patients with SPE compared to MPE group ($p < 0.001$). In addition, confounding lesions such as calcifications were significantly higher in patients with SPE. Several authors have reported similar findings in the literature (**Weiner** *et al.*, **2018**; **Paules** *et al.*, **2019**; **Pietro** *et al.,* **2021**). Moreover, some investigators reported that hyalinization may result from immune attack against trophoblastic tissue due to an immunological reaction inside the villar tissue; since it resembles the amyloid deposition present in immunological disorders (**Agrawal** *et al.,* **2017**).

Conclusion

PE-related placental lesions in our study comprising congested blood vessels, distorted and atrophied villi, hemorrhage in intervillous spaces, incidence of syncytial knots with thickened vasculo-syncytial membrane, hyalinization and disruption of fetal capillaries and calcification in parts of the maternal surface. These changes are multiple and diverse especially in severe stage, and these may be arise as a result of defective maternal vascular perfusion.

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