GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 11 (332) ноябрь 2022

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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Содержание:

GEORGIAN MEDICAL NEWS
No 11 (332) 2022

FREQUENCY OF PLACENTA ACCRETA SPECTRUM DISORDERS IN NINEVAH PROVINCE HOSPITALS: A HISTOLOGIC STUDY

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Abstract.

Objectives: To provide a view on the frequency, and the risk factors of placenta accreta spectrum disorders (PAS) in Nineveh Province, and to assess the morphological alterations associated with these disorders.

Subjects and methods: A prospective and retrospective cross-sectional study was carried out on paraffinized blocks of 19 females, with gestational age ≥32 weeks, presented with peripartum haemorrhage and subjected to emergency hysterectomy at Maternity Teaching Hospitals, Nineveh Province, North of Iraq. Clinical data, including the mother's age and obstetrics history, were recorded when available. All cases were examined for the presence or absence of histological invasion of placentas supported by immunohistochemistry.

Results: The mean age of cases was 34.4 ±1.6 years by the dominance of the fourth decade. The mean gestational age at the time of diagnosis was 35.6±0.8 weeks. The PAS frequency was increasing and reaching up to 1.18 per 1000 live birth. About 60% of the cases gave a history of previous Cesarean section with or without a concomitant placenta previa. According to light microscopic examination, placenta accreta spectrum disorders were identified in 12(63.1%) cases. The immune expression of cytokeratin was significantly correlated with placental invasion, (p=0.001).

Conclusion: The present study reveals an increase in the frequency of abnormal placentation in Nineveh Province. These disorders have well-known predisposing factors. The histo-pathological findings, other than interface decidual loss, may explain the abnormality in placental tissue implantation.

Key words. Placenta accreta, hysterectomy, immunohistochemistry.

Introduction.

Among the critical issues that are threatening the life of females -associated with pregnancy- are placenta accreta spectrum disorders (PAS), which were previously determined as morbidly disciple placenta [1]. It refers to a placental attachment abnormality to the uterine wall [1]. The raised frequency of such disorder was associated with an increase in morbidity and fatality for both mothers and fetuses. Many problems were associated with PAS disorders including emergency hysterectomy, urinary tract injury, transfusion of blood, septicemia, and intensive care unit admission [2].

Several reports have tried to determine the exact frequency of such disorders in different societies [1]. The PAS disorders are presented by variable levels of placental adhesion and assault into the uterus and/or adjacent tissues (placenta accreta, increate, or percreta) [3].

Till now, these disorders remain of unknown pathogenesis [1,3]. It has been proposed that there is a decidual mal-development besides the invasion by intermediate trophoblasts due to a history of instrumentation and uterine injury [4-6]. Several risk factors were correlated with abnormal implantation including the increased rate of cesarean section, pre-eclampsia, history of in vitro fertilization, previous dilation, and curettage, multiparity and placenta previa (PP) [4,6].

The abnormal placental implantation may be suspected clinically, however, it's confirmed by histopathological examination. Microscopically, there are three grades of PAS disorders as follow: placenta percreta in case of the penetration of chorionic villi into the uterine serosa, placenta increta occurs when there is an invasion into the myometrium, then, and finally the placenta accreta in case of close contact of chorionic villi with the myometrium [7]. Immunohistochemistry can assist in the evaluation of extravillous trophoblast myometrial infiltration using specific markers [8].

The incidence of PAS disorders is increasing worldwide [8]. Therefore, there is a need for the precise detection of the PAS patients in order to manage them properly and subsequent better outcomes [9,10].

To our knowledge, this study is the first report on PAS disorders in our locality that aims to highlight the frequency of PAS abnormality, comprehend its various risk factors, and assess the morphological changes associated with these disorders in Maternity -Teaching Hospitals in Nineveh.

Subjects and Methods.

This perspective and the retrospective cross-sectional study was analyzed randomly sampled paraffinized blocks and slides of 19 pregnant females with gestational age ≥ 32 weeks who presented with peripartum haemorrhage and were subjected to an emergency hysterectomy. They were admitted to, AL-Batool, Al-Salam, and Al-Khansaa Maternity- Teaching Hospitals, Province (of Nineveh), North of Iraq. Permission was secured from each patient whose information was dispensed in this work. The study was endorsed by the Ethical Committee of the Medical Researches (at Medicine College, Mosul's University). (UOM/COM/MREC/21-22(41)).

For the hysterectomy cases, uterine tissues with the attached placenta were identified from hospitals' recorded data. The related blocks of paraffin and slides were collected along with the histo-pathological reports.

Hysterectomies due to uterine pathologies other than peripartum haemorrhage were excluded. Other information including the mother's age, the parity status, the presence, or absence of placenta previa, previous cesarean sections, and previous dilation and curettage were also recorded when available.

Gross evaluation: The uterus with the attached placenta was initially examined for any hematoma, bulging and, rupture of the external surface. The suspicious areas of rupture were

inked. Following the guides of Dannheim K et al., in uterine specimen processing, all specimens were fixed in 10% formalin overnight [11]. From suspected zones of myometrial invasion, multiple sections were obtained. Further sections from the lower uterine segment were taken [12]. Blocks of paraffin were 4microns sectioned using a microtome and stained routinely with hematoxylin and eosin(HE) to assess the sections using a light microscope (Optika, Italy) [13-17]. Tabulation of data was done in Microsoft Excel using the percentages for diagnosis. Unstained sections were saved for immunohistochemistry when required.

Histopathological evaluation: The depth of extravillous trophoblasts' myometrial invasion was microscopically evaluated. Immunohistochemistry for cytokeratin (AE1/AE3) was further used as a diagnostic aid for histopathological assessment [18]. Two groups of cases were recorded in this work: Group I; placenta accreta spectrum disorders, which were further classified into 3 subtypes, conforming to the rung of invasion -of placentas- into the myometrium, as follows: when the decidua was absent among the placental villi and myometrium accreta was considered, increta was recorded when the invasion of extravillous trophoblasts into the myometrium was deeper, while full invading through the myometrium was regarded a case of percreta [19], Figure 1 and Group II; Placenta previa/low lying placenta without PAS disorders or extravillous trophoblasts myometrial invasion.

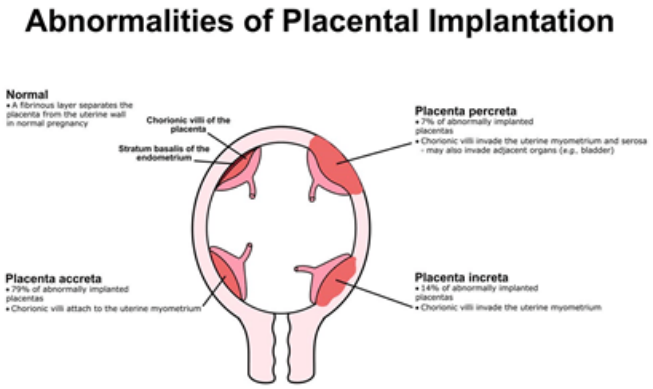

Figure 1. *Abnormalities of placental implantation[20].*

Immunohistochemicalevaluation: Theimmunohistochemical procedure was performed using Pan Cytokeratin (CK) Type I/ II Antibody Cocktail (Catalog # MA5-13156; clone AE1/ AE3, dilution 1:50, Thermo Fisher Scientific, USA), and CD3 Monoclonal Antibody (MA5-14482; clone EP449E, dilution 1:125, Thermo Fisher Scientific, USA), to stain EVT and T lymphocytes, respectively. Briefly, antigen retrieval was performed using sodium citrate (pH 6.0), to expose target proteins, microwaved for 15 min. later, tissues were blocked in 3% H2O2 for 15 min at room temperature, washed, and then probed with the above-mentioned primary antibodies. The detection system was an HRP-conjugated secondary antibody followed by colourimetric detection using a DAB kit. Sections were counterstained with hematoxylin. The positive immune expression of brown staining of the intermediate trophoblasts and T lymphocytes was noticed in the cytoplasm, and the nucleus/cell membrane, respectively [18]. All slides, and blocks were reviewed blindly by two pathologists.

Statistical analysis.

Data were collected and analyzed by the Statistical SPSS version 18. The quantitative data were presented as mean±SD. Descriptive analysis has been used -chi-squared test-, the value of P was considered marked(significant) if it's less than 0.05.

Results.

Throughout the study period, 19 cases of emergency hysterectomy due to severe uncontrolled peripartum haemorrhage were conducted in Maternity Teaching Hospitals in Nineveh Province. Placenta accreta spectrum disorders were diagnosed in 12 (63.1%) specimens, while 7 (36.9%) cases revealed placenta previa/ low lying placenta with no features of PAS disorders.

The baseline characteristics of patients who presented with peripartum haemorrhage are listed in Table (1). Briefly, the mean age of the PAS patients was 34.4±1.6 years, ranging (from 23-39), by the dominance of the fourth decade. Eight (66.7%) women had advanced maternal age (> 35 years). The mean gestational age on the diagnosis time was 35.6±0.8 weeks. About 75% of the patients were multiparous, ranging (from 1-6). Eleven cases reveal placenta previa, 4(44.4%) of them were further involved by PAS disorder (placenta accreta subtype). About 60% of the cases given a history of previous Cesarean section (CS) Range (1-3).

The histopathological features of PAS disorders and PP/low-lying placenta without PAS, among women with peripartum haemorrhage, are illustrated in Table (2).

The uterine specimens via the gross assessment exhibited abnormally attached placental zones enrolling the placental uterine plate up to 25%.

The diagnosis depended on HE-stained tissue sections. Placental normal implantation site reveals the presence of decidual cells(small, rounded cells with the distinct cell membrane, light eosinophilic cytoplasm, and single vesicular nuclei), and the extravillous trophoblast EVT (large polygonal to spindle cells with about amphophilic cytoplasm and large hyperchromatic nuclei), illustrated in Figure (2).

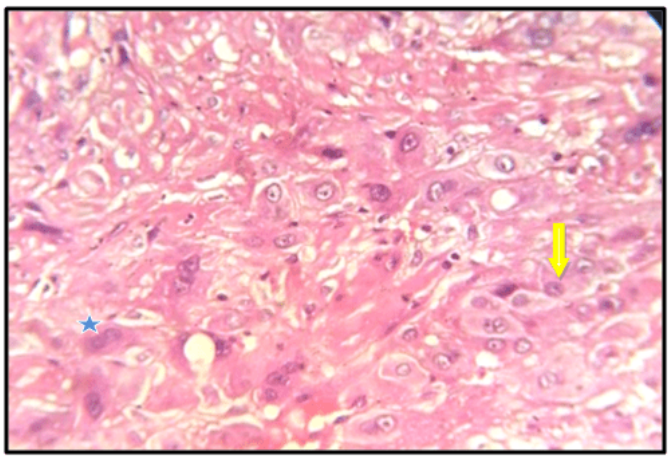

Figure 2. *Placental normal implantational site: Presence of both decidual cells (arrow), and the extravilloustrophoblast (star), (H&E; x10).*

Table 1. *Baseline characteristics of women who presented with peripartum haemorrhage among the two groups.*

Variables	Group I: PAS disorders (n=12)	Group II: PP/low-lying placenta only (n=7)
Age, mean± SD	34.4±1.6	28±0.8
Gestational age, mean± SD	35.6±0.8	36±1.2
Parity status Nulliparous/Multiparous	3/9	3/4
Presence of placenta previa (Yes/No)	4/8	7/0
Previous caesarian section (Yes/No)	8/4	2/5
Previous dilation and curettage (Yes/No)	3/9	0/7

** SD = standard deviation, PAS= placenta accreta spectrum, PP= placenta previa.*

Table 2. *The histopathological features of PAS disorders and PP/ low lying placenta without PAS disorders among women with peripartum haemorrhage.*

Variables No.	Group I: PAS disorder		Group II: PP/low-lying placenta only (n=7)	*P* value
	Accreta (n=10)	Increta (n=2)		
Myometrial scaring	6(60%)	2(100%)	2(0%)	0.027
Excessive fibrin deposits	8(80%)	1(50%)	0(0%)	0.000
Extravillous trophoblast invasion	8(80 %)	2(100%)	1(14.2%)	0.001
Inflammatory T lymphocytes	5(50%)	2(100%)	4(57.1)	0.454

** PAS= placenta accreta spectrum, PP= placenta previa, Differences are critical statistically when p is underneath 0.05.*

Features typical of PAS disorders, such as the nonexistence of a decidual layer in between the myometrial fibres and chorionic villi, were identified by both pathologists with high concordance between them (P = 0.000). According to light microscopic examination, placenta accreta was identified in 10 (83.3%) cases, while features of the placenta increate were diagnosed in the remaining 2 (16.7%) cases cross roading -at a minimum-50% of the uterine wall's thickness. No case of placenta percreta was identified in the current work.

A microscopic myometrial scaring was evident in 8 (66.6%) cases of PAS. Six (75%) PAS cases gave a history of CS and, 2 (75%) with previous uterine instrumentation. While in PP cases only two cases had a history of CS (28.5%). In comparison to placenta previa specimens, 9 (75%) PAS involved uterine tissues showed chorionic villi frequently surrounded by extensive fibrin deposition (0.5-1.5mm thickness) with no evidence of such deposits in PP cases without PAS, (Figure 3).

The fetal-maternal interface significantly revealed EVT deeply invading the myometrium, with thinning of the underlying uterine wall predominantly in increta cases, a feature not reported in PP specimens without PAS(P<000.1). Those invading extravillous trophoblasts were easily identified and qualitatively assessed when highlighted with CK, (Figure 4). In PAS, the placental myometrial interface was often more infiltrated by chronic inflammatory cells with a predominance of T lymphocytes identified by the CD3 marker. A perivascular accentuation of CD3 T lymphocytes was present within the myometrium. However, no marked difference was detected between the two groups, apart from a lower density in the PP/ low lying placental cases (P =0.14), (Figure 5).

Discussion.

The spectrum of placenta accreta disorders is a state of anomalous placental implantation. It is a major cause of severe maternal and fetal morbidity and mortality worldwide because the placenta does not spontaneously detach and leads to severe haemorrhage, often ended by an emergency hysterectomy, and intensive care unit (ICU) admission [21]. Therefore, antenatal screening for PAS is required to identify those high-risk cases. This is usually established through imaging studies using Ultrasonography (US), and magnetic resonance imaging (MRI) [22,23].

Recent studies showed that 50% to two/thirds of PAS disorders cases could be diagnosed at the time of delivery [24]. However, in our study, no cases were antenatally suspected and or diagnosed with PAS disorders. The first diagnosis was made at the time of labor and confirmed by microscopic examination of hysterectomy specimens.

Further, several serum biomarkers might help in the antenatal suspension of PAS disorders like alpha-fetoprotein (AFP), and human chorionic gonadotropin (HCG). However, PAS definite diagnosis is through histopathological examination by the absence of a decidual zone between the chorionic villi and myometrial fibres in hysterectomies [25].

Although imaging studies are important, the absence of US and/ or MRI findings do not exclude the diagnosis of PAS; thus, recognition of clinical risk factors is required as a predictor of the placenta accreta spectrum [26].

This study revealed an increase in the incidence of PAS in our locality from 0.07 per 1000 live birth in 2018 to 0.4 per 1000 live deliveries in 2019, reaching up to 1.18 per 1000 live birth in 2020. Those findings are parallel to the reported overall increase

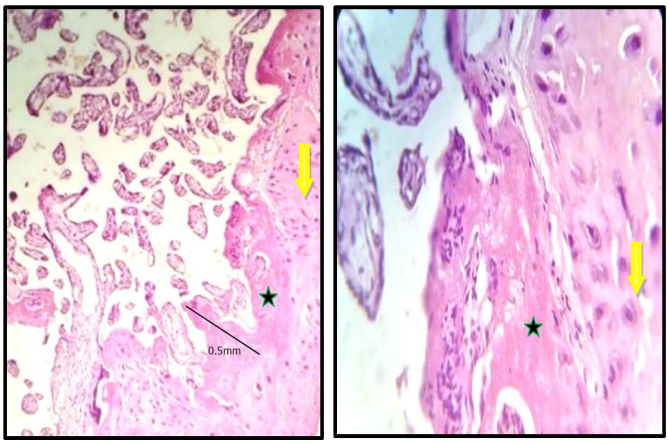

Figure 3. *Placenta accreta spectrum disorders. Loss of decidual layer between villi and myometrium, excessive fibrin layer(star), and extravillous trophoblasts at the placental myometrial interface (arrow). (H& E; ×40 and ×400).*

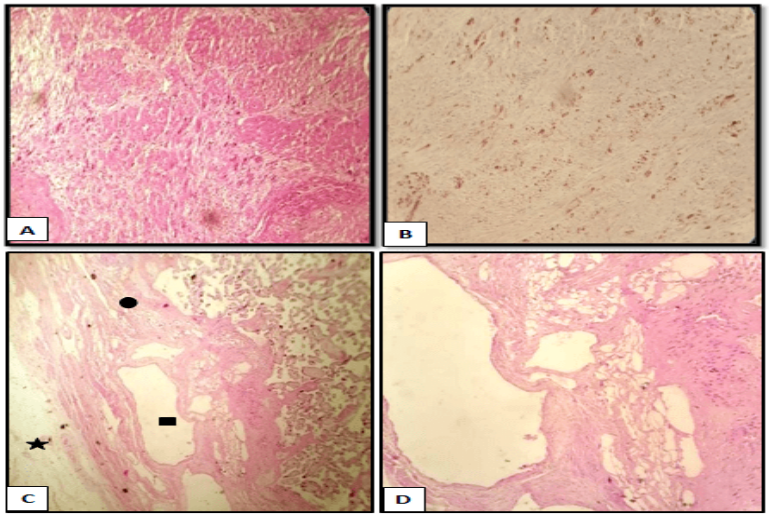

Figure 4. *Placental myometrial interface in PAS disorders. A and B; EVT deeply invading the myometrium, highlighted by CK expression(brown). (H& E; ×40 and IHC ×100). C and D; Chorionic villi infiltration with a very thin layer of the myometrium, is noticed near the perimetrium fat(star). the interface shows mal-perfusion and dilation of myometrial vessels(square). (H& E; ×40 and ×100).*

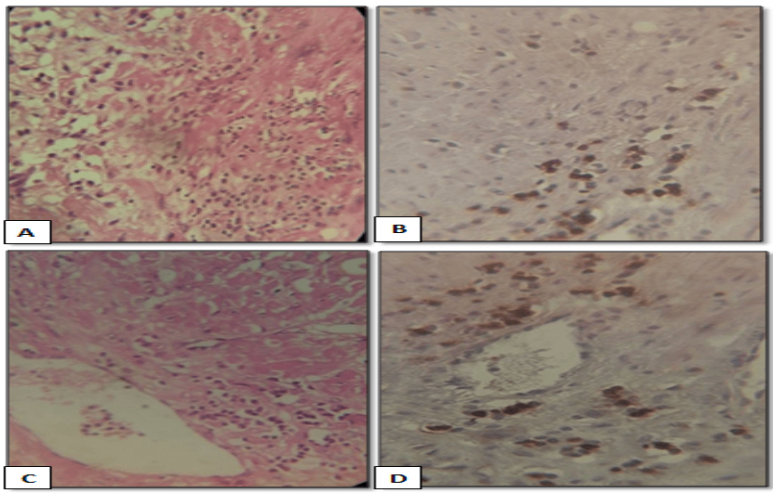

Figure 5. *Chronic inflammatory cell infiltrate in placenta accreta spectrum disorders. A and B; Inflammation within the myometrial fibres with the predominance of CD3 positive T lymphocytes (H&E.×100 and IHC x400). C and D; Perivascular accentuation of T lymphocytes within the myometrium. (H&E×100 and IHC x400).*

in the incidence of the disease in the world [27]. However, a study of Carusi DA, showed that the precise incidence of PAS disorders is difficult to discover, however, it is reaching 1 per 1000 deliveries and this will be steadily more and more with the raising of the threatening factors [28]. In fact, in this work, the sample increases from one diagnosed case in 2018, and four cases in 2019 to seven cases in 2020. The rapid increase in the trend of Cesarean sections in our locality seems to be one of the main predisposing factors, a finding similar to that recorded by Higgins MF and his colleagues [29]. Further, 33.3% of our cases of PAS disorders with prior cesarean sections combined with placenta previa were also recorded, in keeping with Goh WA and Zalud I [30]. It has been found that the existence of placenta previa with a history of Cesarean sections may possess a sixty-one percent increase in the risk of PAS disorders [30]. This parallel relation between the increase of PAS disorders and obstetrics history of previous cesarean sections and placenta previa may be attributed to the hypothesis that a localized uterine injury may result in a locally abnormal decasualization/scarring and aberrant placental adherence in the next pregnancies [31].

On the other hand, we noticed an increase in the incidence of PAS disorders in women >34 years old and with multiparity, a result agreed with those of Fitzpatrick KE et al., and Farquhar CM et al., who reported that older maternal age and multiparity were high-risk factors for PAS disorders [32,33]. Further, similar findings were reached by other workers [34,35].

Microscopically, all PAS specimens reveal an impaired decidualization (at least focally) at the fetal-maternal interface when compared with placenta previa cases, a finding noticed by several other studies [25,36]. Founds SA et al., reported that this recent impairment was suggested to be the cause of placenta accreta recurrent abortion, and preeclampsia [36].

Nearly 75% of cases of invasive placentation reveal an area of myometrial scaring nearby the EVT invasion, a finding that might be supported by the concept of previous localized uterine injury [27]. In a study by Jauniaux E et al., such microscopic myometrial scaring was evident in all his forty cases [19].

The current study revealed evidence of dense fibrin deposits in PAS cases. This finding might explain the failure of parts of the physiological zone of the separation of the placenta from the uterine wall. The deposits were also reported in a recent study [19].

The PAS cases enrolled in this work, mainly increta specimens, an extensive invasion of extravillous trophoblast was recorded in between the myometrial fibres, a finding agreed by Tantbirojn P and his colleagues [37]. This ETV infiltration is nicely highlighted by cytokeratin stain. In our opinion, immunohistochemistry could assist in the detection of the level of EVT myometrial invasion, but it is not necessary for it. Analysis of this work suggested that the absence of decidual cells at the implantation interface besides the presence of uterine scarification might give EVT higher access to the deep myometrium [37]

On the other hand, this work revealed that at the implantation zone, there is an abnormally dilated, empty, thin-walled myometrial vasculature was identified in PAS cases. This reduced vascular remodeling was also reported in other studies [38,39]. However, Hecht JL et al., reported no difference between the vascular alterations of the myometrium in PAS disorders and normal gestation [39].

In this study, PAS placental myometrial interface revealed heavy immune cell infiltrations, with perivascular myometrial condensation of predominantly T lymphocytes which stained by CD3 marker. Although this finding has no statistical significance, it perhaps highlights another PAS microscopic changes [39].

The inflammatory cells seem to have many contributions in both normal implantation and PAS invading sites, especially through keeping immune tolerance between fetus and mother.44 However, future studies are required to understand the molecular biology of different types of inflammatory cells in PAS disorder. In parallel with our findings, Warshak CR et al. noticed that cases of PAS exhibited features of prominent immune cells mainly in those with a history of smoking as a risk factor [40]. However, the history of smoking was inconclusive in our data.

The main limitation of the study is the small sample size, however the strength of the work relied on the microscopic findings. We suggest that, besides the hypothesis of decidual defect, the presence of dense fibrinoid deposits, extensive EVT invasion, and heavy perivascular T lymphocytes at the interface might give a further clarification or explanation for such abnormal placental adhesions. Further studies are required to confirm our suggestions.

Conclusions.

The present study reveals an increase in the frequency of abnormal placentation in Nineveh Province. These disorders have well-known predisposing factors. The histo-pathological findings, other than interface decidual loss, may explain the abnormality in placental tissue implantation.

Acknowledgement.

Thanks to all females who participate with their data to accomplish this work.

Conflict of interests. None.

Funding. None.

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