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Abortion and bacterial causes in women

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Abstract

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Abortion is the termination of a pregnancy, either spontaneously (miscarriage) or intentionally (induced abortion). or it is define a spontaneous loss of pregnancy before 20 weeks. Intentional abortion ends 6 out of 10 unintended pregnancies. Approximately 97% of unsafe abortions occur in developing nations, accounting for Several bacteria are associated with abortion, most notably *Listeria monocytogenes*, *Chlamydia trachomatis*, *Mycoplasma hominis*, and infections linked to bacterial vaginosis**(BV)** which Characterized by a reduction in beneficial *Lactobacillus* species and an overgrowth of anaerobes like *Gardnerella vaginalis*, These pathogens can disrupt pregnancy by causing uterine infection, sepsis, or altering the vaginal microbiome. The maternal infections that are transmissible from mother to fetus are caused by many pathogens.

Introduction

A spontaneous abortion was defined as an involuntary loss of an intrauterine pregnancy before fetal viability (1). The WHO defines spontaneous abortion as the ejection of an embryo or the extraction of a fetus weighing 500g or less. This weight typically corresponds to a gestational age of 20–22 weeks (2). Septic abortion is an infection-related abortion that is complicated by fever, endometritis, and parametritis. It is still one of the biggest risks to women's health worldwide (3).

the bacteria linked to septic abortion are typically polymicrobial, originating from the natural flora of the vagina and endocervix with the significant addition of sexually transmitted infections (4). there are several ways for an infection to enter the intra-amniotic cavity (5). Transplacental spread of infection can happen in women with bacteremia, an infection of the abdominal cavity can spread through the fallopian tubes, but ascending infection from bacteria colonizing the vagina and/or cervix is the most common route (6). The endogenous vaginal microflora, the intestinal microflora, and sexual transmission are the three microbiologic origins of pelvic infections in pregnant women. The infection is caused by organisms migrating from the vagina through the endocervix into the uterus; some organisms may pass through the columnar epithelium, as is the case with infections brought on by Neisseria gonorrhoeae (4)

Six out of ten unwanted pregnancies end with an intentional abortion. Roughly 45% of abortions are performed in developing countries, where 97% of unsafe abortions take place. In addition to being a financial and social burden on individuals, communities, and healthcare systems, unsafe abortion is a significant avoidable cause of maternal death and morbidity and can result in physical and mental health issues(7)

Causes of Bacterial Infection

The relationship between these two infections and abortion are well documented, especially in extra-occidental societies where other causes of spontaneous abortion such as chromosomal abnormalities or hormonal irregularities are less frequent. The Bacterial vaginosis (BV) is a common vaginal infection that happens when some normal bacteria that live in your vagina overgrow, causing a bacterial imbalance (8). is commonly associated with so-called 'intrauterine infection'. Infection of the fetus in utero can cause a clinically apparent illness, severe abnormalities at birth, and in severe cases, fetal death. The link between intrauterine infection and adverse pregnancy outcome is strong (9). Many cases of infection can induce a pro-inflammatory response which can disrupt endocrine function in the placenta and cause preterm labor. Due to the fact that preterm labor is itself a cause of spontaneous abortion (10).

The causes of bacterial infection are those factors which throw the complex ecosystem of normal vaginal flora off balance, allowing overgrowth of potentially harmful bacteria. Vaginal flora is made up of a variety of bacteria and fungi which function protectively to defend the body against potentially harmful organisms (11). When the delicate balance of this environment is disrupted, infection can occur. This is essentially what happens when a woman develops bacterial vaginosis, an infection of the vagina caused by bacteria (12). An infection can cause the amniotic sac to break and rupture of the membranes is a significant risk factor for preterm birth (13). Streptococcus species, which can be separated and identified from the placenta and the aborted fetus, are the most common cause. *Escherichia coli, Pseudomonas species, Klebsiella species, and Staphylococcus species* are among the other organisms found (14).

The most frequent cause of abnormal vaginal discharge in women of reproductive age is bacterial vaginosis (BV). Approximately 30% of women who are of reproductive age have BV (15). Raised vaginal pH and milky discharge are characteristics of BV, where a mixed flora of aerobic, anaerobic, and microaerophilic species replaces typical vaginal flora (Lactobacilli). The vagina is mostly colonized by anaerobic organisms such *as Gardnerella vaginalis*, *Prevotella* spp., *Mycoplasma hominis,* and *Mobiluncus spp*. in BV (16*). Listeria monocytogenes, Chlamydia trachomatis, Mycoplasma hominis*, they also too cause bacterial vaginosis*. Neisseria gonorrhoeae* and *Chlamydia trachomatis* infections are examples of organisms that can pass through the columnar epithelium (4).

Symptoms and Complications

The Abnormal vaginal discharge, which is often yellow or green, accompanied by a strong odor, is frequently symptomatic of an infection. However, it is possible that such an infection has no symptoms, especially at the cervix(17) . In women, Neisseria gonorrhoeae bacteria can cause cervicitis or inflammation of the cervix, urethritis (inflammation of the urethra), and pelvic inflammatory diseases (PID) if the bacteria spread to the uterus and the fallopian tubes (18) . Up to 50% of women with symptoms of gonorrhea actually have a vaginal or bladder infection (19) .

Syphilis is the second bacterial that can affect fetal health. Although the prevalence of syphilis is very low in Canada today, rates are rising again after an all-time low in 2000 and it is still relatively common in other areas of the world (20). Infection with syphilis is quite complex and is staged by severity. Any pregnant woman with an unknown status or high-risk behavior should be tested for syphilis. This is especially important in the prevention of congenital syphilis, in which infection of the infant occurs transplacentally during any stage of the mother's infection and can result in late abortion, stillbirth, congenital infection, or infant death (21). Any person who has had a syphilis exposure in the last year should have a serological test at the time of the exposure and again in 3 months. This is used to rule out late seroconversion of an early infection (22).

Chlamydia can be simply diagnosed through a laboratory test ordered by a physician. There are several methods to test for chlamydia, but the two most common are cell culture and a direct stain test. Urine tests have recently been developed for detection of chlamydia using molecular amplification techniques and are becoming ever more popular due to their ease and relative low cost. If chlamydial infection is diagnosed, treatment should begin as soon as possible to minimize the risk of transmission to the infant, as mother-to-infant transmission during birth can cause eye infections and pneumonia in the newborn (23).

Chlamydia and gonorrhea are the two most common bacterial (sexually transmitted infections (STIs)associated with abortion and stillbirth. Both infections are generally asymptomatic in both men and women, but can cause serious damage to a woman's reproductive health if left untreated (24). Fortunately, in Canada, gonorrhea is a notifiable disease and physicians are required to report all cases to the local Medical Officer of Health. This enables tracking of the infected person's partners and identification of others at risk of infection (25) . If a woman is diagnosed with gonorrhea, it is important that she is referred to a clinic that specializes in the treatment of the disease to ensure eradication of the bacteria. This is especially important during pregnancy to prevent the transmission of the infection to the infant during birth (26) .

Treatment Options

Oral antibiotics are the treatment of choice. However, there's little information on the effects of antibiotics during pregnancy. Tetracyclines are contraindicated due to adverse effects on the fetal skeleton, and it is not recommended that they are used in the first trimester. Erythromycin is considered to be safe (27). During the second and third trimester, management should be as in non-pregnant individuals, with a single dose of azithromycin, erythromycin ethylsuccinate, or amoxicillin being effective against Chlamydia, and ceftriaxone as a single dose being effective against gonorrhoea ((28). The primary reason for recurring infections after treatment comes from re-infection from untreated or new partners. The above treatment should be repeated in these situations. Syphilis is treated with penicillin of varying dosages depending on the stage of the disease, the dosages being the same in pregnancy as in non-pregnant females (29).

The treatment for bacterial infection in pregnancy is not complicated and should follow the same lines as in any other non-pregnant female, with provision for it being safe in pregnancy (30). The initial step is to diagnose the infection correctly. Cultures for Chlamydia trachomatis, Neisseria gonorrhoea, bacterial vaginosis, and specific tests for other organisms need to be undertaken (31). A high vaginal swab is no longer considered sufficient. Testing for other sexually transmitted infections should also be considered (32).

Prevention Strategies

The most viable preventive measure that can be taken to reduce the incidence of abortion due to bacterial infections is vaccination. Efforts should be made to isolate and identify the most common abortifacient pathovars and then develop safe and effective vaccines to induce immunity to these specific pathogens (33) However, this is a long-term goal and would require a significant amount of resources. Availability of a commercial vaccine would offer an economical and viable method to control infection and reduce the incidence of abortion (34).

Another very common method to prevent abortion is the use of antibiotics. This can be useful if the specific cause of an abortion storm can be identified and the microorganism isolated and identified and its susceptibility to antimicrobial agents determined (35). The antibiotics can then be administered to prevent the carrier state or eliminate the agent from the carrier resulting in the prevention of subsequent abortions. Alternatively, knowledge of the common abortifacient organisms in a given area and their susceptibility patterns can lead to the development of strategic or preventative medication programs (36). For vaccines to be a viable control strategy over the long term, there needs to be an effective method of preventing abortion while the immunity is developing, and there is further research to be conducted to identify safe and effective chemotherapeutic agents for use in pregnant (37).

Impact of Bacterial Infection on Female Abortion

Finally, it is now understood that many bacteria and their associated products have an indirect effect on fetal survival. Such products range from endotoxins liberated from the cell wall of gram-negative bacteria, to antigen-antibody complexes, and have been demonstrated to cause fetal death and resorption mediated through the maternal immune response (38). This research effort has largely relied on murine models of disease, but this area of reproduction has the potential to unravel the mysteries of unexplained fetal loss in many species (39). Although not always possible, isolation of the organism and knowledge of its biology permit informed decisions about control of a specific agent and attempts to prevent similar losses in the future (40).

Bacterial abortion resulting from so-called "specific agents" may occur in epizootic form, with many animals becoming infected regardless of their pregnancy status. This pattern has been best described for several zoonotic bacterial infections in which pregnant women have been involved in research (anthrax-missing link, brucellosis, listeriosis) (41). In the later two processes, the information about reproduction in other mammals is largely inferred from what has been observed in human cases and studies in non-pregnant animals (42). Transmission of bacteria to the reproductive tract can be haematogenous or via lymphatics, but some bacteria have a tropism for the placenta and fetus following initial infection elsewhere in the body (43) . This has been shown to be the case with Listeria monocytogenes, which has caused numerous outbreaks of ovine abortion in North America and Europe. (44).The process of understanding the role of bacteria in female abortion follows the pattern set forth above for evaluating the various types of organisms. For purposes of this discussion, bacterial infections will be considered as acute (causing toxic illness or fever) or subacute/chronic (superimposed inflammation leading to late-stage abortion). Most of what we know about acute bacterial diseases comes from unintentional exposure of pregnant women (45). This generally occurs because all species of pathogenic bacteria can cause abortion, and the pregnant animal is always thought to be especially susceptible. The outcome of infection is often the same as in the non-pregnant state, but some bacteria are recognized as being particularly abortigenic (46).

Risk Factors for Bacterial Infection

Women are at particularly high risk for developing postabortal infection if there has been a delay in obtaining abortion services (47). In a study of all women in California who received Medicaid-funded abortions at facilities other than private physicians' offices - a group representing low-income women, two calculable rate ratios comparing infected abortion for women with delay of 28 days or more to those with a delay of 14 days or less, ranged between 2.47 and 2.49. Delay has also been associated with severity of infection, as measured by hospitalization for postabortal pelvic inflammatory disease which occurs in 10-15% of cases (48).

In both the California and Los Angeles County studies, the rate ratios comparing seven or more days of delay to one day of delay were about 1.5. High rates of infection morbidity were obtained for minority women in both studies as well (49). In the Los Angeles County work, rate ratios for various measures of postabortal infection for black or Hispanic women compared to white women ranged between 2.5 and 3.0. This suggests that in the population where availability of abortion services is most restricted, morbidity due to postabortal infection may be even more of a problem (50) . These observations stress the need for strategies to identify and treat infected abortions quickly in order to prevent morbidity. A corollary goal is to investigate the reasons for delay and develop methods to reduce it (51)

In the majority of women who contract infected abortions, little is known about the specific time and place of the original act of infection (48). This is because the symptoms of infected abortion are similar to those of the normal sequelae of abortion and may not become severe enough to warrant treatment(47). Thus, identification of women at risk for developing postabortal infection and appropriate antibiotic treatment could prevent much of the morbidity associated with this condition. Epidemiologic studies have shown that postabortal infection is associated with a number of factors apart from the type of abortion procedure itself (52).

Management of Bacterial Infection during Pregnancy

There are clearly defined regulations and ethical imperatives that influence the type of randomized controlled trial that can be conducted in pregnancy and the extent of investigation and treatment of lower genital tract infections (53) . Despite this, in the case of bacterial vaginosis, it is still unknown what is the best antibiotic to give. High dose metronidazole is contraindicated in early pregnancy, but there may be potential benefits to giving such treatment to women who are at a high risk of preterm delivery. Other antibiotics with minimal systemic absorption may be an alternative for this group of women (54) . Oral clindamycin has been shown to be effective at eradicating bacterial vaginosis and also reducing rates of preterm birth, but there is no data on whether or not it is safe to give in all stages of pregnancy. Topical treatments tend to be better tolerated by patients, and there are some data to suggest that vaginal treatment with metronidazole or clindamycin may be effective and safe in late pregnancy (55).

The management of bacterial vaginosis and other lower genital tract infections, ranging from simple screening and treatment to much more complex treatment algorithms for recurrent infection, all require careful consideration of the potential adverse effects on the pregnancy (56). In the case of bacterial vaginosis, there is also some evidence to suggest that screening and treatment in pregnancy may reduce the risk of preterm birth and preterm prelabour rupture of membranes. However, an effective intervention needs to be devised in a randomized controlled trial setting to confirm these findings (57) . In order to develop a rational management strategy, randomized controlled trials need to be conducted to determine the efficacy of treatment of lower genital tract infections on prevention of adverse pregnancy outcomes. This should involve treating symptomatic and asymptomatic pregnant women and following them up to determine the natural history of infection and whether it is transient or persistent, and whether there are any adverse effects of the infection on pregnancy outcome (58) .

At present, non-specific antibiotic therapy often fails to prevent infection associated preterm birth, with nearly 50% of cases demonstrating microbial invasion of the amniotic cavity, and approximately 25% being diagnosed with clinical chorioamnionitis (59). Although antibiotic treatment of these cases will reduce maternal colonization of pathogenic bacteria and morbidity, the rate of spontaneous preterm birth and fetal death remains high, indicating a requirement for antibiotics that are more effective at eliminating infections within uterine tissues (60).

Characteristics of some pathogenic bacteria that make treatment of associated infections difficult include the ability to form biofilms and invade host cells, and possession of multiple antibiotic resistance mechanisms (61). Antibiotic resistance is the ability of a microorganism to withstand the effects of antibiotics and occurs through a variety of mechanisms, some specific to individual antibiotics, whereas others enable resistance to an entire group or class of antibiotics. The resistant phenotype can be acquired through mutation of chromosomal genes and selection of advantageous genotypes in the presence of antibiotics, or horizontal acquisition of resistance genes, for example, through plasmid transfer (62) . Selection of resistant strains can arise from a single course of antibiotic treatment and increase the difficulty in eradicating infections, as alternative antibiotics may be less effective, more toxic, or unavailable, and treatment failure contributes to increased morbidity, healthcare costs, and progression of infection to long-term complication (63).

Multiple antibiotic resistance mechanisms often possessed by pathogenic bacteria cause a serious global health problem, and there has been an exponential increase in antibiotic resistance with a relative decrease in development of new antibiotics (64). This presents a challenge for treatment and prevention of infection associated pregnancy complications, particularly in cases of abortion related to severe fetal abnormalities where termination of pregnancy may not be considered if there is no means to eliminate intrauterine infection and prevent further complications (65). Alternative strategies for development of antibacterial agents include anti-virulence drugs which do not affect bacterial viability but instead inhibit pathogenic mechanisms, and use of immunomodulatory agents or probiotics to enhance host immunity and bacterial clearance (66) .

Public Health Considerations

In light of the potential costs, an evaluation of the true impact of pelvic inflammatory disease on the public's health is of much importance. A rough judge can be made by the incidence of acute salpingitis, as physicians can differ in their diagnosis of milder cases of PID. If 1 million cases occur annually, by some estimates, the untold cases accumulated over several years, 10% of which will result in chronic tubal changes, could be as high as 20% (67). This leads to around 100,000 cases of tubal factor infertility or ectopic pregnancy each year. Although, in terms of personal suffering by the infected individuals, severe PID is the main offender and recurrent infection can be a source of much misery. These problems, however, are not a public health concern because they come to a halt in the absence of further infection (68).

This section discusses sterilization of infected women in relation to public health. Previous to 1970, the most readily available means of sterilization in the United States was the bilateral tubal ligation (69). This generally occurred after a cesarean section, although at times, some women were sterilized without knowledge or consent. After the public revelation of the eugenic abuses, most states and the federal government established laws and regulations requiring specific written consent and clear statements that the procedure will not deprive the patient of any public assistance (70).

There are still accusations of abuse, such as in the 1973 case in which Mexican women in a Los Angeles County Hospital were allegedly sterilized without proper consent. This brings us back to the question of whether the end justifies the means. It has been suggested that sterilization of infected women could greatly reduce the incidence of premature birth and neonatal death due to incompetent cervix (71). This could potentially be a valid prophylactic method, as worsening pelvic inflammatory disease can lead to chronic tubal changes and repeated infection. The rub is, given the reproductive potential of young women, it is unlikely that sterilization is a sound control measure for any infection short of one causing debilitating illness (72). Unfortunately, while surgical contraception has a very low failure rate and can be cost-effective, it carries permanent implications and alternative long-term methods such as oral contraception may be vulnerable to compliance and usage failure (73).

Research and Future Perspectives

Bacterial infection in the reproductive life of women and its association with female infertility and complications in pregnancy has been increasingly realized. While we now have some knowledge of the affected disease processes, clinical effect, and its effects, optimal treatment is still uncertain (74). The knowledge gained about the nature of bacterial/host interactions and the immune response caused by pathogenic bacteria will allow the development of adjunctive therapies to either ameliorate the effect of the infection or prevent the disease process (75). The former will involve a new approach in the use of anti-inflammatory drugs around the time of antibiotic administration (76).

Immunomodulation therapies might also be useful. If understanding of the disease process is sufficient, it might be possible to develop new agent-specific therapies that will prevent certain aspects of the disease (77). Given the importance of the initial interaction of the pathogen with the host, it may be feasible to develop bacterial receptor blockade therapies. The best example of this is the development of vaccines to prevent infection by leading to the eradication of the disease (78). While vaccine development for the common sexually transmitted infections is unlikely to be a high priority for pharmaceutical companies, public health management of these diseases with the development of free vaccination programs could be the most cost-effective (79).

Conclusion

A large percentage of pregnancy losses worldwide are caused by bacterial infections, which are a major cause of spontaneous abortion (miscarriage) and stillbirth

It is important to look out for the above symptoms of post-abortal infection. Occasionally, a woman may have no symptoms, and the condition may be found later during a routine examination by a doctor (80). An infection can be serious if not treated, and in severe cases, it can lead to infertility. Although the link between infertility and post-abortal infection is not definite, prevention of infection is by far the best option for continuing good uterine health (81).

There are three main ways in which the uterus can become infected. The most common cause of infection is from an incomplete abortion, in which parts of the fetal tissue are left in the uterus(82). The second common cause is after giving birth the bacteria can enter the uterus through the cervix when it is open; the bacteria can then breed in the lining of the uterus. The third cause is from miscarriage Often, with a miscarriage, the uterus is not completely emptied of fetal tissue (83). This provides an opportunity for bacteria to enter the uterus and cause an infection. This can occur if the woman has had a miscarriage at home and performed a self-abortion (84).

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