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Candida albicans and Abortion

Humam Kasem Hussein

Abstract

An abortion that occurs spontaneously is known as a miscarriage. Various effectors associated with abortion such as Genetic and uterine anomalies, Endocrinopathy, immunological dysfunctions, infectious agents, environmental contaminants, psychogenetic elements, and endometriosis. Maternal infections considered the main reason for pregnancy wastage in females with Bad Obstetric History (BOH). *Candida albicans* is a dimorphic fungus that can grow as yeast or filamentous cells and considered one of the limited species of the *Candida* genus that cause humans candidiasis. It is an opportunistic fungus that responsible for mucosal infections in the mouth and genital tract. Excessive growth of *C. albicans* will follow with Vulvovaginal candidiasis (VVC). The incidence of VVC combined with chronic recurrent candidiasis is high in pregnancies than in healthy women. Several scientific researches showed the significance of VVC as an inducer of abortion, candida chorioamnionitis, subsequent preterm delivery, and immunosuppression.

Keywords: *Candida albicans*, Opportunistic fungi, Spontaneous abortion, VVC, Candidemia

1. Introduction

Mycoses considered as most ancient infections, established by Hippocrates and Galen. The fungal infection may be acute, chronic, superficial, or deep [1]. Every year, invasive candidiasis infects about 250,000 persons around the world, which leads to more than 50,000 deaths [2]. In the 19th century, mycoses fixed as infections of newborns and the genital tract in gestation and how affected by each other. The vaginal infections that resulted from yeast-like fungi of the *Candida* genus are the main infections during pregnancy [3]. Even with the presence of placenta and fetal membranes as protective sheets of him against infections, the embryo maybe infected with fungi via ascending (from the vagina) or hematogenic routes in exceptional cases. *Candida albicans* can cross that barrier without damage to the membranes. Watching the placenta plays an important role in the diagnosis of congenital candidiasis [4]. Many infants born at the 23rd week of gestation in serious conditions with congenital candidiasis and the invasion of the membranes by *C. albicans*. Intrauterine infection with *C. albicans* leads to the raising of inflammatory parameters in maternal blood (leukocytes, C-reactive protein, procalcitonin) that also detected in the child blood after delivery. So, early termination of pregnancy becomes prefers [5].

2. Abortion

Termination of the gestation by removing fetus or embryo prior to gaining the ability to survive outside the uterus is called abortion. Nevertheless, if this process happens after the fetus acquires this ability, then it is termed a “late termination of pregnancy“. If the abortion occurs spontaneously, it is termed a miscarriage. In addition, it is titled an induced abortion or “induced miscarriage” if it resulted purposely [6].

Induced abortion does not raise the risk of mental or physical complications if it ensues under legal and secure conditions [7]. Every year nearly 56 million abortion cases happen worldwide [8], half of these cases ended unsafely [9]. Unsafe abortion is considered one of the main challenges of public health in Africa and Middle East areas. In 2003, 1.5 million abortions occur in these regions in unhygienic and unexperienced conditions according to World Health Organization (WHO). From those abortions, 11% of the cases were ended with maternal death. Increasing family planning and birth control make the rate of abortion decline and that what happened in the last two decades globally [10].

In general, the causes of miscarriage are different. Several factors that can form a high degree of risk on pregnancy have been recognized. Health and medical causes have a high rate of incidence in recurrent than in spontaneous miscarriages. Cytogenetic abnormalities are probable reasons for miscarriage particularly earlier to the 9th week of gestation. Autosomal trisomies are the most common chromosomal abnormalities then 45X and triploidy. Gene inactivation in the 4 to 8 cell stages karyotype supposed to be responsible for the non-recognized cases of abortion at an earlier period of gestation.

Miscarriage also occurs by anomalies in the uterus configuration such as the bicornuate and septate uterus, which consider as congenital defects. In addition, submucosal or intramural myomata may lead to early miscarriage [11]. Occasionally, women with spontaneous miscarriage may have endocrine and autoimmune irregularities. The danger of miscarriage will increase in pregnancies who suffered from Hypothyroidism and Polycystic Ovarian Syndrome (PCO). In addition, those with low control on their blood glucose level especially in insulin-dependent diabetes mellitus [12]. The incidence of miscarriage will upsurge with the progression of maternal age. The rate of recurrence increased from 12% before 25 years to 18% after 39 years. At higher ages, anembryonic pregnancies are frequently prevalent. Menarche and menopause are the main factors that influenced maternal age. Social, economic and, cultural situations also affect the preferred family size and period between gestations [13].

Besides smoking, exposure to environmental tobacco smoke (also called passive smoking) holds the same possibility of abortion's occurrence [14]. Consumption of alcohol, caffeine also described as a weak and debatable risk factor of pregnancy loss [15]. Employments with high levels of stress are associated with spontaneous abortion [16]. Miscarriage also resulted from genital infections. *Mycoplasma hominis* and *Chlamydia trachomatis* are established as inducing factors of miscarriage existence. Pregnant women with bacterial vaginosis may be exposed to the risk of late miscarriage [17]. Bacterial vaginosis may follow deficient in lactobacilli with overgrowth of anaerobic bacteria, as well as *Mycoplasma genitalium* and *Gardnerella vaginalis* [18]. Primary infection with genital herpes will increase the risk of miscarriage existence. In addition, other infectious agents such as *Rubella*, Toxoplasmosis, *Cytomegalovirus* and, Listeriosis also fixed as probable causes of miscarriage. *Candida* species are the second most common cause of vulvovaginitis worldwide and *C. albicans* is the most common and clinically significant species

that cause vulvovaginal candidiasis. Untreated vaginal candidiasis may lead to a pelvic inflammatory illness that scar the fallopian tube followed by infertility.

2.1 *Candida albicans*

A dimorphic fungus that can grow as yeast or filamentous cells and considered one of the limited species of the *Candida* genus that cause humans candidiasis [19]. 50–90% of all cases of humans' candidiasis are result from *C. albicans* [20]. Systemic fungal infections (fungemia) caused by *C. albicans* appeared as significant foundations of morbidity and mortality in immunocompromised patients (e.g., AIDS, cancer chemotherapy and, bone marrow transplantation). Today, hospital-acquired candidiasis became a source of major health anxieties.

Candida albicans is a common human flora that noticed in the gastrointestinal tract of 40% of healthy adults [21]. It is commonly a commensal creature, nonetheless, it can turn out to be pathogenic in immunocompetent individuals under various conditions. Candidiasis also can happen due to excessive growth of the fungus, which recurrently detected in immunocompromised cases including HIV-infected patients. It usually befalls the mucous membranes of the mouth or vagina in addition to a number of other parts of the body [22].

2.1.1 Fungal genome

The genome of *C. albicans* characterized by numeric rearrangements of chromosomal structures leads to creating genetic rearrangements called chromosome length polymorphisms, reciprocal translocations, and chromosome deletions. These karyotypic modifications followed by changes in the phenotype, which consider a fungal strategy of adaptation. Two species of candida (including *C. albicans* and *C. tropicalis*) have an uncommon trait in which the CUG codon, which usually specifies leucine, in these species it encodes serine. The main feature of *C. albicans* genome is extremely dynamic, and this changeability is a higher benefit for molecular, epidemiological, and population researches for this species [23].

2.1.2 Heterozygosity

The heterozygosity of the Candidal genome surpasses that persist in other genomes is common among clinical isolates. Two proteins ensued via single-base polymorphisms vary in one or more amino acids will provide the functional variances of each protein. Therefore, this condition significantly raises the number of diverse proteins encoded by the candidal genome [24].

2.1.3 Biology of *Candida albicans*

Candidal colonies seem large, round, white, or cream that emanates a yeasty odor on agar plates at room temperature when grown *in vitro* [25]. By fermentation process, *C. albicans* consumes; glucose and maltose and produce acid and gas, sucrose to acid, but does not ferment lactose, this was a benefit in distinguished it from other *Candida* species. Recently, molecular phylogenetic researches confirm a polyphyletic character in the genus *Candida*. Previously, most yeast that isolated from infected individuals regularly called *Candida* even in absence of a clear indication of relationship to other *Candida* species until the development of molecular methods. For example, three species of candida

which are *C. guilliermondii*, *C. glabrata* and *C. lusitaniae* were misclassified and positioned in other genera until the evolution of phylogenetic reorganization [23].

2.1.4 Epidemiology

Many regions of the human body like skin and mucosal surfaces are inhabited by numerous candidal species, this colonization carried a commensal nature with the host. The immune condition of the individual plays an effect on the severity of the *Candida* infections, so, any disturbance in immunity increase the percentage of the host's illness make the host more susceptible to infection with candidiasis. In immunocompromised patients, Candidal infections create main fungal infections [26]. Generally, oropharyngeal candidiasis is the primary illness presented in those patients, because of that malnutrition developed leading to restriction of the action of the treatment [27]. These invasive infections have many challenges against public health lead to cumulative health and economic significances because of the great mortality proportions and amplified expenditure of medical care [28].

Skin, mouth, throat, genitals, and blood are the main body regions that are usually infected with candidiasis. Generally, *Candida spp* sustains as the fourth supreme isolated pathogen from bloodstream infections (BSIs). Most cases of candidaemia are caused by *C. albicans* have been associated with a high mortality rate, while the non-*albicans* species are responsible for about 23% of candidemia collectively with the rare incidence of mortality. Virulence of these species depends on many elements; capability of biofilms creation, the existence of teleomorph forms, therapeutic difficulty, and resistance to conventional antifungal medicines [29]. Candidal nosocomial infections determined by organ transplantations, an increase of immunosuppression cases, and the clinical procedures that required the usage of invasive devices [30].

2.1.5 Host predisposing factors

Besides the commensalism interaction between *Candida* species and humans and the fundamental existence of it in healthy persons, recent two decades showed an unusual overgrowth in respiratory, gastrointestinal, and urinary tracts in comparison with earlier periods. Shortly after childbirth, species colonize the mucosa of the upper respiratory passages and gastrointestinal tract. Habitually, *C. albicans* exists fluently in the internal warm crinkles and fissures of the gastrointestinal tract and vaginal tract. Candidal colonization rises nearly to 30–40% during pregnancy due to disturbance of immunity, bacterial flora, and pH level variations, while about 10% of these species are found in mucosa and skin of the genitalia in men [31].

2.2 *Candida albicans* and pregnancy

During pregnancy, females exposed to many physiological changes. Gestation is a complicated condition in fetal development that requires various essential substances such as glucose, fatty acids, amino acids, minerals, and vitamins. These nutrients must continuously apply to improve the process of fetal growth and to protect the health condition of pregnant women. Many pathogens that responsible for several sexual and non-sexual transmitted infections invade the women's bodies through the female genital tract (FGT), leading to vaginal infections. The common clinical symptom for female genital tract infection is vaginal discharge, which considers as the second main gynecological problem after menstrual disorders [32]. Vulvovaginal candidiasis (VVC) (also called candidal vaginitis or

moniliasis) initiated by an overgrowth of candida yeast species mainly *C. albicans*. The main features of this disease are curd-like vaginal discharge, itching, erythema, burning, vulvar and vaginal irritation associated with dysuria and dyspareunia [33]. *C. albicans* overgrowth causes superficial infections such as vaginitis that are usually associated with an immuno-compromised state mucosal candidiasis. Scientific researches fixed that near to 75% of women undergo at minimum one incidence of a genital yeast infection at reproductive years of them, In addition, about 10–20% of women acquire asymptomatic vaginal colonization with Candida species during their life. While 5–10% of healthy women suffering from recurrent vaginal candidiasis without any predisposing factors. In the presentation of chronic recurrent candidiasis, pregnant women are less resistant to VVC in comparison with healthy women. The forms of infection may be acute, chronic, superficial, or deep. During pregnancy, rising in estrogen level will be followed by increasing in glycogen production in the vagina, which improves the proliferation of the yeast on the lining of it. Alterations in physiological conditions that affect the beneficial bacteria in the vagina would change the vaginal acidity reducing its pH to 5.0–6.5. This alteration in pH will increase the overgrowth of pathogenic *Candida*. Several factors such as age, menstrual cycle, sexual activity, pregnancy, and excessive use of antibiotics may lead to an increased vaginal pH [34].

Colonization of the vagina by Candida species may be enhanced by numerous factors such as pregnancy, weak immunity, obesity, diabetes, prolonged use of corticosteroids, HIV, malnutrition, consumption of high level of estrogens, Intrauterine Contraceptive Device (IUCDs), tight clothing, poor personal hygiene, intrauterine devices and diet with high carbohydrates contents. VVC is a significant infection that may lead to abortion, candida chorioamnionitis, subsequent preterm delivery, and suppression of the immune system. Even with the isolation of Other candida spp (*Candida tropicalis*) from aborted placenta [35], *C. albicans* considered the main one that can invade the fetal membranes. Uterus infection with candida may be occurring via the usage of IUD that might hold the yeast from contaminated external genitalia into the uterus. In many cases, the pregnancy occurs even with the presence of IUD and that may lead to candidal abortion [5]. In addition, the probability of the presence of *C. albicans* in the uterus was referred to transmit of that yeast via seminal fluid, giving some proves about the role of the male as a reservoir of *C. albicans*. This may lead to re-infection of their sexual partner besides the isolation of that yeast from the genitalia and from semen [36]. In general, the infected male stays asymptomatic carriers and that will add another difficulty to control the yeast spreading. Although its ubiquity in the vagina, intra-amniotic infection with *C. albicans* is rare and that explained the few isolates that detected from the aborted placenta [37].

3. Conclusion

Candida albicans is one of the major normal microbiota found in the human body. It converts to opportunistic microorganisms when the host underwent several physiological and pathological conditions. In pregnant women, it can reach the placenta either by cause ascending infection from the vagina or by infected seminal fluid, which may lead to abortion.

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