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Research Article

Immunohistochemical Evaluation of APAF-1 and E-Cadherin Expression in Placentas of Smoking Women with Premature Rupture of Membranes

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Abstract

Objective: This study aimed to evaluate the immunohistochemical expression of APAF-1 and E-cadherin in placental tissues of smoking women with premature rupture of membranes (PROM).

Materials and Methods: Placental samples obtained from smoking and non-smoking women diagnosed with PROM and from healthy controls were examined immunohistochemically for APAF-1 and E-cadherin expression.

Results: Increased APAF-1 expression and decreased E-cadherin expression were observed in placentas of smoking women with PROM compared to controls.

Conclusion: Smoking may contribute to PROM by enhancing apoptotic activity and disrupting placental cell–cell adhesion.

Keywords: placenta, apaf-1, prom, smoking

INTRODUCTION

Premature rupture of membranes (PROM) is a frequent obstetric complication characterized by the rupture of fetal membranes before the onset of labor and is associated with increased risks of maternal and neonatal morbidity and mortality [1,2]. PROM represents a major contributing factor to preterm birth, which remains a leading cause of neonatal complications worldwide [2,3]. The pathogenesis of PROM is multifactorial and involves infectious, inflammatory, mechanical, and environmental influences that compromise membrane integrity [3,14]. Maternal cigarette smoking during pregnancy is a well-established, preventable environmental risk factor associated with adverse pregnancy outcomes, including PROM [4,5]. Exposure to tobacco smoke introduces numerous toxic substances that induce oxidative stress, vascular dysfunction, and inflammatory responses within placental tissues [4,12]. These pathological effects may weaken placental and fetal membrane structures, increasing susceptibility to premature rupture [5,15].

Apoptosis plays a critical role in placental development and tissue remodeling, and dysregulation of apoptotic pathways has been implicated in pregnancy-related complications [7,13]. Apoptotic protease activating factor-1 (APAF-1) is a key regulator of the intrinsic mitochondrial apoptosis pathway through its involvement in apoptosome formation and caspase activation [8,9].

MATERIALS AND METHODS

Study Design and Tissue Collection

This study was conducted using placental tissue samples obtained from pregnant women who delivered with or without premature rupture of membranes (PROM). Participants were categorized into three groups: smoking women with PROM, non-smoking women with PROM, and healthy non-smoking controls. Informed consent was obtained from all participants, and the study protocol was approved by the institutional ethics committee.

Placental tissues were collected immediately after delivery. Representative samples were taken from standardized regions of the placenta, fixed in 10% neutral-buffered formalin, routinely processed, and embedded in paraffin blocks.

Immunohistochemical Analysis

Paraffin-embedded placental tissues were sectioned at 4–5 µm thickness. Sections were deparaffinized and rehydrated, followed by antigen retrieval using appropriate buffer solutions. Endogenous peroxidase activity was blocked before incubation with primary antibodies against APAF-1 and E-cadherin.

After incubation with secondary antibodies, immunoreactivity was visualized using a chromogenic detection system. Sections were examined under a light microscope, and staining intensity and distribution were evaluated semi-quantitatively. Representative micrographs were captured for documentation.

RESULTS

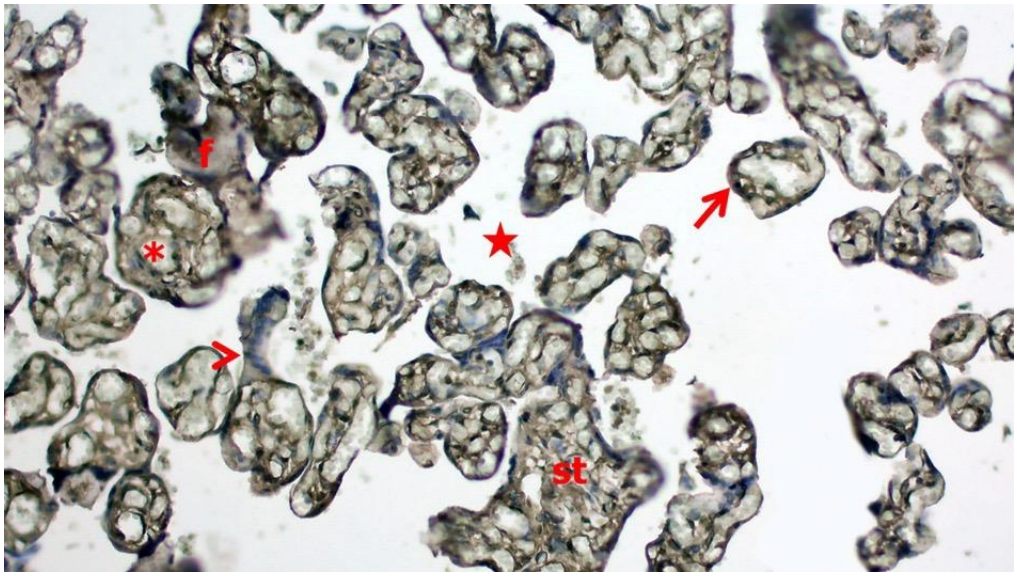

Figure 1. Placental tissue section obtained from the smoking group diagnosed with premature rupture of membranes (PROM), stained with APAF-1 immunoantibody. Prominent cytoplasmic APAF-1 positivity is observed in the syncytiotrophoblast layer (arrow) as well as in cytotrophoblast cells. Moderate to strong immunoreactivity is evident within the stromal region (st) and around the villous capillaries (*). Increased immunopositivity is also noted in the intervillous spaces (★).(Arrow: syncytiotrophoblast layer; arrowhead: syncytial knot; st: stroma; *: villous capillary; f: fibrin deposition; ★: intervillous space; APAF-1 immunostaining; scale bar: 50 µm; magnification: ×20)

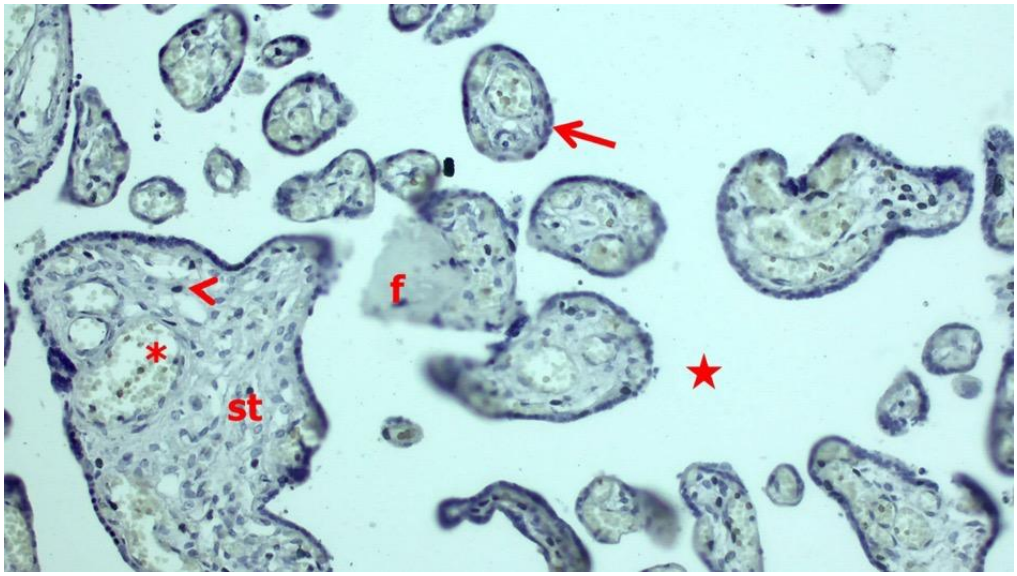

Figure 2. Placental tissue section from the control group stained with the APAF-1 immunoantibody. The villous architecture appears well preserved, while weak cytoplasmic APAF-1 immunoreactivity is observed in both the syncytiotrophoblast (arrow) and cytotrophoblast layers. No marked staining is detected within the stromal compartment (st) or the intervillous space (★).(Arrow: syncytiotrophoblast layer; arrowhead: syncytial knot; st: stroma; *: villous capillary; f: fibrin deposition; ★: intervillous space; APAF-1 immunostaining; scale bar: 50 µm; magnification: ×20)

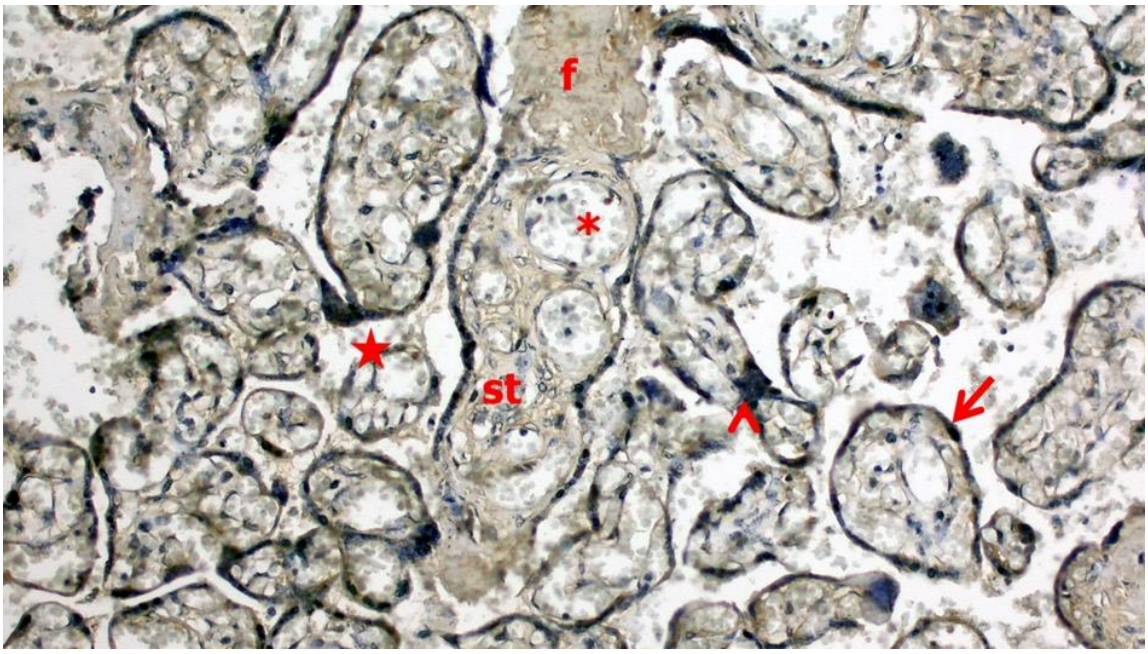

Figure 3. Placental tissue section from the smoking group diagnosed with premature rupture of membranes (PROM), stained with the E-cadherin immunoantibody. A marked loss of staining is observed in the syncytiotrophoblast layer (arrow), while cytotrophoblast cells exhibit irregular and weak immunopositivity. In the stromal region (st), focal areas of moderate E-cadherin immunoreactivity are present, whereas immunostaining in the intervillous space (★) is minimal.(Arrow: syncytiotrophoblast layer; arrowhead: syncytial knot; st: stroma; *: villous capillary; f: fibrin deposition; ★: intervillous space; E-cadherin immunostaining; scale bar: 50 µm; magnification: ×20)

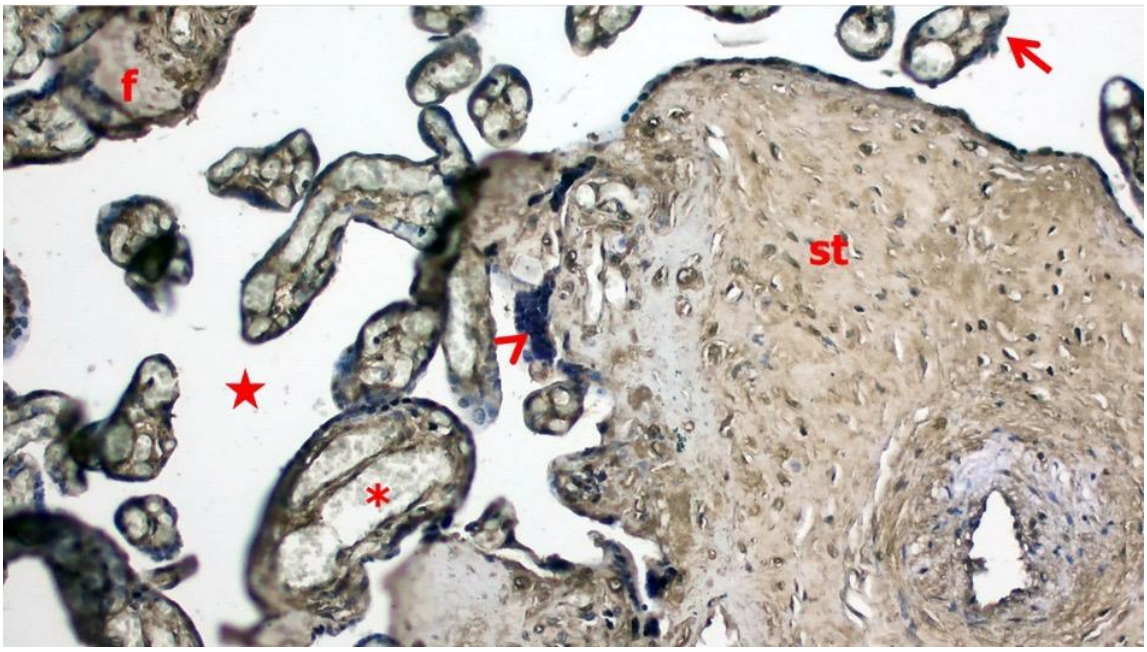

Figure 4. Placental tissue section from the control group stained with the E-cadherin immunoantibody. Moderate immunoreactivity is observed in the syncytiotrophoblast layer (arrow), while cytotrophoblast cells display both cytoplasmic and membranous E-cadherin positivity. More intense E-cadherin staining is evident within the stromal compartment (st); however, no distinct immunoreactivity is detected in the intervillous space (★).(Arrow: syncytiotrophoblast layer; arrowhead: syncytial knot; st: stroma; *: villous capillary; f: fibrin deposition; ★: intervillous space; E-cadherin immunostaining; scale bar: 50 µm; magnification: ×20)

DISCUSSION

The findings of the present study demonstrate that maternal smoking during pregnancy is associated with significant alterations in placental apoptotic and adhesion-related pathways in cases of PROM [4,5]. Increased APAF-1 immunoreactivity observed in placentas from smoking women with PROM suggests enhanced activation of the intrinsic apoptotic pathway [7,9]. This observation is consistent with previous studies indicating that cigarette smoke–induced oxidative stress leads to mitochondrial dysfunction and activation of

apoptosis-related signaling cascades [6,15]. APAF-1 plays a pivotal role in apoptosome assembly and subsequent caspase activation following cytochrome c release from mitochondria [8,9].

Excessive apoptotic activity within placental tissues may compromise cellular viability and structural integrity, thereby contributing to membrane fragility [7,13]. The increased APAF-1 expression observed in the syncytiotrophoblast and stromal compartments in the smoking PROM group supports the hypothesis that smoking accelerates apoptotic processes in the placenta [4,12]. In contrast, E-cadherin expression was markedly reduced in placentas of smoking women with PROM compared to controls, indicating impaired intercellular adhesion [10,11]. E-cadherin is essential for maintaining epithelial cohesion and tissue resistance to mechanical stress, and its downregulation may predispose tissues to rupture [10,11].

Previous studies have reported that oxidative stress and inflammatory mediators can disrupt cadherin-mediated adhesion, further supporting the present findings [11,15]. The combined effect of increased apoptosis and decreased cell–cell adhesion may act synergistically to weaken placental and membrane structures [7,10]. Such molecular alterations may reduce the placenta's ability to withstand mechanical forces during pregnancy, ultimately leading to premature rupture of membranes [14]. These findings highlight the detrimental impact of maternal smoking on placental homeostasis and emphasize the biological plausibility of smoking as a major risk factor for PROM [4,5]. Importantly, smoking cessation during pregnancy may represent a critical preventive strategy to reduce oxidative stress–induced placental damage and lower the risk of PROM-related complications [4,15].

CONCLUSION

The present study demonstrates that placentas from smoking women with PROM exhibit significantly increased APAF-1 expression and reduced E-cadherin expression compared to controls [4,7,10]. These findings indicate that maternal smoking contributes to PROM by enhancing apoptotic activity and disrupting cell–cell adhesion within placental tissues [7,11].

The imbalance between apoptosis and structural integrity may play a crucial role in weakening fetal membranes and promoting premature rupture [13,14]. Understanding the molecular mechanisms underlying smoking-related placental damage provides valuable insight into the pathophysiology of PROM [4,15]. Preventive strategies aimed at smoking cessation during pregnancy may help preserve placental integrity and reduce PROM-associated maternal and neonatal morbidity [4,5].

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Conflict of interest: The authors have no conflicts of interest.

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