Research Article
ISSN (Print): 0971-913X
ISSN (Online): 2455-1244
J Endocrinol Reprod. *Vol 27(4), 253-260, December 2023, DOI: 10.18311/jer/2023/33678*

Histopathological and Immunohistochemical Analysis of Ruptured Tubal Ectopic Pregnancy

Archunan Priya Aarthy[1,2*], Anuradha Monga[1], Sangeeta Sen[1], Narayana Moorthy Bavani[3], Velliyangiri Silambarasan[3], Govindarajan Deepalakshmi[3], Mohammad Abdulkader Akbarsha[5,6] and Govindaraju Archunan[3,4*]

[1]Department of Obstetrics and Gynaecology, Ravindra Nath Tagore Medical College, Udaipur - 313001, Rajasthan, India

[2]Department of Obstetrics and Gynaecology, Saveetha Medical College and Hospital, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai - 602105, Tamil Nadu, India; aartrhyarchun94@gmail.com

[3]Department of Animal Science, Bharathidasan University, Tiruchirappalli - 620024, Tamil Nadu, India; garchu56@yahoo.co.in

[4]Research Dean, The Marudupandiyar Institutions, Thanjavur - 613403, Tamil Nadu, India

[5]Department of Biotechnology and Microbiology, National College (Autonomous), Tiruchirappalli - 620024, Tamil Nadu, India

[6]Mahatma Gandhi-Doerenkamp Centre for Alternatives to Animal Experiments, Bharathidasan University, Tiruchirappalli - 620024, Tamil Nadu, India

Abstract

Ectopic Pregnancy (EP) is reported to be causative of high incidence of maternal death and morbidity. It must be diagnosed during the first trimester immediately after symptoms of severe bleeding, abdominal pain, and cramping. Ultrasonography is the only possible detection method to confirm EP. Patients are at greater risk of EP due to inefficient early detection methods. An early detection of the EP based on cellular markers would possibly improve the diagnosis and clinical management. Therefore, an attempt was made to study the histoarchitecture of, and to identify the biomarkers in, the fallopian tube during rupture of ectopic pregnancy. Histological analysis revealed the formation of hematosalpinx and hydrosalpinx in the fallopian tube. Further, immunohistochemical study of the fallopian tissue of EP patients showed remarkable evidence of protein markers such as Bcl_2 and desmin which may be considered as potential cellular markers for the detection of EP.

Keywords: Bcl_2, Desmin, Ectopic Pregnancy, Histology, Tubal Rupture.

1. Introduction

Ectopic Pregnancy or Extrauterine Pregnancy (EP) is a condition where the implantation and development of a fertilized ovum occurs outside the uterus. In most of the EP cases, implantation occurs in the fallopian tube and it is referred to as tubal pregnancy. In a few cases of ectopic pregnancy, non-tubal conditions prevail wherein implantation occurs in the ovary, cervix, and peritoneal cavity[1]. EP has been a serious problem due to the significant rate of morbidity and maternal deaths. The highest incidence of EP prevails in the African continent. However, the incidence of EP has dramatically increased in America over the past decade. In India, 3.5-7 % of maternal deaths occur due to ectopic pregnancy[2]. The incidence is more common in women of the age group 26-30 years. A recent report by Casadio *et al*. (2020) showed that there is an

**Author for correspondence*

Article Received: 02.05.2023 Revised on: 27.10.2023 Accepted on: 27.10.2023

increased rate of EP in North Italy during the COVID-19 pandemic[3].

Among the tubal EP, the obvious outcome reportedly is tubal hemorrhage that leads to tubal abortion or tubal rupture in certain individuals. Abdominal pain, amenorrhea, vaginal bleeding, and dizziness are the usual symptoms of EP[1]. The possible pathophysiology of the disease includes distortion of the fallopian tube, abnormalities in tubal motility, and trans-peritoneal migration of the zygote[4]. The diagnosis for EP is conducted during the first trimester of pregnancy when the gestation age would be 6 to 10 weeks. Serum measurement of β-hCG and progesterone, and ultrasound imaging are the possible diagnostic methods for EP. Depending on the severity of the condition, surgical methods, and methotrexate medical treatment are the possible clinical management approaches for EP.

The ratio of EP to live births has been increasing with maternal age[5]. Banhart (2009) found that half the percentage of EP-diagnosed people indicate no identifiable risk factors such as a history of sexually transmitted infections, tubal damage, history of EP, *in utero* diethylstilbestrol, and pelvic inflammatory disease[6]. Defective ciliary movement or muscular contractions for embryo transport in the fallopian tube caused by infection or smoking is the possible underlying cause of tubal ectopic pregnancy[7]. Reduction in adrenomedullin, a receptor protein, has a possibility to impair embryo transport in the fallopian tube and lead to tubal EP[8]. Wang *et al*. (2020) concluded that as much as adrenomedullin reduction contributes to the pathophysiology of tubal EP, it does it partly by triggering excessive macrophage-mediated inflammation[9]. The pathology of EP suggests that intraluminal trophoblastic spread along with intratubal hemorrhage leads to destruction of the tubal tissues and, in addition, salpingitis has been noted through histological analysis[10].

We believe that histological examination of the fallopian tube would provide insight into the cellular folding and distribution. Staining is an integral part of histopathology and diagnosis since it expounds defects in cell counts and structure. Immunohistochemistry studies make it possible to visualize the appropriation and restriction of explicit parts inside cells and real tissue settings. Possible cellular biomarkers for EP could also be detected by adopting immunohistochemical tools.

The human body adopts mechanisms such as apoptotic cell death to maintain appropriate cell numbers. During this process, most of the aged cells are eliminated to facilitate normal *milieu interieur* and physiology. As a consequence, in some cases, the expression of important apoptotic pathways is prevented resulting in failure of normal growth and metabolism. B-cell lymphoma 2 (Bcl_2) is a kind of cellular protein widely involved in the regulation of apoptosis and acts as an apoptosis suppressor protein present in the membrane, mitochondria, endoplasmic reticulum, and nuclear envelope. Over-expression of Bcl_2 inhibits apoptosis by preventing the action of caspases[11]. It has been reported that Bcl_2 expression is varied during the entire trimester of pregnancy; however, very high expression of Bcl_2 was found during the third trimester to maintain a successful pregnancy[12]. A lesser intensity of Bcl_2 was noted during both the first trimester and failed pregnancies[13]. High expression of Bcl_2 was reported during the ruptured ectopic pregnancy[14].

Desmin is a muscle-specific type III intermediate filament found in most organs of the human system. It plays an important role in maintaining sarcomere structure, the interconnectors of Z-disks, involved in the formation of myofibrils to provide strength to the muscle fibers[15]. At the time of human endometrial stromal cell differentiation (decidualization), the expression level of desmin was significantly increased[16,17]. The concentration of desmin was considerably increased in the uterine muscle in the pregnant uterus at term[18].

Since the incidence of EP is dramatically increased with increasing mortality rate, there is an urgent need to develop an early diagnostic strategy to detect the EP condition. In the present study, we have examined the cellular changes in the fallopian tube using staining at four different stages of EP. Upon realizing the importance of the two markers, i.e., Bcl_2 and desmin, in addition to histological study, an attempt was made to evaluate these markers in the expression of ectopic tissue to predict the tubal rupture.

2. Materials and Methods

2.1 Sample Collection

The tissue samples were obtained from Ravindra Nath Tagore Medical College, Udaipur. The fallopian tube tissue samples obtained from women who had undergone tubal sterilization were used as control, and tissue samples from women who were diagnosed with tubal ectopic pregnancy, using ultrasound imaging, and

underwent salpingectomy, were taken as test samples. The test samples were categorized into four groups *viz.*,

- First ectopic pregnancy in primigravida
- First ectopic pregnancy in multigravida
- First ectopic pregnancy after abortion
- First ectopic pregnancy with carcinoma

2.2 Tissue Fixation

The tissue samples were fixed in 10% formaldehyde and sent to the histopathology laboratory. The tissue samples, after being assessed by a consultant gynecological pathologist, were embedded in paraffin wax, serially sectioned at 7 to 10 µm thickness in a rotary microtome, and stained with hematoxylin and eosin.

2.3 Hematoxylin and Eosin Staining

The sectioned tissues were immersed in Harris hematoxylin for 10 seconds and kept in running tap water until the water was clear for 30 seconds. Then the sections were stained in 1% aqueous eosin stain for 30 seconds and dehydrated in ascending grades of alcohol [50%, 70%, 80%, 95% (twice), and 100% (twice)] followed by clearing using xylene (3-4 times). Finally, the sections were mounted using a coverslip with DPX mounting medium.

2.4 Immunohistochemistry

One section of the tissue was treated with Bcl_2 antibody and another section of the same sample was treated with antibody for desmin. The sectioned tissues were deparaffinized in three changes of xylene and hydrated using a series of graded alcohol to water. The specimen was incubated for 5–10 minutes with hydrogen peroxide, quenched of any endogenous peroxidase activity, then incubated with monoclonal anti-human Bcl_2 or desmin antibody, followed by incubation with the PolyExcel Target Binder for 10 minutes, with a PolyExcel HRP labeled polymer for 10 minutes, and with 3,3'-diaminobenzidine (DAB) substrate-chromogen for 5 minutes which resulted in a brown-colored precipitate at the antigen site. The tissue sections were stained with hematoxylin. The slides were dehydrated through a graded series of alcohol, cleared in xylene, and mounted with a cover slip. The histological and immunocytochemical preparations were critically observed in a Carl Zeiss (Germany) research microscope and areas of interest were photographed.

3. Results

3.1 Critical Observation of Histoarchitecture

The histomorphological analysis of the fallopian tube revealed well-defined and extensive mucosal folds, a sandwich of smooth muscle, and a serosal coat. Microscopic examination of the control sample showed non-ciliated cells with granular cytoplasm and oval nucleus, ciliated cells with finely granular cytoplasm and round nuclei, and peg cells with dark nuclei. The smooth muscle cells interspersed with loose connective tissue were found normal (Figure 1).

The ectopic pregnancy in primigravida displayed occasional intraluminal chorionic villi (Figure 2). The appearance of a large round vacuole in the center of

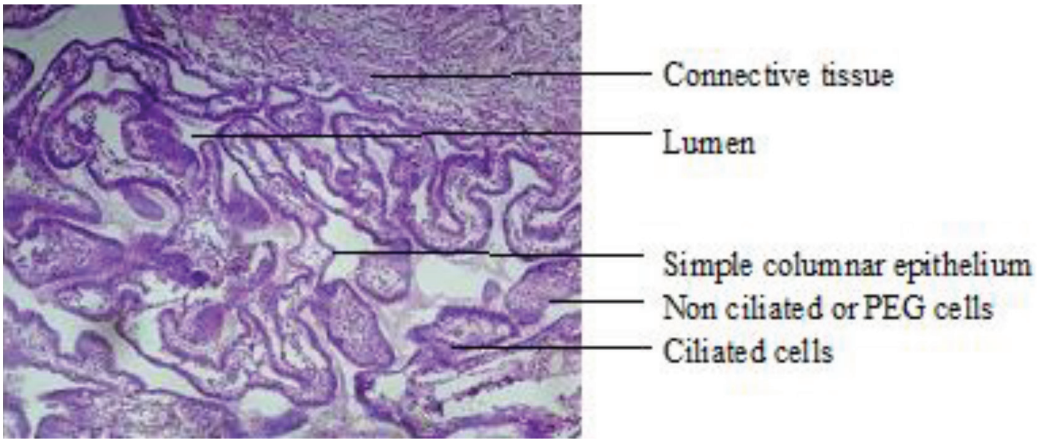

Figure 1. Photomicrograph of section of normal fallopian tube tissue collected immediately after sterilization (H and E).

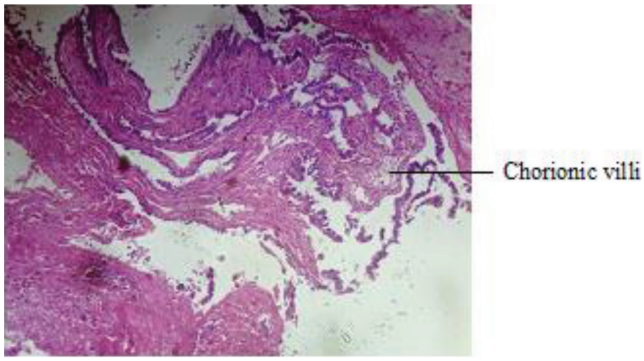

Figure 2. Photomicrograph showing chorionic villi in the ectopic pregnancy of primigravida (H and E).

Figure 3. Photomicrograph showing decidual change (De) in ectopic pregnancy of primigravida (H and E).

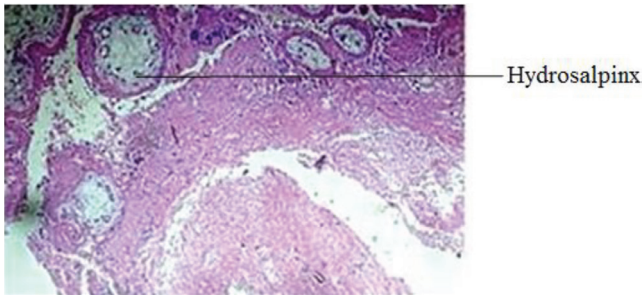

Figure 4 Photomicrograph showing hydrosalpinx in ectopic pregnancy of multigravida (H and E).

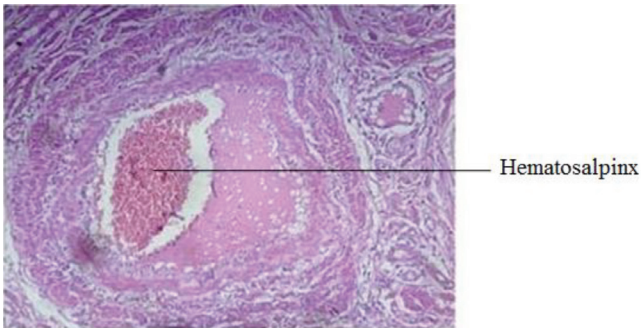

Figure 5. Photomicrograph showing hematosalpinx in ectopic pregnancy of multigravida (H and E).

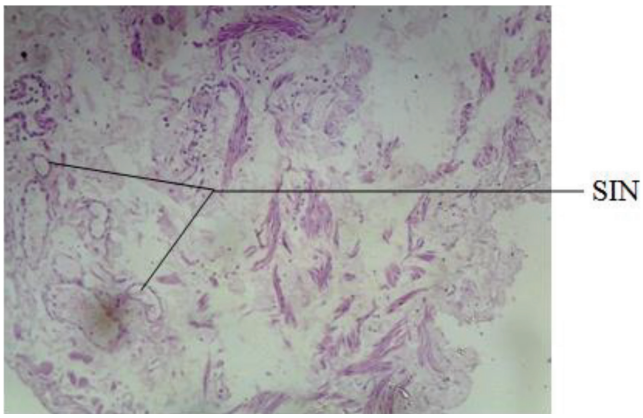

Figure 6. Photomicrograph of salpingitis isthmic nodosa (SIN) in ectopic pregnancy after abortion (H and E).

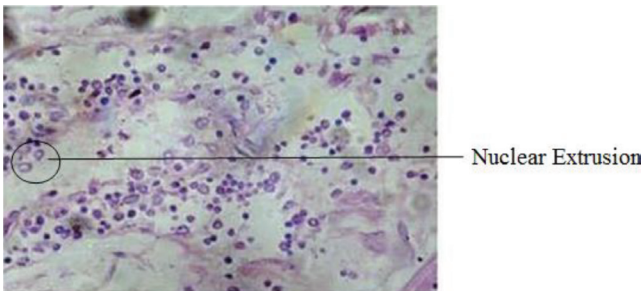

Figure 7. Photomicrograph showing nuclear extrusion (NE) in ectopic pregnancy after abortion (H and E).

the cell with displacement of the nucleus towards the periphery was observed. Extravillous trophoblast and no embryonic parts were found. Decidual change in lamina propria (Figure 3) appeared in a primigravida.

Mucosal folds were absent. Glandular cells were found as in the control sample. The nuclei of most of the epithelial cells had degenerated, and the tissue reflected a fibroid appearance. The fluid buildup in the fallopian tube showed hydrosalpinx (Figure 4) and the blood-filled fallopian tube showed hematosalpinx (Figure 5) in multigravida. Marked deciliation was also found subsequent to tubal ectopic pregnancy.

Salpingitis Isthmica Nodosa (SIN) was microscopically identified from the tubal epithelia-lined glands surrounded by hypertrophied smooth muscle cells (Figure 6). The out-pouching of the fallopian tube epithelium into the tubal wall displayed SIN in ectopic

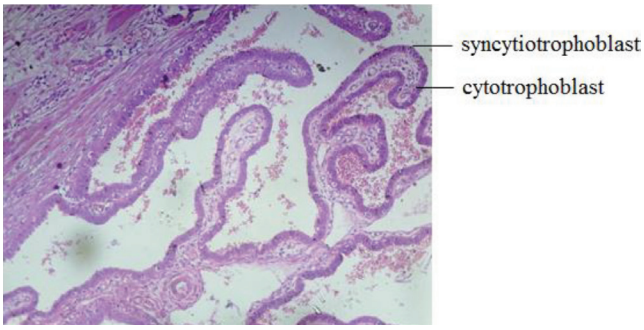

Figure 8. Photomicrograph showing cytotrophoblast and syncytiotrophoblast in ectopic pregnancy after abortion (H and E).

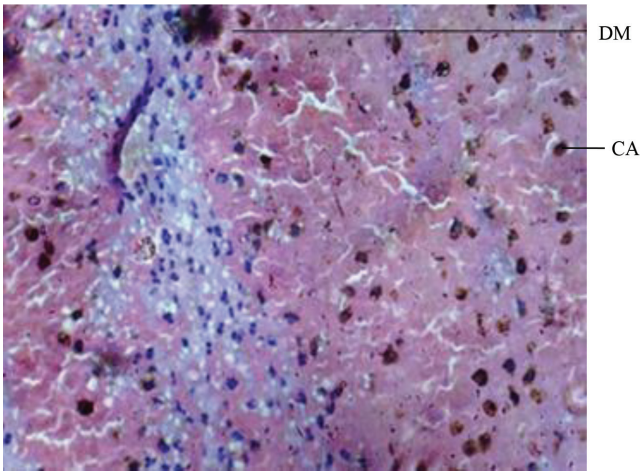

Figure 9. Photomicrograph showing dark masses (DM) and cytologia atypia (CA) in ectopic pregnancy with carcinoma (H and E).

pregnancy after abortion. Extrusion of the nucleus due to pyknosis was found. The lumen was completely obstructed, which showed the severity of this case (Figure 7). The cytotrophoblast was an inner layer of trophoblast formed of small round mononuclear cells with clear cell boundaries. The syncytiotrophoblasts were multinucleated giant cells (Figure 8).

The massive, destructive, single-to-multiple dark masses with hemorrhage and variable amounts of necrosis with striking cytologic atypia were observed (Figure 9). Characteristically, chorionic villi were absent.

3.2 Immunohistochemistry

Bcl_2 and desmin were immunopositive in all three categories except the control group. The control group did not express either Bcl_2 or desmin. Among the tested

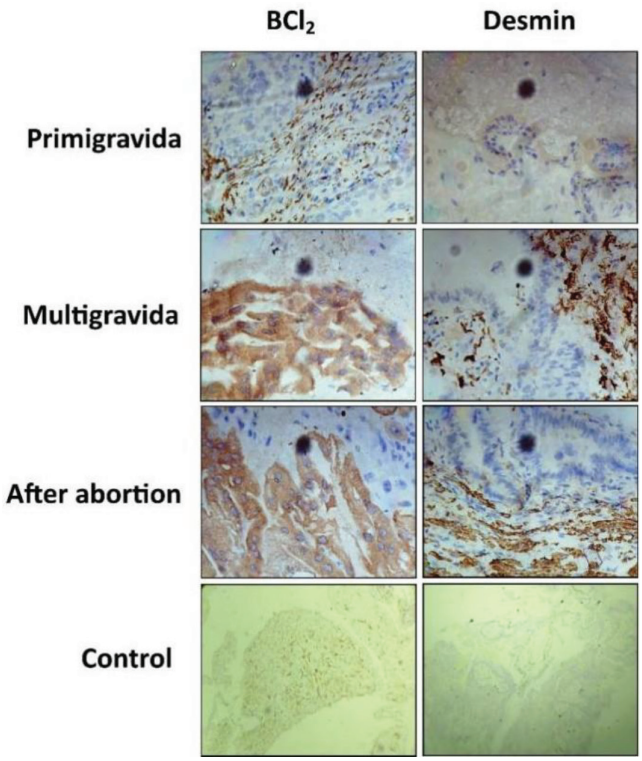

Figure 10. Immunohistochemical analysis of desmin and Bcl_2 expression.

groups, the ectopic pregnancy of primigravida displayed a low level of Bcl_2 and desmin. EP multigravida category had a higher level expression of both Bcl_2 and desmin. But in the case of the abortion group, the levels of Bcl_2 and desmin were much higher when compared to the other two groups (Figure 10).

4. Discussion

The fallopian tube is an elongated funnel-like organ, divided anatomically into infundibulum, ampulla, isthmus, and interstitial part. The wall of the tube consists of internal mucosa (endosalpinx), intermediate muscular layer (myosalpinx), and outer serosa which is continuous with the peritoneum of the broad ligament and uterus, the upper margin of which is the mesosalpinx. Mesothelium lines the serosal layer and the broad ligament. The muscular wall is formed of inner circular and outer longitudinal muscles. The tube is lined on the inner side by mucosa arranged in the shape of longitudinal branching folds known as plicae, which merge with the fimbriae. Our microscopic findings on control samples correlate with Hendrickson's (1997) finding that there are three

distinct cell types in the epithelium: secretory, ciliated, and intercalated (peg)[19].

The decidua at the implantation site involutes rapidly with degeneration of the chorionic villi, whereas distant decidua in the tubes, uterus, or elsewhere sometimes persists after degeneration of the trophoblast and completes involution of the local decidua[20]. Also, the absence of chorionic villi is a histological characteristic of choriocarcinoma. The thinning of the fallopian tube due to the trophoblastic infiltration, uncontrolled by decidual cells and the mechanical distension of the lumen of the tube due to the growth of the ovum result in early rupture of the tube. The observations in the present cases support this inference.

Osiakina and Schmatok (1933) reported decidual reaction in the tube in 21% of 21 tubal pregnancies independent of the presence of the implanted ovum[21]. Variations in the size and shape of ectopic decidual cells and vacuoles in the cytoplasm are common. Surely, the cytoplasmic vacuolization is an initial stage in decidual cell involution[22]. The present findings also show the decidual change in the lamina propria of the fallopian tube in the ectopic pregnancy of primigravida which happens as a response to high levels of estrogen and progesterone. The extravillous trophoblast may degenerate during these decidual changes. The high levels of estrogen and progesterone in the context of pregnancy induce mesenchymal fibroblast differentiation into decidual cells[23,24].

Studies showed the highest incidence of ectopic gestation in women with two to three children[25,26]. The multigravida shows the blockage in the fallopian tube with hematosalpinx and hydrosalpinx, which may be due to pelvic infection or sexually transmitted infection[27]. Repeated cycles of hemorrhage result in fibrosis. This can lead to retraction of the tube and formation of hydrosalpinx.

The loss of ciliated cells also influences the implantation of zygotes in ectopic sites. An important finding in our study is marked deciliation in primigravida. Ciliation and deciliation are continuous cyclical processes all through the menstrual cycle. Ciliation during the peri-ovulatory period, particularly in the fimbria, is the highest. Estrogen facilitates ciliation, whereas progesterone inhibits it. A great extent of deciliation occurs in ectopic pregnancy as the progesterone level goes down. Further, deciliation of the lining cells plays a significant role in the pathogenesis of tubal ectopic pregnancy[28]. Marked deciliation is sometimes seen subsequent to tubal ectopic pregnancy and in biopsies from women undergoing tubal surgery who later develop a tubal ectopic pregnancy[29].

Dahiya *et al.* (2011) reported an incidence of 6% salpingitis isthmic nodosa (SIN), while Homm *et al.* (1987) and Dubuisson *et al.* (1986) showed it to be 45.9% and 36.4%, respectively[30-32]. There was a significant association with SIN which is a known as an etiological factor for infertility and ectopic pregnancy. *Chlamydia trachomatis* is considered capable of producing silent salpingitis. According to Mårdh *et al.* (1977), there is an excess of *C. trachomatis* seropositivity among women with ectopic pregnancy[33]. Our study shows a remarkable association of ectopic pregnancy with SIN and a very marked association with acute salpingitis in women with ectopic pregnancy after abortion. These findings suggest that inflammation is an indicative contribution of the causation of ectopics. Majhi *et al.* (2007) noted ectopic pregnancy in patients with a history of tubectomy (14.4%) and abortion (26.1%)[34].

A high level of desmin was observed during decidualization[35]. The specific expression of structural protein desmin was observed as a marker protein for the EP condition. The expression of desmin was also observed during the decidualization of stromal cells in mouse[36] and rats[37]. Bcl_2 is a proliferation marker of trophoblast during pregnancy of humans[38]. Similarly, high proliferative activity brought about by Bcl_2 expression in syncytiotrophoblast might have an impact on tubal rupture[14]. The syncytiotrophoblast produces proteolytic enzymes which are essential for the blastula to get implanted. Bcl_2 expression has been observed in intrauterine[39] and ectopic pregnancies[14].

Thus, the present study is a preliminary attempt to find specific cellular protein biomarkers in relation to ectopic pregnancy adopting an immunohistochemical technique. The outcome of the study explains that Bcl_2 and desmin are overexpressed in the causation of ectopic pregnancy. Further protein expression studies among EP patients might reveal the potential early diagnostic biomarker for the prediction of EP.

5. Acknowledgments

The authors thank R.N.T. Medical College, Udaipur, India, for access to the women patients who were part of this study, and the sample collection. GA is grateful to INTI International University, Malaysia, for the award of Research Fellowship.

6. References

1. Sokol AI, Sokol ER. General gynecology: the requisites in obstetrics and gynecology. Elsevier Health Sciences; 2007. https://doi.org/10.1016/B978-032303247-6.10011-5
2. Tahmina S, Daniel M, Solomon P. Clinical analysis of ectopic pregnancies in a tertiary care center in Southern India: a six-year retrospective study. Journal of Clinical and Diagnostic Research: JCDR. 2016; 10(10):QC13. https://doi.org/10.7860/JCDR/2016/21925.8718
3. Casadio P, Youssef A, Arena A, Gamal N, Pilu G, Seracchioli R. Increased rate of ruptured ectopic pregnancy in COVID-19 pandemic: analysis from the North of Italy. Ultrasound in Obstetrics and Gynecology. 2020; 56(2):289. https://doi.org/10.1002/uog.22126
4. DeCherney AH, Agel WO, Yauger BJ. Ectopic Pregnancy. In: Dadelszen PV, Editor. The Global Library of Woman's Medicine. DOI 10.3843/GLOWM.10047
5. Mann LM, Kreisel K, Llata E, Hong J, Torrone EA. Trends in ectopic pregnancy diagnoses in United States emergency departments, 2006–2013. Maternal and Child Health Journal. 2020; 24:213-21. https://doi.org/10.1007/s10995-019-02842-0
6. Barnhart KT. Ectopic pregnancy. New England Journal of Medicine. 2009; 361(4):379-87. https://doi.org/10.1056/NEJMcp0810384
7. Ankum WM, Mol BW, Van der Veen F, Bossuyt PM. Risk factors for ectopic pregnancy: a meta-analysis. Fertility and Sterility. 1996; 65(6):1093-9. https://doi.org/10.1016/S0015-0282(16)58320-4
8. Li HW, Liao SB, Chiu PC, Tam WW, Ho JC, Ng EH, Ho PC, Yeung WS, Tang F, Wai Sum O. Expression of adrenomedullin in the human oviduct, its regulation by the hormonal cycle and contact with spermatozoa, and its effect on the ciliary beat frequency of the oviductal epithelium. The Journal of Clinical Endocrinology and Metabolism. 2010; 95(9):E18-25. https://doi.org/10.1210/jc.2010-0273
9. Wang X, Lee CL, Vijayan M, Yeung WS, Ng EH, Wang X, Wai-Sum O, Li RH, Zhang Y, Chiu PC. Adrenomedullin insufficiency alters macrophage activities in fallopian tube: a pathophysiologic explanation of tubal ectopic pregnancy. Mucosal Immunology. 2020; 13(5):743-52 https://doi.org/10.1038/s41385-020-0278-6
10. Pal A, Gupta KB, Sarin R. A study of ectopic pregnancy and high-risk factors in Himachal Pradesh. Journal of the Indian Medical Association. 1996; 94(5):172-3. PMID: 8855569
11. Wei P, Jin X, Zhang XS, Hu ZY, Han CS, Liu YX. Expression of Bcl-2 and p53 at the fetal-maternal interface of rhesus monkey. Reproductive Biology and Endocrinology. 2005; 3(1):1-0. https://doi.org/10.1186/1477-7827-3-4
12. Soni S, Rath G, Prasad CP, Salhan S, Saxena S, Jain AK. Apoptosis and Bcl-2 protein expression in human placenta over the course of normal pregnancy. Anatomia, Histologia, Embryologia. 2010; 39(5):426-31. https://doi.org/10.1111/j.1439-0264.2010.01012.x
13. Lea RG, Al-Sharekh N, Tulppala M, Critchley HO. The immunolocalization of bcl-2 at the maternal-fetal interface in healthy and failing pregnancies. Human reproduction (Oxford, England). 1997; 12(1):153-8. https://doi.org/10.1093/humrep/12.1.153
14. Kucera E, König F, Tangl S, Grosschmidt K, Kainz C, Sliutz G. Bcl-2 expression as a novel immunohistochemical marker for ruptured tubal ectopic pregnancy. Human Reproduction. 2001; 16(6):1286-90. https://doi.org/10.1093/humrep/16.6.1286
15. Hnia K, Ramspacher C, Vermot J, Laporte J. Desmin in muscle and associated diseases: beyond the structural function. Cell and Tissue Research. 2015; 360:591-608. https://doi.org/10.1007/s00441-014-2016-4
16. Glasser SR, Lampelo S, Munir MI, Julian J. Expression of desmin, laminin, and fibronectin during in situ differentiation (decidualization) of rat uterine stromal cells. Differentiation. 1987; 35(2):132-42. https://doi.org/10.1111/j.1432-0436.1987.tb00161.x
17. Can A, Tekeliioğlu M, Baltaci A. Expression of desmin and dimentin intermediate filaments in human decidual cells during first-trimester pregnancy. Placenta. 1995; 16(3):261-75. https://doi.org/10.1016/0143-4004(95)90113-2
18. Leoni P, Carli F, Halliday D. Intermediate filaments in smooth muscle from pregnant and non-pregnant human uterus. Biochemical Journal. 1990; 269(1):31-4. https://doi.org/10.1042/bj2690031
19. Hendrickson MR. Normal histology of the uterus and fallopian tube. In Histology for Pathologists. 1997; 879-928. ISBN:0397517181 9780397517183
20. Kline BS. The decidual reaction in extrauterine pregnancy. American Journal of Obstetrics and Gynecology. 1929; 17(1):42-8. https://doi.org/10.1016/S0002-9378(29)90579-2
21. Osiakina AJ, Schmatok KD. über die Dezidualreaktion der Tube bei intrauteriner und Tubenschwangerschaft und ihre Bedeutung für die ätiologie der letzteren. Gynecologic and Obstetric Investigation. 1933; 94(6):329-37. https://doi.org/10.1159/000310513
22. Hofbauer J. Decidual formation on the peritoneal surface of the gravid uterus. American Journal of Obstetrics and Gynecology. 1929; 17(5):603-12. https://doi.org/10.1016/S0002-9378(29)90977-7
23. Kim JH, Nam KH, Kwon JY, Kim YH, Park YW. A case of ovarian deciduous in pregnancy. Korean Journal of Obstetrics and Gynecology. 2011; 54(7):373-76. https://doi.org/10.5468/KJOG.2011.54.7.373

24. Markou GA, Goubin-Versini I, Carbunaru OM, Karatzios C, Muray JM, Fysekidis M. Macroscopic deciduous in pregnancy is finally a common entity. European Journal of Obstetrics and Gynecology and Reproductive Biology. 2016; 197:54-8. https://doi.org/10.1016/j.ejogrb.2015.11.036
25. Hlavin GE, Ladocsi LT, Breen JL. Ectopic pregnancy: an analysis of 153 patients. International Journal of Gynecology and Obstetrics. 1978; 16(1):42-7. https://doi.org/10.1002/j.1879-3479.1978.tb00390.x
26. DeCherney AH, Minkin MJ, Spangler S. Contemporary management of ectopic pregnancy. The Journal of Reproductive Medicine. 1981; 26(10):519-23. PMID: 6458698
27. Foti PV, Ognibene N, Spadola S, Caltabiano R, Farina R, Palmucci S, Milone P, Ettorre GC. Non-neoplastic diseases of the fallopian tube: MR imaging with emphasis on diffusion-weighted imaging. Insights into Imaging. 2016; 7:311-27. https://doi.org/10.1007/s13244-016-0484-7
28. Vasquez G, Winston RM, Brosens IA. Tubal mucosa and ectopic pregnancy. BJOG: An International Journal of Obstetrics and Gynaecology. 1983; 90(5):468-74. https://doi.org/10.1111/j.1471-0528.1983.tb08946.x
29. Vasquez G, Boeckx W, Brosens I. Infertility: Prospective study of tubal mucosal lesions and fertility in hydrosalpinges. Human Reproduction. 1995; 10(5):1075-8. https://doi.org/10.1093/oxfordjournals.humrep.a136097
30. Dahiya N, Singh S, Kalra R, Sen R, Kumar S. Histopathological changes associated with ectopic tubal pregnancy. International Journal of Pharmaceutical Sciences and Research. 2011; 2(4):929. https://doi.org/10.13040/IJPSR.0975-8232.2(4).929-33
31. Homm RJ, Holtz G, Garvin AJ. Isthmic ectopic pregnancy and salpingitis isthmic nodosa. Fertility and Sterility. 1987; 48(5):756-60. https://doi.org/10.1016/S0015-0282(16)59525-9
32. Dubuisson JB, Aubriot FX, Cardone V, Vacher-Lavenu MC. Tubal causes of ectopic pregnancy. Fertility and Sterility. 1986; 46(5):970-2. https://doi.org/10.1016/S0015-0282(16)49846-8
33. Mårdh PA, Ripa T, Svensson L, Weström L. Chlamydia trachomatis infection in patients with acute salpingitis. New England Journal of Medicine. 1977; 296(24):1377-9. https://doi.org/10.1056/NEJM197706162962403
34. Majhi AK, Roy N, Karmakar KS, Banerjee PK. Ectopic pregnancy--an analysis of 180 cases. Journal of the Indian Medical Association. 2007; 105(6):308-10. PMID: 18232175
35. Halperin R, Fleminger G, Kraicer PF, Hadas E. Desmin as an immunochemical marker of human decidual cells and its expression in menstrual fluid. Human Reproduction. 1991; 6(2):186-9. https://doi.org/10.1093/oxfordjournals.humrep.a137302
36. Zorn TM, de Oliveira SF, Abrahamsohn PA. Organization of intermediate filaments and their association with collagen-containing phagosomes in mouse decidual cells. Journal of Structural Biology. 1990; 103(1):23-33. https://doi.org/10.1016/1047-8477(90)90082-N
37. Glasser SR, Julian J. Intermediate filaments of the midgestation rat trophoblast giant cell. Developmental Biology. 1986; 113(2):356-63. https://doi.org/10.1016/0012-1606(86)90170-3
38. Kim CJ, Choe YJ, Yoon BH, Kim CW, Chi JG. Patterns of bcl-2 expression in placenta. Pathology-Research and Practice. 1995; 191(12):1239-44. https://doi.org/10.1016/S0344-0338(11)81132-5
39. Sakuragi N, Matsuo H, Coukos G, Furth EE, Bronner MP, VanArsdale CM, Krajewsky S, Reed JC, Strauss JF. Differentiation-dependent expression of the BCL-2 proto-oncogene in the human trophoblast lineage. Journal of the Society for Gynecologic Investigation. 1994; 1(2):164-72. https://doi.org/10.1177/107155769400100212