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ORIGINAL ARTICLE

BACTERIAL INFECTION CAUSES OF PREGNANCY LOSS AND PREMATURE BIRTH IN THE WOMEN IN UKRAINE

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ABSTRACT

The aim: To find out whether or not the presence of pregnancy loss and preterm birth was associated with the history of healthcare-associated infection (HAI) of women reproductive tract.

Materials and methods: We performed a retrospective cohort study was based on surveillance data. This study included 1,027 fertile women aged 21-50 years admitted to 8 hospitals from 2017-2019 with complaints to pregnancy loss or preterm birth. Definitions HAI of women reproductive tract were used from the CDC/ NHSN.

Results: Of 1,027 fertile women with complaints to pregnancy loss or preterm birth, 702 (68.4%) HAIs of reproductive tract were detected. The predominant HAIs were: postpartum endometritis (19.1), bacterial vaginitis (15.8%), chorioamnionitis (11.3%), vaginal cuff infection (9.1%), and parametritis (5.6%). According to the statistical data, a significant association between HAI of women reproductive tract and the history of pregnancy loss ($p < 0.05$) was determined. The presence of HAI had no effect on the first trimester miscarriage ($p > 0.05$), but HAI women reproductive tract had strongly affected the second trimester pregnancy losses ($p < 0.05$). Main causative agents of HAI were *Escherichia coli* (31.5%), *Enterobacter* spp. (18.4%), *Klebsiella pneumoniae* (12.5%), *Enterococcus faecalis* (11.6%),*Staphylococcus aureus* (10.2%), *Pseudomonas aeruginosa* (8.4%).

Conclusions: This study identified a significant association between healthcare-associated infection of women reproductive tract and a history of miscarriage. However, there was no association between HAI and a history of preterm birth.

KEY WORDS: pregnancy loss, miscarriage, preterm birth, healthcare-associated infection, reproductive tract infection, bacterial pathogen, antimicrobial resistance

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INTRODUCTION

Pregnancy loss and preterm birth in women is an important public health care concern in worldwide. The term reproductive loss is often associated with miscarriage, which manifests itself as spontaneous abortion during the first trimester of pregnancy before 12 weeks (early miscarriage) or 12 to 24 weeks of gestation (late miscarriage) in women [1]. Miscarriage can be also classified as embryonic loss (or early miscarriage) when it occurs before 10 gestational weeks and fetal loss (or fetal miscarriage) when it occurs after 10 gestational weeks [2, 3].

According to literature, research suggests that between 10% and 20% of women with a medically confirmed pregnancy will end in miscarriage [4]. In an Australian prospective cohort women the rate of miscarriage varied from 11.3 to 86.5 per 100 live births; overall, miscarriage occurred in 25% of the women in the study [5]. Early pregnancy loss in women is a relatively common event, occurring in 15%–25% of pregnancies, and increasing in prevalence with maternal age [6]. The risk is between 9% and 12% in women aged ≤35 years, but increases to 50% in women aged >40. According to the American College of Obstetricians and Gynecologists, risk of miscarriage in women aged 45 years but increases to 80% [7]. Recurrent pregnancy loss is an important reproductive health issue, affecting 2%–5% of couples [6, 8]. However, almost half of the cases remain unexplained and are empirically treated [8].

Miscarriage is one of the most common reproductive losses, however, the causes and adverse outcomes of pregnancy remain poorly understood. According to literature, common established causes include uterine anomalies [9], age of both parents [5, 6], antiphospholipid syndrome [10], hormonal and metabolic disorders [11], and cytogenetic abnormalities [12]. Other etiologies have been proposed but are still considered controversial, such as chronic endometritis [13, 14] and inherited thrombophilias [15]. In addition, there is evidence in the literature that obesity [6, 16], smoking [17], excessive caffeine consumption [17], and cocaine [18] is associated with an increased risk of miscarriage.

Can be difficult to pinpoint exactly what causes pregnancy loss, there are some infections that are associated with an increased risk of miscarriage. According to literature,

bacterial vaginosis, brucellosis, syphilis, cytomegalovirus, dengue fever, human immunodeficiency virus, rubella, and malaria are more frequently found in women with miscarriage [1]. However, no trials have been published to date, remain concerning the impact of healthcare-associated reproductive tract infection on reproductive outcome.

THE AIM

The aim of this study was to find out whether or not the presence of pregnancy loss and preterm birth was associated with the history of healthcare-associated infection of women reproductive tract.

MATERIALS AND METHODS

SETTING AND PATIENTS

Over a 36-month period (January 2017 to December 2019), this a retrospective cohort study was performed in 8 Ukrainian women's hospitals, which are similar in terms of medical equipment, personnel, laboratory facilities, and number of beds. All participating hospitals were required to have a clinical microbiology laboratory with the capacity to process cultures. This study included fertile women aged 21-50 years admitted to hospitals with complaints to pregnancy loss or preterm birth. All women were local residents. Patients who were referred from other hospitals were excluded. Exclusion criteria were patients with current pregnancy, positive serological test for syphilis or other sexually transmitted infections.

DEFINITIONS

For the purposes of this study miscarriage is defined as the spontaneous loss of a pregnancy during the first 24 weeks of gestation. Diagnosis of healthcare-associated infection (HAI) women reproductive tract was based on criteria from the CDC/NHSN Surveillance Definitions for Specific Types of Infections [19].

DATA COLLECTION

All data on outcome of pregnancy (pregnancy loss and preterm birth) and HAIs of women reproductive tract, and their causative pathogens, were collected retrospectively on a form specifically designed by the investigators using medical records comprising charts, daily flow sheets, and laboratory (microbiology) results.

ETHICS

The Shupyk National Healthcare University of Ukraine Ethics Committee approved the waiver of informed consent to participate in this study due to its retrospective design. All women's data were anonymised prior to the analysis.

MICROBIOLOGICAL METHODS

All samples were obtained from women with clinical symptoms of HAIs. Microbial isolates were identified using standard microbiological techniques, including automated microbiology testing (Vitek-2; bioMe´rieux, Marcy l'Etoile, France).

STATISTICAL ANALYSIS

The aim of this study was to find out whether or not the presence of early pregnancy loss or preterm birth was associated with the history of HAI of women reproductive tract. For these comparisons, $\chi 2$ or Fischer's exact test was used, and P values less than 0.05 were considered as statistically significant.

RESULTS

During the study period, 68.4% [95% confidence interval (CI) 66.9 -69.8] (702 of 1,027) fertile women with complaints to pregnancy loss and preterm birth were found to have healthcare-associated reproductive tract infections. Of these cases, 1.7% (17/1027) pelvic abscess or cellulitis, 1.8% (18/1027) infection of the uterine appendages, 2.5% (26/1027) infection of the Fallopian tubes, 1.7% (17/1027) infection of the ovaries, 5.6% (57/1027) infection of the supporting ligaments, 11.3% (116/1027) chorioamnionitis, 15.8% (162/1027) infection of the vagina, 19.1% (196/1027) postpartum endometritis, and 9.1% (93/1027) vaginal cuff infection were identified (Table I).

The women in the study population were also evaluated in view of the miscarriages whether it has happened in the first or second trimester of gestation. 518 (73.8%) of the 702 women had the first trimester miscarriage (≤12 weeks), and the remaining 184 (26.2%) of 702 women had the second trimester miscarriage (>12 weeks).

When we examined the study population with of healthcare-associated infection (HAI), 511 (72.8%) of the 702 women were detected as having the history of a early pregnancy loss in the last 6 months, 191 (27.2%) of 702 women had recurrent pregnancy losses.

In the study population, 511 of 702 (72.8%) women with HAI had a history of early pregnancy loss in the last 6 months and only 191 of 702 (27.2%) women with HAI had recurrent pregnancy losses (Table II). According to the statistical data, a significant association between HAI and the history of pregnancy loss ($P < 0.05$) was determined. However, there was no association between HAI and the history of preterm birth ($P > 0.05$).

In additional, the effect of HAI women reproductive tract on the gestation periods was also examined. The presence of HAI had no effect on the first trimester miscarriage ($P > 0.05$), but HAI women reproductive tract had strongly affected the second trimester pregnancy losses ($P < 0.05$).

In our study, a total of 987 pathogens isolated from 702 cases HAIs of women reproductive tract. Main causative agents of HAI were *Escherichia coli* (31.5%), *Enterobacter* spp. (18.4%), *Klebsiella pneumoniae* (12.5%), *Enterococcus faecalis* (11.6%), *Staphylococcus aureus* (10.2%), *Pseudomonas aeruginosa* (8.4%). The distribution of microorganisms causing HAIs of women reproductive tract is shown in Table III.

Table I. Frequency of pregnancy outcomes in fertile women in Ukraine between 2017 and 2019 by healthcare-associated reproductive tract infection (n=1027)

HAI[a] type	Number of miscarriages	
	n	%
A pelvic abscess or cellulitis	17	1.7
Infection of the uterine appendages (*Adnexa utery*)	18	1.8
Infection of the Fallopian tubes (*Salpingitis*)	26	2.5
Infection of the ovaries (*Oophoritis*)	17	1.7
Infection of the supporting ligaments (*Parametritis*)	57	5.6
Chorioamnionitis	116	11.3
Infection of the Vagina (*Bacterial Vaginitis*)	162	15.8
Postpartum endometritis	196	19.1
Vaginal cuff infection	93	9.1
Total	702	68.4

Note: [a]HAI, healthcare-associated infection

Table II. Relationship among the presence of early pregnancy loss or preterm birth, history of healthcare-associated reproductive tract infection (n=1,027).

Pregnancy outcomes	HAI (+) (n=702, %)	HAI (-) (n=325, %)	*P* value
Pregnancy loss	511 (72.8)	137 (42.2)	*P* <0.05
Preterm birth	191 (27.2)	188 (57.8)	*P* <0.05

Table III. The distribution of microorganisms (n =987) causing HAIs of women reproductive tract

Microrganism	All isolates	
	n	%
Gram-positive cocci	246	24.9
Enterococcus faecalis	114	11.6
Staphylococcus aureus	101	10.2
Streptococcus spp.	14	1.4
Staphylococcus epidermidis	12	1.2
Enterococcus faecium	3	0.3
Other Gram-positive cocci	2	0.2
Gram-negative bacilli	741	75.1
Escherichia coli	313	31.7
Enterobacter spp.	182	18.4
Klebsiella pneumoniae	123	12.5
Pseudomonas aeruginosa	83	8.4
Proteus mirabilis	13	1.3
Serratia spp.	9	0.9
Citrobacter spp.	8	0.8
Klebsiella oxytoka	7	0.7
Other Gram-negative bacilli	3	0.3

DISCUSSION

Although miscarriage is considered the most common adverse pregnancy outcome worldwide, figures are for Ukraine is not available. The aim of this study was to find out whether or not the presence of early pregnancy loss and preterm birth was associated with the history of healthcare-associated infection of women reproductive tract. In our study, HAI women reproductive tract was detected in 68.4% fertile women by criteria from the CDC/NHSN Surveillance Definitions for Specific Types of Infections [19]. Of these cases, 1.7% pelvic abscess or cellulitis, 1.8% infection of the uterine appendages, 2.5% infection of the Fallopian tubes, 1.7% infection of the ovaries, 5.6% infection of the supporting ligaments, 11.3% chorioamnionitis,

15.8% infection of the vagina, 19.1% postpartum endometritis, and 9.1% vaginal cuff infection were identified.

In our study 73.8% women had the first trimester miscarriage, and the remaining 26.2% women had the second trimester miscarriage. When we examined the study population with of HAI, 72.8% women were detected as having the history of a early pregnancy loss in the last 6 months, 27.2% women had recurrent pregnancy losses. In the study population, 72.8% women with HAI had a history of early pregnancy loss in the last 6 months and only 27.2% women with HAI had recurrent pregnancy losses. According to the statistical data, a significant association between HAI and the history of pregnancy loss was determined. However, there was no association between HAI and the history of preterm birth. In additional, the effect of HAI women reproductive tract on the gestation periods was also examined. The presence of HAI had no effect on the first trimester miscarriage, but HAI women reproductive tract had strongly affected the second trimester pregnancy losses.

In our study many women who miscarry do not have any risk factors prior to their miscarriage. In contrast, some women have many risk factors for miscarriage, but end up carrying a normal pregnancy to term.

Reproductive loss is an inclusive term for women, related to reproductive health, fertility, the outcomes of a pregnancy, and includes experiences of miscarriage, stillbirth, infertility, abortion, pregnancy loss, and loss of a child.

According to literature, the definition of recurrent pregnancy loss differs among international societies. For the European Society for Human Reproduction and Embryology [2, 20], and the Royal College of Obstetricians and Gynaecologists [21]. recurrent pregnancy loss refers to three consecutive pregnancy losses, including nonvisualized ones. However, according to the American Society for Reproductive Medicine [6], it is defined as two or more clinical pregnancy losses, but not necessarily consecutive. Early pregnancy loss, also referred to as miscarriage or spontaneous abortion, is defined as the loss of a clinical pregnancy before 20 completed weeks of gestational age (18 weeks after fertilization) or, if gestational age is unknown, the loss of an embryo/fetus of <400 g. [22]. Ectopic, molar, and biochemical pregnancies are thus not included.[6].

We analyzed a large number of bacterial infectious agents to determine if they are associated with an increased risk of miscarriage. Further research is required to clarify whether certain infections do increase miscarriage risk. This issue is of particular importance for public health practitioners as it could alter current policies of prevention of infection, diagnosis and treatment in pregnant women.

CONCLUSIONS

This study identified a significant association between HAI of women reproductive tract and a history of miscarriage. However, there was no association between HAI and a history of preterm birth. For most of the bacterial pathogens the mechanism that leads from infection to miscarriage is unknown. Further research is required to clarify whether certain reproductive tract infections do increase miscarriage risk.

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The Authors declare no conflict of interest

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