

Biochem Cell Biol., 30, 1998, 1285-90.

25. Radaelli, T. et al. Gestational diabetes induces placental genes for chronic stress and inflammatory pathways. *Diabetes*, 52, 2003, 2951-8.

26. Retnakaran, R. et al. Pre-gravid physical activity and reduced risk of glucose intolerance in pregnancy: the role of insulin sensitivity. *Clin Endocrinol.*, 70, 2009, 615-22.

615-22.

27. Veena, S.R. et al. Glucose tolerance and insulin resistance in Indian children: relationship to infant feeding pattern. *Diabetologia.*, 54, 2011, 2533-7.

28. Zhang, Y. et al. Positional cloning of the mouse obese gene and its human homologue. *Nature.*, 372, 1994, 425-32.

СЛБ ПРИ ЕНДОМЕТРИАЛЕН КАРЦИНОМ - МЯСТОТО Й В СЪВРЕМЕНОТО ОПЕРАТИВНО ЛЕЧЕНИЕ

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Резюме.

След рака на млечна жлеза, ендометриалният карцином е най-честата неоплазма засягаща жените. Един от най-важните прогностични критерии на това заболяване е състоянието на регионалните лимфни възли (ЛВ). Няма единно мнение нито за мястото, нито за обема на лимфната дисекция (ЛД) при I стадий. Сентинелната лимфна биопсия (СЛБ) търси мястото си в съвременното оперативно лечение на ендометриалния рак.

Ключови думи: ендометриален карцином, сентинелна лимфна биопсия

SENTINEL LYMPH NODE BIOPSY IN ENDOMETRIAL CANCER - A PART OF MODERN OPERATIVE TREATMENT

Abstract.

After breast cancer the endometrial cancer is the most common gynaecological malignancy. The lymph node status is with great prognostic value. There is no agreement for the therapeutic value and the contents of the lymph node dissection in early stages. That is why the sentinel lymph node biopsy is a part of modern operative treatment of endometrial cancer.

Key words: endometrial cancer, sentinel lymph node biopsy

След рака на млечна жлеза, ендометриалният карцином е най-честата неоплазма засягаща жените. Честотата му расте ежегодно като долната възрастова граница непрекъснато пада. Един от най-важните прогностични критерии на това заболяване е състоянието на регионалните лимфни възли (ЛВ). Това има отношение както към последващата терапия, така също и към преживяемостта на пациента. Ето защо и към хирургичното стадиране задължително трябва да включва информация за лимфния статус.

Поради анатомичните особености на лимфосъбирателната система на маточното тяло и факта, че лимфната дисекция с неясен терапевтичен ефект, то няма единно мнение нито за мястото, нито за обема й при I стадий на ендометриалния карцином. Някои автори

извършват хирургично стадиране за всички пациенти в I стадий на заболяването, а други приемат, че в този случай това е излишно. Между тези две крайности е мнението за осъществяване на дисекция само при високо рискови за екстарутеринно разпространение на заболяването пациенти (серозен или светлоклетъчен хистологичен вариант, грейдинг - G3, дълбочина на миометрална инвазия над 50 %, ангажиране на истмуса). Съществуват дебати и за обема на дисекцията - от лимфна биопсия, през селективна до тотална такава. Не трябва да се забравя, че риска от тазово лимфно метастазиране при I стадий на ендометриалния карцином е само 10-12%, а общият риск за парааортално засягане е 4-6% (1).

Ако се извършва сентинелна лимфна биопсия

into consideration: diagnosis of anaemia during pregnancy; dosing of corticosteroid therapy; possibility of giving birth to a viable foetus and prognosis for next pregnancies.

Owing to the inter-disciplinary efforts, the life and health of this pregnant woman were preserved, but the foetus was lost.

ПЪРВИЧЕН МАЛИГНЕН МЕЛАНОМ НА ВЛАГАЛИЩЕТО И ВЪЗМОЖНОСТИТЕ ЗА ЛЕЧЕНИЕ: ПРИНОС НА ЕДИН СЛУЧАЙ

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Цел: Да бъдат представени и анализирани клиничната характеристика, лечението и възможностите за лечение на пациентка с първичен малигнен меланом на влагалището и да се направи преглед на литературата.

Клиничен случай: Пациентка на 71 год. с анамнеза за вагинално кръвотечение, предизвикано от 4 туморни формации разположени във влагалището. Размерът на формациите беше около 2 см., като три от тях бяха разположени в проксималните две трети на предната стена на влагалището и една в дисталната трета. Извърши се ексцизионна биопсия на формацията, разположена в близост до входа на влагалището. Хистопатологичното изследване разкри, че се касае за малигнен меланом на влагалището, което беше потвърдено и имунохистохимично. След изключване на първичен тумор от друго място, на пациентката беше извършена радикална хистеректомия клас IV, тотална вагинектомия и тазова лимфна дисекция. На патохистологичния препарат беше доказана клинично неизявена меланомна лезия на маточната шийка. Пациентката беше подложена на следоперативна химиотерапия с Dacarbasine и ежемесечна имунотерапия с BCG ваксина. Болната преживя 21 месеца след операцията, без да развие локален рецидив и почина от далечни метастази в гръбначния стълб.

Извод: Радикалната хирургия при първичен меланом на влагалището е сигурен начин за постигане на локорегионален контрол на заболяването при мултифокален тумор. Широката локална ексцизия може да се използва при унифокална лезия и сигурност в постигането на чисти резекционни линии.

PRIMARY MALIGNANT MELANOMA OF THE VAGINA AND TREATMENT OPTIONS: A CASE REPORT

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Objective: To present and analyze the clinical characteristics, treatment, and treatment options for a patient with primary malignant melanoma of the vagina and review of literature.

Clinical case: A 71-year-old patient with a history of vaginal bleeding caused by four tumor growths located in the vagina is presented. The size of each formation was about 2 cm. Three of them were located in the proximal two-thirds of the anterior wall of the vagina and one in the distal third. Excisional biopsy was performed of the lesion located near the entrance of the vagina. Histopathological examination revealed that it was a malignant melanoma of the vagina, which was confirmed immunohistochemically. After ruling out a tumor of an unknown primary site, the patient underwent radical hysterectomy type IV, total vaginectomy and pelvic lymph node dissection. Hystological examination proved a clinically asymptomatic melanoma lesion of the uterine cervix. After surgery, the patient was given chemotherapy with Dacarbasine and monthly immunotherapy with BCG vaccine. The patient survived 21 months after surgery without developing a local relapse and died of distant metastases in the spine.

Conclusion: Radical surgery for primary melanoma of the vagina is a secure way of achieving locoregional control of multifocal disease. The wide local excision can be used in unifocal lesions with security in achieving clean surgical margins.

Am J Obstet Gynaecol 1996; 174: 654-658

3. Seracchioli R, Rossi S, Govoni F et al. Fertility and obstetric outcome after laparoscopic myomectomy of large myomata: a randomized comparison with abdominal myomectomy. *Hum Reprod* 2000; 15: 2663-2668

4. Rossetti A, Sizzi O, Soranna L et al. Long-term results of laparoscopic myomectomy: recurrence rate in comparison with abdominal myomectomy. *Hum Reprod* 2001; 16: 770-774

5. Alessandri F, Lijoi D, Mistangelo E et al. Randomized study of laparoscopic versus minilaparotomic myomectomy for uterine myomas. *J*

Minim Invasive Gynaecol 2006; 13: 92-97

6. Holzer A, Jirecek ST, Ilievich UM et al. Laparoscopic versus open myomectomy: a double-blind study to evaluate postoperative pain. *Anesth Analg* 2006; 102: 1480-1484

7. Laudi S, Zaccoletti R, Ferrari L et al. Laparoscopic myomectomy: technique, complications and ultrasound scan evaluations. *J Am Assoc Gynaecol Laparosc* 2007; 8: 231-240

8. Chu J, Yan H, Xia et al. Laparoscopic versus open myomectomy – a meta analysis of randomized controlled trials. *Obstet Gynaecol* 2009; 145: 14-21

СЕНТИНЕЛНА ЛИМФНА БИОПСИЯ ПРИ ЕНДОМЕТРИАЛЕН КАРЦИНОМ – НАШ ОПИТ

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Резюме

Цел. Целта на проучването бе да се изследва възможността за детекция на сентинелени лимфни възли (СЛВ) при ендометриален карцином, използвайки метода на Altgassen et al.

Пациенти и методи. На 12 пациенти с ендометриален карцином бе инжектирано 4 мл метиленово синьо на 8 места субсерозно. След 10 мин бе извършена оценка на лимфния статус.

Резултати. Отчете се 91.6 % успеваемост като само при една пациентка не се визуализираха СЛВ, а при друга се намери СЛВ само едностранно. Не се отчетоха странични ефекти.

Заключение. Този метод за детекция на СЛВ е многообещаващ, бърз и лесен за изпълнение, но се налага извършването на допълнителни изследвания за да стане част от стандарта за оперативно лечение на ендометриалния карцином.

Ключови думи: ендометриален карцином, сентинелен лимфен възел

SENTINEL LYMPH NODE BIOPSY IN ENDOMETRIAL CANCER - OUR EXPERIENCE

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Abstract

Purpose. The objective of the study was to determine the feasibility of a method described for the first time by Altgassen et al. of labeling sentinel lymph nodes in patients with endometrial cancer using blue dye.

Patients and methods. 4 ml of blue dye was administered in 12 patients with endometrial cancer subserosally at eight sites. After 10 min sentinel lymph nodes were harvested.

Results. Detection rate was 91.6 %. In only one patient there was no detection of sentinel lymph node and in one patient the sentinel lymph node was marked only in one hemipelvis.

Conclusions. This method for detection of sentinel lymph nodes in patients with endometrial cancer is promising, fast and easy to implement, but need to conduct additional studies to become part of the standard for the surgical treatment of endometrial cancer

Key words: endometrial cancer, sentinel lymph node

examination 10 days after the FETO demonstrated an increased LHR to 1.1. Treatment with FETO for severe CDH has been performed for the first time in Bulgaria and this procedure addressed several questions for optimal management by an experienced interdisciplinary team.

ЛЕЙОМИОСАРКОМ НА ВЛАГАЛИЩЕ – ПРЕДСТАВЯНЕ НА ЕДИН СЛУЧАЙ С КРАТЪК ЛИТЕРАТУРЕН ОБЗОР

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Резюме

Лейомиосаркома на влагалището е изключително рядко състояние и поради тази причина няма стандартна схема на лечение. Представяме случай на 35 годишна пациентка с такова заболяване, на която бе извършена радикална хирургическа интервенция и не е провеждала следоперативна терапия. Шест месеца след това няма данни за метастазиране и рецидив на основното заболяване.

Ключови думи: лейомиосаркома, влагалище

LEIOMYOSARCOMA OF THE VAGINA: A CASE REPORT AND REVIEW FROM THE LITERATURE A Jordanov¹, N Hinkova¹, I Ivanov², S Popovska²

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Abstract

Leiomyosarcoma of the vagina is a very rare condition and that is why there is no standard treatment of this disease. We describe a 35 year old woman with vaginal leiomyosarcoma to whom was accomplished a complete surgical treatment and no postoperative radiation or chemotherapy. Tumor recurrence was not detected for the last 6 months.

МЕТАСТАЗА В ГЪРДАТА ОТ ПЛОСКОКЛЕТЪЧЕН КАРЦИНОМ НА МАТОЧНАТА ШИЙКА. КЛИНИЧЕН СЛУЧАЙ.

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Резюме

Млечната жлеза е изключително рядък таргетен орган за метастазиране на екстрамамари неоплазми. Честотата варира от 1.7% - 6.6%, като аутопсионна находка до 1.2%-2%, като клинична изява и около 2.7% в цитологични серии. Според първичната туморна локализация в по-голям процент се срещат метастази от лимфом меланом, рабдомиосарком, тумори на бял дроб и овариални тумори. Метастази в млечната жлеза от карцином на маточната шийка са казуистична находка. Според литературни обзори, до момента са описани около 30 случая със сходна патология. Представяме клиничен случай на 48 годишна жена с плоскоклетъчен карцином на маточната шийка, хистологично верифициран през 2010г. Три години след поставяне на диагнозата на първичния тумор, след провеждане на лъче- и химиотерапия, пациентката е с кистична туморна формация в гърдата, болезнена при натиск. Извършена е квадрантектomia с отворена биопсия. Хистологично и имунохистохимично е отхвърлена диагнозата първичен плоскоклетъчен карцином на гърдата. Диференциалната диагноза на метастатични лезии в гърдата е проблематична

ЛАПАРОСКОПСКИ УСЛОЖНЕНИЯ В ГИНЕКОЛОГИЯТА

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Резюме. Въпреки все по-широкото използване на лапароскопията в гинекологията, нейните усложнения не трябва да се подценяват и пациентите трябва адекватно да се информират за рисковете от така наречената мини инвазивна хирургия.

LAPAROSCOPIC COMPLICATIONS OF GYNECOLOGIC SURGERY

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Abstract. Despite the growth of laparoscopic surgery, its complications must not be underestimated and patients must be informed of the risks of so-called ,minimally' invasive surgery.

ПЪРВИЧЕН НЕХОЧКИНОВ ЛИМФОМ (НХЛ) НА ВЛАГАЛИЩЕ – ПРЕДСТАВЯНЕ НА СЛУЧАЙ С ЛИТЕРАТУРЕН ОБЗОР

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Резюме:

Първичните неходжкинови лимфоми ангажиращи женската полова система са изключително редки, особено тези на влагалището. Представяме случай на 71 годишна пациентка с първичен НХЛ, на която след поставяне на диагнозата се проведе стандартно за заболяването химиотерапия и 2 години по-късно няма данни за рецидивирание и метастазирание на основния процес.

Ключови думи: Първичен неходжкинов лимфом, влагалище

PRIMARY VAGINAL NON-HODGKIN LYMPHOMA – A CASE REPORT AND REVIEW FROM THE LITERATURE

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Abstract

Primary vaginal non-Hodgkin lymphoma is really uncommon disease. We describe a 71 year old woman with primary vaginal non-Hodgkin lymphoma to whom was made a standart chemotherapy after diagnosis. Tumor recurrence was not detected for the last 2 years.

ЗА ПРАКТИКАТА

ЧЕСТО СРЕЩАНИ ПРАВНИ ПРОБЛЕМИ В ПРАКТИКАТА НА ГИНЕКОЛОГА

Петрова М.

Резюме: Предмет на настоящата статия е нормативната уредба и съдебна практика, касаеща отговорността на лекарите гинеколози. Целта е да се запознаят медицинските специалисти – гинеколози с основните видове отговорност, различията помежду им, както и обстоятелствата, които ги пораждат. Запознаването на лекарите – гинеколозите с правната рамка, в която упражняват своята професия, ще доведе до нарастване на тяхната увереност и сигурност при работа.

Ключови думи: юридическа отговорност на гинеколога,

LEFT AND RIGHT UTERINE ARTERY DOPPLER AS EARLY SCREENING TEST OF THREATENED ABORTION OUTCOME

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Human reproduction entails a fundamental paradox: although critical to the survival of the species, many aspects are inefficient and wastage seems excessive. Only 50-60% of all conceptions advance beyond 20 weeks of gestation. Miscarriage was defined by WHO as a loss of pregnancy before 20 weeks of gestation or weight of baby under 500 gr. Threatened abortion is the first, reversible phase of miscarriage. The pregnancy outcome doesn't always correlate to severe of its cardinal symptoms- vaginal bleeding and abdominal pain. The measure of HHG can't accurately predict the pregnancy outcome. Ultrasound scanning is probably the best single diagnostic and prognostic test in managing cases of threatened abortion. Uterine artery Dopler waveforms analysis in patients with threatened abortion is non-invasive method, which can find pathological signs in the beginning of pregnancy. Development of a molecular biology give an opportunity to find out problems of pregnancy in the process of implantation, a technical progress in ultrasound give a chance to study changes in uterine blood flow in early deadlines and to finding new additions between uterine perfusion and embryo development.

ЗАТРУДНЕНИЯ В ДИСЕКЦИЯТА НА ПИКОЧНИЯ МЕХУР

ПРИ ТОТАЛНА ЛАПАРОСКОПСКА ХИСТЕРЕКТОМИЯ

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Резюме: Дисекцията на пикочния мехур е критичен етап при извършването на лапароскопската хистеректомия.

Предшестващи оперативни интервенции като цезарово сечение, конизация на маточната шийка, наличие на цервикални или истмични миоми възли, както и недостатъци на оперативната техника могат да затруднят допълнително отпрепарирването на пикочния мехур.

Оптималното извършване на лапароскопската хистеректомия е функция на спазването на някои основни принципи: познания върху анатомията на малкия таз и топографските взаимоотношения между тазовите органи; отчитане на наличните рискови фактори; интраоперативен скрининг за настъпили усложнения и ранното им овладяване.

DIFFICULTIES IN DISSECTION OF URINARY BLADDER IN TOTAL LAPAROSCOPIC HYSTERECTOMY

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Abstract: The dissection of urinary bladder is a crucial phase of the laparoscopic operation of hysterectomy. The latter dissection may become even more difficult in the context of history of operative interventions as cesarean section or cervical conization, presence of cervical or isthmic myomatous nodes, as well as upon a bad operative technique.

The obeying of some basic principles (knowledge of pelvic anatomy and topographic interrelations; considering of present risk factors; intraoperative screening for complications and their early treatment) results in the optimal performance of laparoscopic hysterectomy.

Влияние на медикосоциалните и акушерските фактори при бременни за раждане на деца преди и след 37 гестационна седмица с ниско и нормално тегло

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Ключови думи: медикосоциални фактори, акушерски фактори, родилки, недоносени деца, преждевременно раждане

УВОД

В достъпната научна медицинска литература се посочват различни медикосоциални и акушерски фактори, които се свързват с изявата на спонтанно предтерминно раждане на незрял плод. Незрялостта на плода е определяща за развитието на хронична белодробна болест, забавено психомоторно развитие, различни форми на неврологичен дефицит, зрителни нарушения, както и за появата на проблеми от медикосоциално и етично естество, които имат отложен във времето ефект върху семейството, обществото и здравните системи [1, 3-6, 8].

В световен мащаб 15.5% от новородените са с тегло под 2500 г, а 67% са родени преди 37 гестационна седмица (г.с.). Делът на преждевременно родените деца в развитите страни е между 5 и 10%, като при повече от 50% етиологията е неясна.

Една от основните причини за провеждане на настоящото проучване е липсата на комплексно проучване в България през последните 20 години върху ролята на медикосоциалните и акушерските фактори за раждането на деца преди 37 г.с. с тегло под 2500 г. Програмите за идентифициране и контрол на рисковите фактори за раждане на деца под 37 г.с. и с тегло под 2500 г у нас са недостатъчно ефективни и изискват координирани действия с участието на различни институции и сектори в обществото.

Целта на проучването е да се извърши сравнителен анализ на медикосоциалните и акушерските фактори на бременните жени за раждане на деца преди и след 37 г.с. с тегло под и над 2500 г.

МАТЕРИАЛ И МЕТОДИ

През 2017 г. е проведено проучване „случай-контрол“. В проучването са обхванати 1212 родилки и 1212 живородени деца от едноплодна бременност, които са регистрирани в УМБАЛ „Д-р Г. Странски“ ЕАД, Плевен и за които е налице информация, събирана за целите на проучването (критерии за включване).

Родилките и живородените деца са разпределени в четири групи. Трите групи на случаите включват:

преждевременно родени деца преди 37 г.с., с тегло при раждането под 2500 г (1 група, ПРНТ, n=120), преждевременно родени деца преди 37 г.с. с тегло над 2500 г (2 група, ПРНТ, n=100), родени след 37 г.с. с тегло под 2500 г (3 група, РТНТ, n=37). Контролната група включва родените след 37 г.с. с тегло при раждането над 2500 г (4 група, РТНТ, n=955).

Във всяка от четирите групи е изследвана и сравнена честотата на различни рискови фактори: медикосоциални фактори (възраст, местоживеење, образование, социален статус, семеен статус, наблюдение на бременността, фамилна обремененост, минали операции, общи и гинекологични заболявания, менархе-цикличност, поредна бременност и раждане, аборт, усложнения на бременността) и акушерски фактори (особености поотгълно на таз, околоплоден мехур и ципи, плацентата, пъпна връв, предлежание на плода, механизъм на раждане).

Данните са събрани от „История на бременността и раждането“ и са обработени със SPSS v.24.0. Качествените променливи са описани чрез тяхната абсолютна и относителна честота. За описание на количествените променливи са използвани средноаритметична и стандартно отклонение ($X \pm SD$) при нормално разпределение и медиана и обхват (Me, Min-Max) - при асиметрично разпределение. Приложени са ANOVA и хи-квадрат на Пирсон. За сигнификантни се приемат различията, които са установени при ниво на значимост $p < 0.05$.

РЕЗУЛТАТИ

Средната възраст на родилките на ПРНТ (28 ± 7.4) е сигнификантно по-висока спрямо тази на останалите три групи (табл. 1). По-голяма част от родилките на ПРНТ са с ниско образование (51.85%), безработни (46.6%) и без регистрирано наблюдение на бременността (27.5%), като различията са статистически значими ($p < 0.05$).

Медикосоциалните фактори на родилките имат по-висока честота на проявление при ПРНТ (1 група), с някои особености (табл. 1). Всяка пета родилка в тази група е фамилно обременена (20.0%) и с данни за минали общи заболявания (23.01%), а всяка трета е преживяла



Analysis of abdominal vs. robotic radical hysterectomies for patients with cervical cancer: a Bulgarian experience

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Received: 16 March 2021 / Accepted: 17 April 2021

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Abstract

To assess and compare the peri-operative, oncologic, and survival outcomes for women with cervical cancer (CC) treated with abdominal radical hysterectomy (ARH) versus robotic radical hysterectomy (RRH) approaches in Bulgaria. We retrospectively analyzed patients with histologically diagnosed CC operated via ARH or RRH methods during January-2008 to April-2019. The data analyzed include patients and tumor characteristics, peri-operative outcomes, and disease status. Kaplan–Meier method and Cox regression analysis were performed to determine disease-free survival (DFS) and overall survival (OS). There were consecutive 1347 patients (ARH = 1006, RRH = 341), which formed the basis of study analyses. Women in the RRH group had significantly shorter median hospital length-of-stay than ARH cases (7 vs. 11 days, $p < 0.001$), higher post-operative hemoglobin (116 vs. 108 g/L, $p < 0.001$), and fewer blood transfusions (7.3% vs. 21.5%, $p < 0.001$), respectively. The overall incidence of post-operative complications was also lower in the RRH vs. ARH group (2.1% vs. 9.4%, $p < 0.001$). Median follow-up time for ARH vs. RRH groups was 4.32 vs. 5.24 years, respectively ($p < 0.001$). Kaplan–Meier analysis demonstrated that the RRH cohort had a significantly higher survival rate compared to the ARH group (CC-specific death 8.5% vs. 16.5% respectively). Mean time to recurrence did not differ significantly in either surgical approach ($p = 0.495$). Cox multivariate regression showed no significant impact of surgical approach on DFS or OS. No significant difference in DFS or OS between ARH vs. RRH for CC was observed. RRH approach does not lead to inferior oncologic outcomes and is associated with better peri-operative outcomes. In regard to “all stages” of CC, we found robotic surgery safer compared to laparotomy, and thus consider RRH a better surgical treatment option for patients with CC.

Keywords Cervical cancer · Radical hysterectomy · Abdominal vs. robotic surgery · Peri-operative outcomes · Oncologic factors · Survival analysis

Introduction

Traditionally, the operative approach for cervical cancer (CC) has been radical hysterectomy (RH) [1, 2], nevertheless, abdominal radical hysterectomy (ARH) is associated with sizable complications regarding the peri-operative and

long-term post-operative periods [3–5]. In recent years, women with CC underwent RH most frequently by ARH or minimally invasive surgery (MIS) [6, 7], however, the MIS approach correlates better with peri-operative and oncologic outcomes.

The first laparoscopic RH with pelvic and para-aortic lymph node dissection was performed by Nezhat in 1989 and published [8], followed by Canis et al. in 1990 [9]. After that, numerous studies in peer-reviewed literature have demonstrated better outcomes for MIS as compared to ARH, with respect to hospital length-of-stay (LOS), estimated blood loss (EBL), and complications [6, 9–17]. Several retrospective cohort studies illustrated lower peri-operative morbidity and no appreciable difference in the survival rates and shorter LOS [18–20]. However, the MIS potential

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Peri-operative and survival outcomes analysis of patients with endometrial cancer managed by three surgical approaches: a long-term Bulgarian experience

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Received: 28 September 2021 / Accepted: 21 January 2022
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Abstract

The study aim was to assess the peri-operative, oncologic, and survival outcomes for patients with endometrial cancer (EC) managed by abdominal hysterectomy (AH), laparoscopic hysterectomy (LH), or robotic hysterectomy (RH) approaches at premier centers in Bulgaria. We analyzed histologically diagnosed EC cases operated via any of the three surgical methods during 2008–2019. Data analyses included patients and tumor characteristics, peri-operative outcomes, and disease status. We grouped FIGO stages I and II to represent early-stage EC and to investigate their survival. Kaplan–Meier and Cox regression analyses were performed to determine disease-free survival (DFS) and overall survival (OS). Consecutive 917 patients (AH=466; LH=60, RH=391) formed the basis of study analyses. Most of demographics and tumor characteristics of the patients were comparable across the groups except few minor variations (e.g., LH/RH cases were younger, heavier, more stage IA, endometrioid, G1, low-risk group). LH and RH group cases had significantly lower operative time than AH ($p < 0.001$), shorter hospital length-of-stay ($p < 0.001$), higher post-operative Hgb ($p < 0.001$). RH cases had fewer blood transfusions than AH or LH ($p < 0.001$). Cox multivariate analyses indicate that OS was not influenced by the type of surgical approach. Despite the fact that the DFS in “early-stage” EC is significantly better in AH group than RH, the type of surgery (i.e., AH, LH, or RH) for “all stages” is insignificant factor for DFS. With our long-term experience, minimally invasive surgical approach resulted in superior peri-operative, oncologic, and survival outcomes. Specifically, RH is not only safe in terms of post-operative results, but also for mortality and oncologic rates.

Keywords Endometrial cancer · Abdominal vs. laparoscopic vs. robotic surgery · Peri-operative outcomes · Oncologic factors · Survival analysis · Bulgarian experience

Introduction

Globally, the second most common gynecologic malignancy is endometrial cancer (EC) [1]. Surgical treatment is considered to be the standard of care for this disease. In the past decades, total abdominal hysterectomy (AH) was the most common approach and considered to be a gold standard for surgical management of EC. Technological innovations and evolution in medicine, particularly in surgery, played integral part of the process for the treatment of malignant tumors. Such processes led to the development of minimally invasive surgical (MIS) approaches for EC in recent decades, i.e., total laparoscopic hysterectomy (LH) and robotic-assisted hysterectomy (RH). Nowadays, these three surgical approaches for the treatment of EC vary across the globe

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INCISIONAL ENDOMETRIOSIS: FOUR CLINICAL CASES

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Received: May 11, 2017

Revision received: June 01, 2017

Accepted: November 02, 2017

Summary

The presence of functioning endometrial glands and stroma outside the uterine cavity is defined as endometriosis. Its incidence is approximately 10-15% of women of fertile age. Incisional endometriosis following obstetric or gynecologic surgery is reported in 0.03-1.08% of women. Most of the cases reported in the literature are related to caesarean section and have required a differential diagnosis with a hernia, abscess, granuloma or lipoma. The diagnosis is based on histological findings. We describe incisional endometriosis in four patients operated on at St. Marina Hospital – Pleven for one year.

Key words: endometriosis, incisional endometriosis

Introduction

Endometriosis is a benign gynecologic condition, in which endometrial glands and stroma are found outside the uterus. Worldwide, endometriosis is diagnosed in about 10% (89 million) of women of fertile age [1, 2]. Most often, the pelvic peritoneum, ovaries, ovarian tubes and the uterine body are involved. Endometrial lesions can also be found along the rectovaginal septum, ureters, and the urinary bladder. Endometriosis at the site of incision is a rare extragenital location, seen in 0.03-1.08% of patients after obstetric or gynecologic surgery [3-5]. The onset of endometriosis can be explained by several theories: dysontogenetic (ectopic Mueller's epithelium growth), transplantational (regurgitation of viable endometrial cells and their translocation on the peritoneal mesothelium), metastatic (metastasizing from the uterine cavity by lymphatic or blood vessel route), metaplastic theory (metaplasia of the coelomic epithelium into the endometrial epithelium under the influence of estrogenic hormones) [6-8]. Endometriosis associated with the surgical cicatrix is explained by the transplantational and metastatic theory. The factors responsible for implantation and growth of the endometrial lesions can be divided into anatomical, immunological, genetic and hormonal. Locally, immunologic dysfunction in endometriosis is associated with higher concentration of activated macrophages and proinflammatory and growth cytokines – IL-1, 6,

PREVENTION OF PRETERM BIRTH

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Received: June 12, 2018

Revision received: December 01, 2018

Accepted: January 17, 2019

Summary

Preterm birth (PTB) is a worldwide problem with great social significance because it is a leading cause of perinatal complications and perinatal mortality. PTB is responsible for more than a half of neonatal deaths. The rate of preterm delivery varies between 5-18% worldwide and has not decreased in recent years, regardless of the development of medical science. One of the leading causes for that is the failure to identify the high-risk group in prenatal care. PTB is a heterogeneous syndrome in which many different factors interfere at different levels of the pathogenesis of the initiation of delivery, finally resulting in delivery before 37 weeks of gestation (wg). The various specificities of risk factors and the unclear mechanism of initiation of labour make it difficult to elaborate standard, unified and effective screening to diagnose pregnant women at high-risk for PTB correctly. Furthermore, they make primary and secondary prophylaxis less effective and render diagnostic and therapeutic measures ineffective and inappropriate. Reliable and accessible screening methods are necessary for antenatal care, and risk factors for PTB should be studied and clarified in search of useful tools to solve issues of risk pregnancies to decrease PTB rates and associated complications.

Key words: preterm birth, high-risk group, screening

Introduction

According to the World Health Organization (WHO), preterm birth (PTB) is birth before 37 weeks of gestation (wg) or 259 days before the first day of the last menstrual period [1]. Defining the borderline between birth and abortion varies across different countries. Historically, this borderline moved from 28 wg toward earlier gestations, because of the improved survival before 28 wg following the introduction of corticosteroid prophylaxis of the respiratory distress syndrome, postnatal surfactant therapy and the advances in intensive neonatology. There are centres where this borderline moved to 22 wg. The WHO definition of PTB is based on a statistical analysis of the gestational age at birth, and this should be clearly distinguished from the concept for prematurity, which reflects the lack of maturity of different organs and systems of



UTERINE AND OVARIAN SARCOMAS: CLINICAL AND HISTOPATHOLOGICAL CHARACTERISTICS

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ABSTRACT

Purpose: To investigate the clinical and histopathological characteristics of patients with uterine and ovarian sarcomas and analyse surgical operations already performed.

Material and Methods: The retrospective study included 17 patients with uterine and 2 patients with ovarian sarcomas, who were diagnosed and operated on for three years at St. Marina University Hospital in Pleven, Bulgaria.

Results: In the group of uterine sarcomas, the highest incidence was that of leiomyosarcomas (53.3%), followed by endometrial stromal sarcomas (33.3%) and the homologous carcinosarcomas (13.3%). Most of the patients were diagnosed in the first clinical stage (73.3%), and the most common surgery performed was total abdominal hysterectomy with salpingo-oophorectomy, with or without omentectomy (53.3%). The two patients with ovarian tumours were histologically diagnosed with carcinosarcoma.

Conclusions: Genital sarcomas are a heterogeneous group of rare malignant diseases with poor prognoses. Early detection, adequate histological diagnosis and staging are of utmost importance for control.

Keywords: uterine sarcoma, ovarian sarcoma

INTRODUCTION

Sarcomas account for about 5% of uterine neoplasms [1]. The most common histological ones are carcinosarcoma (50%), leiomyosarcoma (30%) and endometrial stromal sarcoma (10%) [2]. Carcinosarcomas are a variable mixture containing malignant epithelial and malignant mesenchymal components. These malignancies can occur in any part of the genital tract, though the most common location is in the uterus [3]. The epithelial component can be endometrioid, clear-cell, serous or squamous. The malignant mesenchymal components defined as homologous or heterologous. If the sarcomatous part contains elements of the Müllerian system (endometrial stromal sarcoma, leiomyosarcoma, and other), it is classified as homologous. The

heterologous ones contain malignant tissues such as cartilaginous, bone, and transversely striated muscle tissue, which are not generally found in the genital system. It is suggested that carcinosarcomas belong to the group of carcinomas and be treated as such, rather than as sarcomas, as they are now categorized in the current FIGO classification [4]. Sarcomas account for $\leq 1\%$ - 4% of all ovarian tumors [5]. The etiology and pathogenesis of these mesenchymal neoplasms remain largely unknown yet, and any subtype is characterized by a variety of risk factors, specific genetic aberrations, clinical course, staging and prognosis.

MATERIALS AND METHODS

Patients

This retrospective study included 17 patients with uterine sarcomas, and 2 patients with ovarian sarcomas, diagnosed and operated on between July 2015 and July 2018 at St Marina University Hospital in Pleven, Bulgaria. The mean age of the patients with uterine sarcomas was 55.5 years (age range 40-76), and ten of them were in menopause. They accounted for 6.3% of all patients operated on for malignant diseases of the uterus at the clinic. The two patients with ovarian sarcomas were 14 and 50 years old and were 0.8% of all patients treated for malignant diseases of the ovaries. We assigned the stage of uterine sarcomas using the FIGO 2009 system. Ovarian tumors were staged according to FIGO 2014.

Statistical analysis

To evaluate the results, we applied the descriptive method.

RESULTS

Of the patients with uterine sarcomas, 11 were admitted for primary surgical treatment, and six because of recurrences or need for additional surgery. Two of them were only diagnosed by testing abrasion/biopsy but were not operated on at the clinic. The rest of the patients underwent surgical operations as follows:

NORMS FOR PHYSICAL GROWTH OF THE FULL-TERM BABIES BORN FROM SINGLETON PREGNANCY IN PLEVEN

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Received: September 02, 2019

Revision received: November 15, 2019

Accepted: December 01, 2019

Summary

The aim of the study was to develop the norms for physical growth (birth weight-, birth height- and head circumference-for age) of the full-term babies born from singleton pregnancy in UMHAT „Dr. G. Stranski” – Pleven (total, by gender and gestational age at birth). A cross-sectional study was carried-out in 2017; 1092 live infants born from singleton pregnancy between 38 and 42 weeks were included in the study. We obtained information about three anthropometric measurements (birth weight-, birth height- and head circumference-for age). Data were processed by SPSS v.24.0. Norm group ranges (3, 5 and 7 groups) were developed for three indicators using percentile methods. Kruskal-Wallis test was used. The mean birth weight- and height-for age were higher for baby boys (P50, 3280 g and 50 cm) compared with baby girls (P50, 3150 g and 49 cm). Baby boys and girls weighed <2570 g at birth fell into the group „very slow growth” (P3). A „very fast growth” (P97) was found in baby boys weighed >4120 g at birth (vs. >3870 g for baby girls). Norm group ranges allow to identify the newborns with a higher risk and to focus efforts and health resources to them; it should be updated periodically.

Key words: birth-weight-for age, birth height-for age, head circumference-for age, norm group ranges, percentile

Introduction

Nowadays, need of the local child growth standards discussed many times. These standards are very important for planning of the prevention programs and health care for children fall into the groups „very slow growth” and „very fast growth” in terms of birth weight and birth length [1].

It has been proven that physical growth indicators (including in the infants) are dynamic and it is unacceptable these indicators to be used for a long time. Therefore, the standards should be updated periodically and the studies should be repeated every 8-10 years [2] or 10-15 years [3].

In 2006, World Health Organization (WHO) published the new child growth standards (The WHO Child Growth Standards) [4] and over 140 countries had adopted them in 2011 [5]. The WHO Child Growth Standards replaced the CDC growth charts for United States (US CDC 2000 growth charts) [5, 6]. According to the WHO Child Growth Standards, the baby boys



ASSESSMENT OF RISK FACTORS OF OBSTETRIC STATUS ASSOCIATED WITH PREMATURE BIRTHS IN WOMEN IN CHILDBIRTH

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SUMMARY

Purpose: To identify and assess the prevalence of the risk factors of obstetric status associated with premature births – total and according to maternal age at pregnancy.

Material and Methods: A case-control study was carried out in 2017 at the University Hospital – Pleven, including 1212 women in childbirth and 1212 live-born babies after single pregnancies. The women were divided into three age groups: under 19, 20-35 and over 35 years. The live-born infants were divided into two groups. The cases included 120 preterm and low-birth-weight newborns (PLBWN). The controls included 955 full-term newborns with normal birth weight (FTNNBW). We did not include 37 full-term newborns with low birth weight (FTNLBW) and 100 preterm newborns with normal birth weight (PNNBW) in the study to control confounding effects. The role of 8 risk factors (RFs) on premature births was investigated.

Results: The prevalence of most RFs was higher in women under 18 and over 35 years of age compared with aged 20-35 years. Maternal pelvic size abnormalities (OR=3.31), breech presentation (OR=7.35), placental abnormalities (OR=4.23), caesarean birth (OR=2.28) increased the risk of preterm births and low birth weight.

Conclusions: There are many RFs associated with preterm births and low birth weight. These RFs need to be identified during pregnancy to reduce the prevalence of PLBWN and the health, economic and social consequences for children and their families, and for the health system and society.

Keywords: risk factors, obstetric status, women in childbirth, age groups, premature births

INTRODUCTION

The multifactor aetiology of pregnancy and premature birth in different age groups of mothers are still not well understood in Bulgaria. During the last 20 years, no complex assessment has been made of protective and risk

factors for premature birth and low birth weight.

Prematurity has a greater impact on the physical and neuropsychological development of the children throughout their lives [1]. The risk of neurological diseases, problems with vision and learning deficits increases [2]. A number of poor health outcomes in preterm newborns occur later in life and increase the risk of developing chronic non-infectious diseases at an older age [3-7]. Prematurity has been one of the leading global burden of disease [8-12] and has negative effects on families, society and health systems [13].

Currently, the efforts of obstetricians, neonatologists and pediatricians are mostly oriented towards new health technologies to improve survival rates of preterm infants.

It is a challenge for both researchers and physicians to identify individuals or groups with high risk for pregnancy and delivery complications [14-16]. The preventive interventions to reduce preterm births and low-birth weight [17-19] should be effective and focused on reducing morbidity and health problems occurring in later life among premature infants.

The aim of the study was to identify and assess the prevalence of RFs of the obstetric status associated with premature births – total and according to maternal age at pregnancy.

MATERIAL AND METHODS

A case-control study was carried out in 2017 at the University Hospital – Pleven. There were 1248 births registered in 2017. The study included 1212 women in childbirth and 1212 live-born babies after single pregnancies. Respondents were chosen according to the following criteria: they should be registered at university hospital in Pleven in 2017 and data collected for the purpose of the study should be available.

The women were divided into three age groups: under 19 (n=193), 20-35 (n=862) and over 35 years (n=157). The live-born infants were divided into two groups: cases and controls. The cases included 120 preterm low-birth-

СЪСТОЯНИЕ И ТЕНДЕНЦИИ НА РАЖДАНИЯТА И ЗДРАВНОТО СЪСТОЯНИЕ НА НОВОРОДЕНИТЕ ДЕЦА В ГР. ПЛЕВЕН ЗА ПЕРИОДА 2010-2017 Г.

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STATUS AND TRENDS IN BIRTHS AND HEALTH STATUS OF THE NEWBORNS IN PLEVEN, 2010-2017

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Резюме. Целта на проучването е да се анализират тенденциите в броя на ражданията при жените в три възрастови групи (до 19 г., 20-35 г. и над 35 г.) и в здравното състояние на новородените деца в Плевен от 2010 до 2018 г. В проучването са обхванати изчерпателно родилки (N = 17 859) и живородени деца (N = 18 149). Събрана е информация за броя на родилките (общо и по възраст), броя на живородените деца (общо, доносени и недоносени) и регистрираните заболявания при доносените и недоносените деца. При анализа на динамични редове са използвани: абсолютен прираст, темп на ръста и на прираста при постоянна основа – база 2010 г. За моделиране на тренда на недоносеността е използван SPSS Forecasting module. За изследвания 8-годишен период се наблюдава: нарастване на дела на родилките до 19- и над 35-годишна възраст и на недоносените деца; значително нарастване на дела на децата, родени с тегло 1999÷1500 г и 1499÷1000 г. Заболяемостта при доносените и недоносените нараства сигнификантно през изследвания период и остава трайно по-висока при недоносените деца. Резултатите от настоящото проучване са полезни при определяне на ресурсите и при планиране на здравните грижи в акушеро-гинекологичната практика и педиатрията.

Ключови думи: тенденции, родилки, недоносени деца, тегло при раждане, заболяемост

Abstract. The aim of the study was to analyze the trends in births of women in three age groups (under 19, 20-35 and over 35 years of age) and in the health status of the newborns in Pleven from 2010 to 2018. All women in childbirth (N = 17 859) and newborns (N = 18 149) were included in the study. Data about the number of women in childbirth (total and by age), number of live-born babies (total, full-term and preterm infants) and diseases registered in full-term and preterm infants were collected. The absolute change, dynamic index and rate of increase (decrease) with fixed base (2010) were calculated. SPSS Forecasting module was used for time series analysis of the prematurity. During the 8-year period, we established the increasing of the proportion in women in childbirth aged less than 19 and more than 35 years, as well as the proportion in preterm infants; the considerable increasing of the proportion in babies with birth weight less than 1999 ÷ 1500 grams (g) and less than 1499 ÷ 1000 g. Morbidity rates of the full-term and preterm infants increased statistically significantly in the period of the study, however the rates were higher in the preterm infants. The results of the study are useful to identify and planning the resources and healthcare in obstetrics and gynecology, as well as in pediatrics.

Key words: trends, women in childbirth, preterm infants, birth weight, morbidity

EMBRYOLOGICAL ASPECTS AND ANATOMICAL VARIATIONS OF THE INFERIOR VENA CAVA – ITS IMPORTANCE IN GYNECOLOGIC ONCOLOGY SURGERY

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Received: February 13, 2022

Revision received: March 08, 2022

Accepted: May 11, 2022

Summary

Surgical procedures of the retroperitoneum are often performed in gynecologic oncology surgery clinics. The most complex among them is paraaortic lymphadenectomy. It is generally performed in cases of bulky lymph nodes in ovarian carcinomas and sarcomas to achieve optimal cytoreduction. In the early stages of ovarian cancer, type II non-endometrioid endometrial cancer, and in advanced stages of cervical cancer, paraaortic lymphadenectomy is an integral part of staging. Moreover, the retroperitoneum is approached in cases of retroperitoneal gynecologic sarcomas. The largest vessels of the human body – the inferior vena cava and the abdominal aorta are localized in the retroperitoneum. Therefore, iatrogenic vessel injury during oncogynecological surgery is more likely to affect the inferior vena cava. Anatomical variations of the vein additionally increase the risk of vascular lesions. Therefore, surgeons should be aware of possible anatomical variations. The present article aimed to highlight the heterogeneity of anatomical variations of the inferior vena cava related to gynecologic oncology surgery. Embryogenesis of the vein and its variations are also discussed. Additionally, some anomalies of the ureter, associated with the embryogenesis of the inferior vena cava, are mentioned.

Keywords: inferior vena cava, embryological aspects, anatomical variations, gynecologic oncology surgery

Introduction

The inferior vena cava (IVC) is derived by the convergence of both common iliac veins (CIVs) at the level of the 5th lumbar vertebra. It leaves the abdomen by piercing the diaphragmatic central tendon at the caval opening at the level of the eighth thoracic vertebra [1]. Generally, the IVC is a single and right-sided vessel formed by four pairs of veins in the embryo. It is posterior to the duodenum, vena portae, and liver [2]. It is the largest vessel that drains blood from the pelvis and lower limbs [3]. Variations

Immunological Risk Factors in Recurrent Pregnancy Loss in Patients With Hereditary Thrombophilia

Review began 03/13/2024
Review ended 03/16/2024
Published 03/20/2024

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Abstract

Background: Recurrent pregnancy loss (RPL) is a complicated reproductive disorder with underlying genetic and immunological causes. RPL may be influenced by hereditary thrombophilia, a class of blood clotting-related genetic abnormalities, via the vascular and immune systems. This study examines the immunological characteristics that hereditary thrombophilia patients have in common with RPL.

Methods: A prospective cohort study included 300 patients split into two groups: a control group without hereditary thrombophilia and a group with the condition. Interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- α), and interferon-gamma (IFN- γ) levels were measured, along with demographic specifics, antiphospholipid antibodies, natural killer (NK) cell counts, and other cytokines. Group differences were found using statistical analysis.

Results: Antiphospholipid antibodies were significantly more common in the thrombophilia group (42% testing positive, $p=0.001$) compared to the control group (12% testing positive), despite demographic factors being similar between groups ($p=0.372$ and $p=0.093$). When body mass index (BMI) was taken into account, the study found a statistically significant difference ($p=0.046$), with the thrombophilia group having a higher mean BMI (26.3 kg/m^2 , standard deviation (SD): 2.8) than the control group (24.7 kg/m^2 , SD: 3.1). IL-6 (14.8 pg/mL , SD: 3.2, $p=0.029$) were higher than the control group (12.4 pg/mL , SD: 2.1), and TNF- α levels were higher in the thrombophilia group (10.5 pg/mL , SD: 2.0, $p=0.012$) compared to the control group (8.9 pg/mL , SD: 1.5), but NK cell counts did not differ significantly ($p=0.213$).

Conclusion: This study emphasizes the role of elevated pro-inflammatory cytokines (IL-6 and TNF- α) and antiphospholipid antibodies in RPL among people with hereditary thrombophilia. In this population, early detection and immunomodulatory interventions may improve pregnancy outcomes. To fully comprehend these mechanisms and create customized treatments, collaborative research is required.

Categories: Obstetrics/Gynecology, Allergy/Immunology

Keywords: pregnancy outcomes, cytokine levels, antiphospholipid antibodies, immunological factors, hereditary thrombophilia, recurrent pregnancy loss

Introduction

Recurrent pregnancy loss (RPL), defined as the unsatisfactory recurrence of two or more consecutive pregnancy losses before the 20th week of gestation, continues to be a challenging reproductive issue for couples hoping to become parents and causes significant distress [1,2]. RPL has a complex etiology that involves complex interactions between genetic, immunological, and environmental factors [3].

Hereditary thrombophilia, a group of heritable genetic mutations that include the prothrombin gene mutation, the factor V Leiden mutation, and deficiencies in the proteins C and S, as well as antithrombin III, is at the center of our investigation [4]. Notably, thrombotic events that occur during pregnancy can potentially impair placental blood flow, raising the risk of miscarriage as a result [5]. The link between hereditary thrombophilia and repeated miscarriages, however, goes beyond vascular issues. Recent studies have revealed fascinating relationships between hereditary thrombophilia and the immune system, suggesting that immunological changes may cause these individual repeated miscarriages [6].

The focus of this study is on immunological factors, which include a wide range of mechanisms from immune tolerance to immune dysregulation, each of which significantly impacts the outcome of pregnancy [7,8]. The maternal immune system must carefully maintain the delicate balance between identifying the fetus as a genetically distinct entity and protecting against potential pathogens. This delicate balance can be upset, resulting in immunological intolerance and subsequent fetal rejection, increasing the risk of

How to cite this article

Kirovakov Z, Konova E, Hinkova N, et al. (March 20, 2024) Immunological Risk Factors in Recurrent Pregnancy Loss in Patients With Hereditary Thrombophilia. Cureus 16(3): e56555. DOI 10.7759/cureus.56555

Thromboprophylaxis during pregnancy for prevention of adverse complications in patients with inherited thrombophilia: a literature review

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Summary

Compared with non-pregnant women, pregnancy alone carries a three- to fivefold higher risk of venous thromboembolism (VTE). Despite the increasing use of low-molecular-weight heparin in identified high-risk patients, pulmonary embolism is still the leading cause of maternal mortality. However, evidence for optimal use of thromboprophylaxis is scarce. Thrombophilia (hereditary or acquired) is thought to predispose to both VTE and is also associated with complications of pregnancy, such as recurrent miscarriages and preeclampsia. This review discusses the current evidence for optimal thromboprophylaxis during pregnancy by focusing primarily on VTE prevention strategies, the potential to prevent recurrent complications during pregnancy with low molecular weight heparin (LMWH), aspirin, and Nattokinase in pregnant women with congenital thrombophilia.

Key words: Aspirin, low molecular weight heparin, nattokinase, thrombophilia



Academic editor: Zornitsa Kamburova

Received: 22 March 2024

Accepted: 17 April 2024

Published: 10 June 2024

Citation: Kirovakov Z, Gyokova E, Hinkova N, Konova E (2024)

Thromboprophylaxis during pregnancy for prevention of adverse complications in patients with inherited thrombophilia: a literature review. Journal of Biomedical and Clinical Research 17(1): 115–126.

<https://doi.org/10.3897/jbcr.e123690>

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<https://doi.org/10.3897/jbcr.e123690>

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Introduction

The overall care for pregnant women with thrombophilia involves careful monitoring. Problems associated with blood clots in pregnancies with thrombophilia can be detected early through attentive observation (Schreck et al. 2022). These issues include deep vein thrombosis, pulmonary embolism, and placental blood clots (Antic et al. 2022). Healthcare professionals can swiftly identify symptoms related to blood clots by regularly examining the patient's clinical status, conducting specific diagnostic tests, and using medical imaging techniques such as ultrasound. Proactively addressing these problems and minimizing their impact on the health of both the mother and the fetus is crucial. Close monitoring allows for the timely detection of problems and quick intervention. Issues related to blood clots can be swiftly treated to reduce risks (Kujovich 2018). Healthcare practitioners can promptly alter anticoagulant therapy to minimize blood clots and bleeding after discovering deep vein thrombosis (Sharma and Kriplani 2018). If a pulmonary embolism is detected, stabilization and treatment can commence immediately (Samuel end Saw 2020). Obstetricians-gynecologists, hematologists,

epididymal proteins. *Rev Reprod*1998; 3: 86–95.

6. Bingle L, Singleton V, Bingle CD. The putative ovarian tumour marker gene HE4 (WFDC2), is expressed in normal tissues and undergoes complex alternative splicing to yield multiple protein isoforms. *Oncogene*2002; 21: 2768–73.

7. Clauss A, Lilja H, Lundwall A. A locus on human chromosome 20 contains several genes expressing protease inhibitor domains with homology to whey acidic protein. *Biochem J*2002; 368: 233–42.

8. Sonoda G, Palazzo J, du Manoir S, et al. Comparative genomic hybridization detects frequent overrepresentation of chromosomal material from 3q26, 8q24, and 20q13 in human ovarian carcinomas. *Genes Chromosomes Cancer*1997; 20: 320–8.

9. Kiechle M, Jacobsen A, Schwarz-Boeger U, Hedderich J, Pfisterer J, Arnold N. Comparative genomic hybridization detects genetic imbalances in primary ovarian carcinomas as correlated with grade of differentiation. *Cancer*2001; 91: 534–40.

10. Moore R, McMeekin D, Brown A, DiSilvestro P, Miller M, Allard W, Gajewski W, Kurman R, Bast RJ, Skates S. A novel multiple marker bioassay utilizing HE4 and CA125 for the prediction of ovarian cancer in patients with a pelvic mass. *Gynecol Oncol.* 2009;112:40–46.

11. Drapkin R, Hecht JL. The origins of ovarian cancer: hurdles and progress. *Women's Oncol Rev*2002; 2: 261–8.

12. Zhou C, Smith JL, Liu J. Role of BRCA1 in cellular resistance to paclitaxel and ionizing radiation in an ovarian cancer cell line carrying a defective BRCA1.

*Oncogene*2003; 22: 2396–404.

13. Moore R, Brown A, Miller M, Badgwell D, Lu Z, Allard W, Granai C, Bast RJ, Lu K. Utility of a novel serum tumor biomarker HE4 in patients with endometrioid adenocarcinoma of the uterus. *Gynecol Oncol.* 2008b;110:196–201.

14. Hellström I, Hellström K. SMRP and HE4 as biomarkers for ovarian carcinoma when used alone and in combination with CA125 and/or each other. *Adv Exp Med Biol.* 2008;622:15–21.

15. Hellström I, Raycraft J, Hayden-Ledbetter M, Ledbetter J, Schummer M, McIntosh M, Drescher C, Urban N, Hellström K. The HE4 (WFDC2) protein is a biomarker for ovarian carcinoma. *Cancer Res.* 2003;63:3695–3700.

16. „HE 4 – туморен маркер за овариален карцином” - В.Манолов, Б.Маринов, В.Василев, А.Андреева; XV^{та} Национална Конференция по Гинекология – 10.03-12.03.2011 г., к-кв „Боровец”

17. Moore R, Brown A, Miller M, Skates S, Allard W, Verch T, Steinhoff M, Messerlian G, DiSilvestro P, Granai C, Bast RJ. The use of multiple novel tumor biomarkers for the detection of ovarian carcinoma in patients with a pelvic mass. *Gynecol Oncol.* 2008a;108:402–408.

18. Hellstrom I, Raycraft J, Hayden-Ledbetter M, et al. The HE4 (WFDC2) protein is a biomarker for ovarian carcinoma. *Cancer Res*2003; 63: 3695–700.

19. Манолов В., Б. Маринов, В. Василев, А. Андреева – „HE4 – туморен маркер за овариален карцином”; сп. „Акушерство и Гинекология” vol. 50, 2011, 11-15

ТОТ'НЕМА - ПРЕПАРАТ НА ИЗБОР ПРИ ЖЕЛЯЗОДЕФИЦИТНА АНЕМИЯ В АКУШЕРО - ГИНЕКОЛОГИЧНАТА ПРАКТИКА

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Резюме: Цел: Нашата цел беше да тестваме ефективността на железния препарат Tot'hema при лечението на желязодефицитна анемия (ЖДА) при пациенти, претърпели оперативно лечение по повод гинекологични заболявания.

Материал и методи: Бяха изследвани общо 110 пациентки, оперирани в нашата клиника по повод на малигнени и бенигнени заболявания. Разделени бяха по групи, в зависимост от степента на анемията. Всички те бяха изписани с предписание да приемат Tot'hema в дневна доза от 2 до 4 ампули и след 30 дни да се изследва хемоглобин (Hb).

Резултат: При всички пациентки, без значение на първичната диагноза, се наблюдава повишаване на хемоглобина с 10 до 15 g/l за период от 30 дни.

Извод: Tot'hema е препарат, който бързо повишава нивата на хемоглобина следоперативно,

няма странични ефекти от приема му и лесно се понася от пациентите.

Въведение: Най-честата анемия в световен мащаб е желязодефицитната анемия. Според критериите на СЗО анемична е всяка жена с Hb под 120 g/l. В зависимост от нивото на хемоглобина заболяването се разделя на три степени:

I степен – 120 g/l – 95 g/l

II степен – 95 g/l – 65 g/l

III степен – под 65g/l

Честотата на разпространение в България е: при бременни – 29,7 %, деца – 26,7 % и жени в детеродна възраст – 17,7% [1]. Основните причини

ПРОФИЛАКТИКА И ЛЕЧЕНИЕ НА РАННИТЕ УСЛОЖНЕНИЯ ОТ СТРАНА НА ЛИМФНАТА СИСТЕМА ПРИ РАДИКАЛНО ОПЕРИРАНИ ОНКОБОЛНИ В ОНКОГИНЕКОЛОГИЯТА

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Резюме:

Цел: Целта е да представим нашия опит в медикаментозната профилактика на следоперативното лимфоцеле /Л/ с препарата Phlebodia при пациентки, претърпели лимфна дисекция /ЛД/ в процеса на оперативно лечение на онкогинекологични заболявания.

Пациенти и методи: В проучването са включени 283 пациентки с онко- гинекологични заболявания, оперирани в УМБАЛ „Г. Странски“, Плевен, Клиника по Онкогинекология за периода от 01.01.2014 до 01.01.2015г.

На всички пациентки е извършена ЛД, като следоперативно е прилагана стандартна постоперативна терапия и е включен медикамента Phlebodia.

Резултати: За 2013г. са извършени общо 232 ЛД за всички локализации, като регистрираните и третирани Л са общо 12. За 2014г. са извършени с 51 бр. повече ЛД т.е. 283, като диагностицираните Л са общо 6.

Заключение: Познавайки етиологията и механизмите на появата на Л, прилагането на медикаменти, използвани достатъчно рано следоперативно, в достатъчна дозировка и продължително време позволяват адекватната му профилактика.

PROPHYLAXIS AND TREATMENT OF EARLY COMPLICATIONS OF LYMPH NODE SYSTEM IN RADICAL TREATED PATIENTS WITH ONCOGYNAECOLOGICAL DISEASES

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Summary:

Aim: The aim is to present our experience with Plebodia in patients with lymph node dissection for prophylaxis of lymphocelle.

Patients and methods: Our study represents 283 patients with oncogynecology diseases, hospitalized in UMBAL G. Stranski for 1 year.

Results: For 2013, 232 lymph node dissections are made. 12 of them have lymphocelles. In 2014, 283 lymph node dissections are made and only 6 of them have lymphocelle.

Discussion: The usage of Phlebodia reduces the postoperative lymphocelles.

Лимфогенното метастазиране е един от основните начини за разпространение на туморни клетки от първичния туморен процес. Извършването на лимфни дисекции /ЛД/ в различен вид са необходими за пълния обем хирургично лечение на тези заболявания. Усложненията, свързани с тях са известни и за съжаление неизбежни. Непрекъснато се търсят консервативни и минимално инвазивни методи за профилактика и лечение на усложненията.

Появата на усложнения от ЛД се определя от обема, локализацията на ЛД, добрата хирургична техника, анатомичните особености на лимфните

съдове, състава на лимфата, лимфния дренаж, съотношението между резорбция и излив на лимфна течност.

Честотата на лимфоцелето/Л/ е различна, варирайки от 0.4% до 58.7%. %*(1), като симптомни са 5-18 %. Wu K(2) съобщава за 7.8%, Conte M за 22.2%, като количеството е вариabilно от 46 до 300 мл. на 12-24 следоперативен ден. /2,3/

Клинично Л бива асимптомно, симптомно и усложнено, като изявата му зависи от локализацията, големината и наличието на инфекция.

Профилактиката на следоперативната лимфорея и лимфоцеле могат да се разделят на:

ЕНДОМЕТРИОЗА НА РЕКТОВАГИНАЛНИЯ СЕПТУМ

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МБАЛ „Света Марина“, Клиника по Гинекология

Резюме

Ендометриозата на ректовагиналното пространство е предизвикателство в хирургичната и гинекологичната практика. Въпреки че заболяването е бенигнено и изисква хирургично отстраняване, поради инвазивността си често влиза в диференциалната диагноза на авансирало, с гранична операбилност онкологично заболяване. Представяме клиничен случай на дълбоко инфилтрираща ендометриоза, поставил диференциално - диагностични трудности.

Ключови думи: дълбоко инфилтрираща ендометриоза, лечение, клиничен случай

ENDOMETRIOSIS OF RECTOVAGINAL SEPTUM

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Summary

Endometriosis of the rectovaginal septum is a challenge in surgical and gynecological practice. Although the disease is benign, it is invasive and requires surgical removal. Because of its invasiveness, deep endometriosis may be misdiagnosed as advanced and inoperable cancer. We present a case of deep infiltrating endometriosis that caused diagnostic difficulties.

Keywords: deep infiltrating endometriosis, treatment, clinical case

Въведение

Ендометриозата се дефинира като наличие на ендометриални жлези и строма извън маточната кухина. При тазовата ендометриоза лезиите могат да бъдат повърхностни перитонеални, яйчникови и дълбоко инфилтриращи (1). При дълбоко инфилтриращата ендометриоза лезиите са над 5 мм под перитонеалната повърхност и могат да се представят като солидни, комплексни нодули. Разграничават се 3 типа дълбоко инфилтрираща ендометриоза. При тип I се касае за мултифокални лезии с дълбочина на инфилтрация над 5 мм. Тип II се характеризира с чревна ретракция. При тип III се наблюдават най- често от 1 до 3 ендометриозни нодули над или в ректовагиналния септум. Най- честите локализации са ретроцервикалното пространство, сакроутеринните връзки, tunica muscularis на ректума и влагалището, както и ректовагинални септум (2). Ректовагиналната ендометриоза се засяга между 3,8% и 37% от пациентите (3) и се отнася към IV стадий на заболяването (4, 5).

Схематично стадирането на ендометриозата е представено на фигура 1. (6)

В клиничен аспект ендометриозата на ректовагиналния септум се счита за една от най- активните, тежки и агресивни форми. Тежестта на симптомите корелира с дълбочината на инвазия и с броя на лезиите (7). Характерна

е цикличността на проявите и постепенното нарастване на интензитета им във времето. Инвазивният характер на тези импланти причинява значителна болка - дисменорея, дълбока диспареуния, дисхезия; дисфункция на червата, чревна стеноза до обструкция, перфорация, вагинално или ректално кървене, инфертилитет. Асимптомни са едва 5 % от заболялите (8). Дълбоката ендометриоза представлява предизвикателство в диагностичен и лечебен план. Диагностичният алгоритъм включва ректален и вагинален преглед, трансвагинално и трансректално ултразвуково изследване, ядрено-магнитен резонанс, компютърна томография, колоноскопия, цистоскопия. Най- често при преглед се установяват болезненост и нодуларни формации, уплътнения на сакроутеринните връзки и параметриумите (9). Четирите образни методики се допълват в предоперативната оценка на дълбоко инфилтриращата ендометриоза. Ултразвуковото изследване има висока сензитивност - до 78% - и специфичност - до 90% (10, 11). Най- честата находка е хиперехогенен слой между вагината и предната стена на ректума, с дължина от 2,1 см - за нераждащите жени, до 3,3 см - за многократно раждали (12, 13). Ядрено - магнитният резонанс показва специфичност до 90,3% при диагностициране ендометриоза на ретроцервикалната област,

БРЕМЕННОСТ СЛЕД АРТ И РИСК ОТ ПРЕДТЕРМИННО РАЖДАНЕ

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PREGNANCY AFTER ART AND THE RISK OF PRETERM BIRTH

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Резюме

Предтерминното раждане (ПТР) е проблем със социална значимост в световен мащаб, произтичаща от факта, че е водеща причина за перинатални усложнения и перинатална детска смъртност и за изразходване на ресурси в здравеопазването. Бременностите след приложение на асистирана репродуктивни технологии (АРТ) се асоциират с повишен риск от ПТР и се сочат като една от причините за увеличаване на честотата на тези раждания в световен мащаб.

Това е обсервационно и проспективно проучване на 334 неселектирани бременни по време на рутинните антенатални визити. Събирани са данни за рискови фактори, като анамнеза за предхождащо ПТР, начин на забременяване (спонтанно или след АРТ), дължина на маточна шийка във втори триместър за оценка на превалентността и значението на тези фактори и да се определи алгоритъм за оценка на индивидуалния риск от ПТР.

Установи се повишен риск от прематуритет при бременностите след АРТ, като е необходимо да се проучат факторите, обуславящи тази асоциация.

Ключови думи: Асистирана репродуктивни технологии, предтерминно раждане.

Summary

Preterm delivery (PTD) is a worldwide problem with a great social significance, considering the fact, that it is a leading cause for perinatal complications and perinatal mortality and spending resources in healthcare. Pregnancies after ART are associated with an increased risk of preterm birth and are being cited as one of the reasons for the increase of the preterm birth rates worldwide.

This was observational and prospective study of 334 unselected pregnant women during the routine antenatal visits. Data were collected about risk factors, such as history of previous PTD, conception method (spontaneous or after ART), second trimester cervical length to estimate the prevalence and the significance of these factors and to define an algorithm to estimate the individual risk of PTD.

It was found an increased risk of prematurity in pregnancies after ART. There is a necessity for further evaluation of the factors which determine this association.

Key words: Assisted reproductive technologies, preterm birth.

Въведение

Предтерминното раждане (ПТР) е проблем със социална значимост в световен мащаб, произтичаща от факта, че е водеща причина за перинатални усложнения и перинатална детска смъртност и за изразходване на ресурси в здравеопазването. ПТР е отговорно за повече от половината от неонаталната детска смъртност. Предтерминно родените са с висок риск за усложнения, хронична инвалидизация и смъртност. Ромею и съавтори определят ПТР като хетерогенен синдром с неизяснена мултифакторна етиология, при когото множество рискови фактори водят до общ краен резултат раждане преди 37 г.с.^{1,21}. Три основни категории описват ПТР: ПТР по медицински индикации (ятрогенни) (25%; 18.7–35.2%),

предтерминна прелаборна руптура на околоплодния мехур (ППРОМ) (25%; 7.1–51.2%) и спонтанно ПТР (50%; 23.2–64.1%). Повечето многоплодни бременности (10% от всички ПТР) се раждат предтерминно (50% по медицински индикации). Въпреки развитието на медицината честотата на предтерминните раждания не намалява през последните десетилетия и причините за това са комплексни¹³.

Асистираните репродуктивни технологии (АРТ) са медицински процедури за лечение на безплодие. АРТ помагат на много безплодни двойки да постигнат бременност и решават редица проблеми свързани с демографската ситуация, но тези бременности често са предизвикателство за здравеопазването,



A Case-Control Study of Obstetric Risk Factors for Low Birth Weights and Preterm Births

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DOI: [10.36348/sjmps.2020.v06i01.004](https://doi.org/10.36348/sjmps.2020.v06i01.004)

| Received: 30.12.2019 | Accepted: 06.01.2020 | Published: 15.01.2020

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Abstract

To study the role of the obstetric risk factors for low birth weight and preterm birth. A case-control study was carried out in 2017 at the University Hospital – Pleven; 1212 women in childbirth and 1212 live-born babies after single pregnancies were included in the study. The live-born infants were divided into two groups. The cases included the preterm low-birth-weight (PLBW) newborns weighing less than 2500 grams (g). The controls included full-term newborns with normal birth weight (FTNBW). The role of 8 obstetric risk factors (RFs) on PLBW was studied (maternal age, type of birth, amniotic fluid deficiency and congenital abnormalities, maternal pelvic size abnormalities, placental abnormalities, abnormalities of fetal membranes, umbilical cord abnormalities, and presentation of the fetus). The obstetric RFs were significantly associated with PLBW. Risk of PLBW is significantly higher ($p=0.001$) in breech presentation (exp (β)=6.622), placental abnormalities (exp (β)=5.556), maternal pelvic size abnormalities (exp (β)=4.426) and amniotic fluid deficiency and congenital abnormalities (exp (β)=2.903). The results of that study can be useful for effecting prevention programming of pregnancy and prematurity.

Keywords: women in childbirth, preterm low-birth-weight, newborns, breech presentation, placental abnormalities, maternal pelvic size abnormalities, amniotic fluid deficiency and congenital abnormalities, binary logistic regression.

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INTRODUCTION

Prematurity has more significant impact on the physical development of the children and has been one of leading global burden of disease [1-6]. Preterm babies have a high risk for neurological diseases, more common problems with vision and learning deficits [7] and chronic non-communicable diseases in adulthood [8-12].

Prematurity birth rates reported in different populations range between 9% and 50%. In Bulgaria, these rates have increased from 6.1% in 80 years of 20th century (6.1% in EU, 5.5% in Norway, 4.1% in Finland) to 8.1% in 2011; these values were higher compared with the lowest values in Europe (Norway – 4.8%, Finland – 4.1%) and lower compared with the highest European values (Cyprus – 13.1%) [1, 4, 7, 13-17].

Over the last 20 years, no comprehensive assessment has been made of risk factors for premature

birth and low birth weight despite the fact that it is associated with the all costs which are paid by preterm newborns, their families and society [13].

The study aimed to evaluate the role of the obstetric RFs for low birth weights and preterm births.

MATERIAL AND METHODS

The case-control study was carried out in 2017 at the University Hospital – Pleven; it was a part of dissertation and approved by Research Ethics Committee.

The study included 1212 women in childbirth (26.6±6.5 years) and 1212 live-born babies after single pregnancies were included in the study. Inclusion criteria were: women in childbirth and live-born infants should be registered at the University hospital in Pleven in 2017 and data collected for the study should be available. We did not include 37 full-term low-birth-weight (FTLBW) newborns and 100 preterm births with

ВЛИЯНИЕ И ОЦЕНКА НА МЕДИКО-СОЦИАЛНИТЕ И АКУШЕРСКИ ФАКТОРИ ВЪРХУ ФИЗИЧЕСКИТЕ ХАРАКТЕРИСТИКИ НА НОВОРОДЕНИТЕ ДЕЦА СПОРЕД ВЪЗРАСТТА НА МАЙКАТА

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Резюме

Целта на проучването е да се направи комплексна оценка на влиянието на медико-социалните и акушерските фактори при бременни жени на възраст до 19 г., 20-35 г. и над 35 г. върху физическите характеристики на новородените деца.

Материал и методи: През 2017 г. е проведено проучване на 1212 бременни жени и 1212 новородени деца от едноплодна бременност. Жените са разпределени в три възрастови групи: до 19 г. (n=193), 20-35 г. (n=862) и над 35 г. (n=157). Новородените деца са разпределени в четири групи: преждевременно родени с ниско тегло (ПРНТ, n=120), преждевременно родени с нормално тегло (ПРНрТ, n=100), родени на термин с ниско тегло (РТНТ, n=37) и родени на термин с нормално тегло (РТНрТ, n=955).

Резултати и изводи: Идентифицираните рискови фактори за раждане на деца преди навършена 37 г.с. с тегло под 2 500 г са еднакви по вид, но различни по сила и значимо по-високи стойности на риска при родилки до 19 г. и над 35 г. в сравнение с родилки на възраст 20-35 г. Вероятността за преждевременно раждане на дете с тегло под 2500 г е около 3 пъти по-висока при отворен околоплоден мехур, 4.4 пъти – при анатомично тесен таз, около 6 пъти – при особености на плацентата и почти 7 пъти – при седалищно предлежание.

Ключови думи: медико-социални фактори, акушерски фактори, оценка, влияние, недоносени деца.

IMPACT AND ASSESSMENT OF MEDICO-SOCIAL AND OBSTETRIC FACTORS IN WOMEN IN CHILDBIRTH IN DIFFERENT AGE GROUPS ON THE PHYSICAL CHARACTERISTICS OF THEIR NEWBORN BABIES

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Abstract

This study aimed to assess the impact of medico-social and obstetric factors in women in childbirth aged 19 yrs. and younger, 20-35 yrs., and older than 35 yrs. on the physical characteristics of the newborn babies.

Material and Methods: The study was carried-out in 2017. All 1212 women in a singleton pregnancy and 1212 newborn babies were included in the study. Women were divided into three age groups: 19 yrs. and younger (n=193), 20-35 yrs. (n=862), and older than 35 yrs. (n=157). Babies were classified into four groups: group 1 (preterm and low-birthweight newborns, n=120), group 2 (full-term newborns with normal birth weight, n=955), group 3 (low-birthweight babies born at term, n=37), and group 4 (preterm babies of normal birth weight, n=100).

Results and conclusions: Risk factors for preterm birth and low birthweight indentified in the study were the same by type and different by power in women in childbirth aged 19 yrs. and younger and older than 35 yrs. than women in childbirth in age 20-35 yrs. The risk for preterm birth with low birthweight was 3 times higher in preterm rupture of membranes, 4.4 times higher – in maternal pelvic size abnormalities, 6 times higher – in placental abnormalities and 7 times higher – in breech presentation.

Key words: medico-social factors, obstetric factors, assessment, impact, premature babies.

Въведение

През последните няколко десетилетия в България не е извършвана систематична оценка на влиянието на медико-социалните и акушерските фактори при бременни жени в различни възрастови групи върху

физическите характеристики на новородените деца. Необходимостта от използването на подобен подход се обуславя от няколко причини. Установено е, че възрастта под 19 години и над 35 години са рискови по отношение на здравето на новородените, като това

The Role of Gestational Management and use of LMWH and Aspirin in Patients with Inherited thrombophilia

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Article History

Received: 06.02.2024

Accepted: 26.02.2024

Published: 07.03.2024

Abstract: Recurrent pregnancy loss (RPL) is multiple pregnancy losses. Inherited thrombophilia, which increases blood clot risk, contributes to RPL. Pre-gestational therapy with Low-Molecular-Weight Heparin (LMH) and Aspirin may improve pregnancy outcomes in these patients. This study aims to evaluate the effectiveness of pre-gestational management and the combination of LMH and Aspirin in patients with RPL and inherited thrombophilia. A hereditary thrombophilia test was performed on each of the 459 pregnant research participants, whose gestational ages ranged from 6 to 38 gestational week Medical center - Prime Clinic and KIRM- Pleven in Bulgaria period from January 2021- May 2023 were collected. Based on the treatment method, patients in a dataset with RPL and hereditary thrombophilia were split into three groups. Group I (Control) patients did not get any pre-gestational care or anticoagulant treatment. Group II: Patients who only received aspirin treatment with 100 mg. Group III: Patients receiving LMH and aspirin therapy. Compared to the treated groups (Group II and Group III), the pregnancy success rate was noticeably lower among the patients in Group I (Control). In addition, Group I experienced more thrombotic events than the groups that received treatment. Pre-gestational therapy with aspirin alone or in combination improves pregnancy outcomes and reduces thrombotic events in RPL and hereditary thrombophilia patients. LMH combined with aspirin may increase pregnancy success more than aspirin alone. These findings need further investigation and larger trials to maximize treatment for this patient population.

Keywords: *pre-gestational management, recurrent pregnancy loss (RPL), Low-Molecular-Weight Heparin (LMH), inherited thrombophilia, Low-Molecular-Weight Heparin (LMH), Aspirin.*

1. Introduction

Losing a pregnancy is a major tragedy that greatly impacts the couple that loses it. Recurrent pregnancy loss (RPL), characterized by its repeated occurrence and unknown etiology in 50% of instances, is a frustrating and difficult issue in reproductive medicine [1]. A miscarriage occurs when a pregnancy spontaneously ends in utero before the fetus is viable. This term covers pregnancies up to 23 weeks and six days; in contrast, several nations have a definition that covers pregnancies up to 20 weeks. Even though RPL was defined as the loss of three successive pregnancies in the “2011 Green-top Guideline from the Royal College of Obstetricians and Gynecologists”, 1, the organization's most recent draft guideline makes it clear that consecutive miscarriages are not required to qualify as recurrent miscarriage. Two or more clinical miscarriages are considered RPL by the “American Society for Reproductive Medicine (ASRM)” [2]. Negative outcomes are associated with all forms of diabetes:

“type 1 (T1 Diabetes mellitus), type 2 (T2 Diabetes mellitus)”, and pre-gestational (PGDM).

Pregnant women with pre-existing diabetes mellitus are more likely to experience surgical delivery, preterm labor, congenital abnormalities, stillbirth, perinatal mortality, macrosomia, prematurity, and cesarean section (CS). However, the caliber of treatment provided to women with diabetes mellitus can influence unfavorable birth outcomes by lowering congenital disabilities and stillbirths. Pregnant women with diabetes do better when they receive more support. The success of pregnancies is improved when women with pre-existing diabetes mellitus receive the proper therapeutic care [3]. Despite the increased risk of RPL among these women, routine screening for acquired or genetic thrombophilia is not always warranted if no venous thromboembolism has occurred. Due to a lack of knowledge regarding the factors that contribute to these pregnancy challenges and a lack of evidence demonstrating the effectiveness of therapies, it is challenging to assess if screening women who have had pregnancy issues is beneficial. The existence of this association with placental vascular thrombosis led



Frequency of Thrombophilic Factors in Patients with Recurrent Pregnancy Loss

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Article History

Received: 24.02.2024

Accepted: 01.03.2024

Published: 23.03.2024

Abstract: Background: A category of hereditary diseases known as Thrombophilia induces irregular blood clotting. Pre-eclampsia, late miscarriages, premature delivery, fetal growth restriction, and deep venous thrombosis are all associated with Thrombophilia. A higher incidence of recurrent pregnancy loss (RPL) or recurrent early pregnancy loss (REPL) in the initial 6–10 weeks of conception may be seen in homozygous individuals for particular thrombophilic variables. A healthy uteroplacental circulation is necessary for a favorable pregnancy outcome. It has been hypothesized that maternal Thrombophilia could raise the probability of preeclampsia and intrauterine growth retardation (IUGR). ACE D/D (angiotensin-converting enzyme deletion/deletion) genotype and PAI 4G/4G (plasminogen activator inhibitor-1 4G/4G) genotype have been associated with an increased risk for these conditions and high blood pressure (hypertension).

Aim of this study is to determinate the frequency of the different thrombophilic mutations in patients with recurrent pregnancy loss.

Methods: A prospective cohort study included 309 pregnant patients with gestational age from 6 to 12 gestational weeks. The patients have a history of recurrent pregnancy loss in the past. Inherited Thrombophilia test was performed on each research participants as part of preconception counseling.

Results: Plasminogen activator inhibitor 1 (PAI – I) 4G/4G was the most prevalent form of thrombophilic mutation identified (82,83%), followed by MTHFR mutation (85.43%), mutations in the prothrombin gene (12,61%) and factor V Leiden (12.29%). Additionally, (12.62%) of pregnant women had IUGR babies, (29,44%) of patients had preeclampsia as a diagnosis and gestational diabetes (24,27%).

In conclusion - The genetic landscape significantly impacts the trajectory of pregnancy-related complications. This study sheds light on the pivotal roles played by genetic mutations, elucidating potential avenues for refined clinical management and targeted interventions. The early detection of these genetic variations paves the way for enhanced personalized care strategies, ultimately benefitting the well-being of both maternal and fetal domains.

Keywords: *Thrombophilia, hereditary, pregnancy, genetic disorders, fetal growth.*

1. Introduction

Thrombophilia is an inherited (hereditary) propensity for thrombosis that can also be identified in later life (acquired). Thrombosis occurs when haemostasis, the process by which blood clots are formed and broken down, is disrupted in any way. Variables in blood clotting, plasma proteins, blood movement, vascular walls, and cell components all contribute to an abnormally high propensity for blood clotting. This causes thrombosis to form in the affected blood vessel. The first step in treating a patient with thrombosis rationally is determining if the patient's hypercoagulable disease is inherited or acquired. The haemostatic

system is altered throughout pregnancy, becoming hypercoagulable, a condition that is unavoidable near the time of delivery. About 5% of reproductive-age women have RPL, defined as two or more unexpected losses. Recent research has linked thrombophilia as a cause of RPL. Some mutations in a gene that codes for a plasmatic protein involved in the anticoagulant mechanism lead to the development of an inherited condition [1]. Hereditary thrombophilia is a genetic susceptibility to developing thrombi due to an inadequacy in anticoagulant factors such antithrombin (AT), protein C (PC), or protein S (PS). People under the age of 40 with this syndrome are at increased risk for getting potentially fatal thrombosis. Vein thromboembolism (VTE) is a