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Brucellosis and its relationship to miscarriage in pregnant women

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Abstract

Brucellosis, worldwide prevalent zoonotic disease also consider a major public health concern predominantly in developing area where livestock and humans cooperate frequently. Brucella is cause by *Brucella* species for instance *Brucella abortus* and *Brucella melitensis* then it is transmit primarily via direct contact with infected animals or the ingesting of unpasteurized animal products. Brucella has role in spontaneous abortion in women link between brucellosis and mistake in pregnant women is receiving cumulative attention. Developing indication proposes that brucellosis can restrict to triggering inflammatory responses, specific peripheral tissues, and harm to the embryo, donating to opposing pregnancy consequences, with miscarriage and stillbirth, where the neonatal begins to convert infected. Diagnosis remains interesting in pregnant women because of symptoms are nonspecific and restrictions of serological test difficult molecular methods for detailed detection. Treatment are further complicated by essential to endorse maternal efficacy and fetal safety with routines often narrow to rifampicin and trimethoprim-sulfamethoxazole via pregnancy. Brucella infection endures to carriage an important social and economic load, emphasizing need for developed diagnostic strategies, improved clinical consciousness and safe therapeutic involvements designer exactly to pregnancy. Association with miscarriage is dangerous to successful maternal health consequences and easing public health worries in endemic regions. Aim to understanding link between brucellosis and miscarriage in pregnant women.

Keywords: Brucellosis, miscarriage, pregnant, public health, treatment.

Introduction

. Brucellosis, generally famous as “Malta fever” ,“Mediterranean fever” is a lead reason of zoonosis universal produced by bacteria genus *brucella*. *Brucella* is gram-negative, aerobic , facultative intracellular ,non-fermenting, non-motile, non-spore-forming, cocci, short rods or coccobacilli base on DNA homology and be sole species[1]

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In pregnant women, Brucellosis is occasional disease which is related with several obstetric problems include Consumption of unpasteurized dairy product , specially raw milk, , butter, soft cheese and ice cream, is greatest public mode of transmission[2]. Transmission through Human-to-human because of tissue transplantation, blood transfusion, breastfeeding, congenital transmission, sexual contact, and hospital infection has also been conveyed in rare cases[3]

Brucellosis in pregnancy allied with adversative consequences for instance spontaneous abortion, chorioamnionitis, preterm delivery, and fetal death. [4] . Still, it is not pure whether consequences are more public than in other infectious diseases[6]. Occurrence of abortion is greater and ready therapy be able to be life-saving for fetus[5].

Brucellosis offerings insistent challenge in regions universally, particularly Middle Eastern countries for instance Iraq. The country has contended with brucellosis subsequently its early isolation in 1937 [6]. In Iraq, small reflective sector, including sheep and goats, play a vital role in maintenance nation's food security. Lately, Iraq is household to an valued 7–8 million sheep then 1.5–2.0 million goats, serving such as major cause of meat and milk production however given that livelihoods and constancy to those affianced in agriculture [7]

Aim to understanding link between brucellosis and miscarriage in pregnant women.

Brucellosis

Brucellosis is recognized by WHO as one of seven-neglected zoonosis because of its predominant nature and vital socioeconomic problem, specifically in endemic areas [8]. *Brucella* is consider intracellular pathogen which displays a extensive spectrum of clinical performances in humans that extending from acute febrile infection to chronic devastating conditions distressing multiple organ systems [9]. Clinical manifestations comprising fever, night sweats, malaise and arthralgia [10].While nonspecific symptoms often cause misdiagnosis that is more difficult to precisely assess true occurrence and impact of disease [11]

Implications in Public health

Brucella infection residues major public health worldwide largely because of obstinate zoonotic infections and inherent problems in diagnosis [12]. Different species within genus *Brucella* for instance *B. abortus*, *B. miltensis*, and *Brucella suis* that infect a widespread range of animal hosts generating reservoirs which preserve transmission to humans which often breath of contaminated aerosols [13]. *B. abortus* and *B. melitensis* are considered zoonotic potential that mainly infect respectively sheep ,goats and cattle that often related with cases of brucellosis in humans [14]. *Brucella melitensis* biotype three has been recognized as a source of miscarriage in pregnant women, which are through consumption of unpasteurized milk [15]

In human, brucellosis is remains high that especially in resource limited settings where *B. abortus*, *B. melitensis*, and *B. suis* are endemic and exceedingly virulent to both human and natural hosts [16] .

The economic losses attributed to brucellosis in cattle are significant, including reduced milk production, infertility, and spontaneous abortion, exacerbating poverty in affected areas[17,18] .

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In humans, brucellosis is characterized by nonspecific symptoms for instance undulant night sweats, fever, weight loss, splenomegaly, joint pain, muscle pain and depression with chronic manifestations that may lead to severe complications for instance neurobrucellosis, osteoarticular brucellosis and endocarditis, the latter being a occasional but fatal outcome [19]. The projected global incidence of human brucellosis, although often underreported due to diagnostic challenges and surveillance limitations, is substantial, with some sources citing figures ranging from 500,000 to over 12 million new cases annually [20]

In endemic areas, prevalence of human brucellosis is significantly higher among occupational groups for instance farmers and slaughterhouse workers, confirming the role of direct contact with animals in disease transmission [21,22]. Public health efforts in affected areas that have to address in elevation healthcare costs requisite for diagnosis and treatment which along with non-health expenses owed to public education to diminish disease transmission [23]. Brucellosis is existing in numerous forms comprising prolonged convalescence or chronic local infection ,relapses and is often revealed by symptoms such as joint pain, fever, sweating, splenomegaly and hepatomegaly [24.]. Incubation period of *Brucella* infection varieties from (5 to 30) days that it can be highly flexible and may extend much lengthier depending on infection with Brucella species and size of sample [25.]

Brucellosis in pregnant women

There are relationship between infection of *brucella* and miscarriage in pregnant women; the bacteria's transferring to reproductive tissues and their capability to encourage inflammatory responses that can directly affect integrity of placenta and fetal viability[26]. Bacteria existence intracellular, in macrophages enable them to escape host immune responses thus leading to persistent infections, which can cooperation maternal and fetal health[17]. This positioning to reproductive tissues particularly placenta, is supposed to be intermediated by factors such as erythritol that acts as growth promoter for *Brucella* species consequently enabling their multiplication and pathological effects indoors pregnant uterus [27]

In women, spontaneous abortions could be related with isolation of *brucella* from placenta of an aborted fetuses[28] . It is trusted which brucellosis reasons less spontaneous abortions in humans than it does in animal owing to the lack of erythritol in human placenta and fetus[29] . Erythritol is a component of normal ungulate fetal and placental tissue , in cases of abortion in bovine, encourages devastating infection of fetus and placenta. Furthermore, reason for slighter starring role of abortion in human brucellosis is existence of anti-brucella activity in human amniotic fluid[30].

While selective accumulation within placenta can cause inflammation in placental and uterine then ensuing disruption of fetal-maternal interface, eventually leading to spontaneous abortion [15]. The influence of *Brucella* infection extends elsewhere direct fetal loss such as infection of pregnancies that lead to premature births, little birth weight, and infect of neonate, increasing load of opposing pregnancy consequences [15]. Systemic inflammatory response reason by infection with Brucella that contribute to adversative consequences by stimulating contractions of uterine and impairs placental blood flow, additional negotiating fetal growth [31].

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- Brucellosis is an vital health problem in endemic regions، for instance India ,South and Central America , Mediterranean basin, Balkans, and Middle East. Turkey is between endemic areas with rate of 25.7 cases per 100,000 population [32]. Brucellosis is unusual in pregnancy, with incidence in endemic areas from 1.3% to 12.2% 3-5 [33].

Above 500,000 new cases of brucellosis are described worldwide respectively year, with about 10 cases per 100,000 populations [34]. Nevertheless, this statistic might undervalue true epidemiological scope, with estimations proposing 5,000,000 to 12,500,000 cases per year [35] . Twelve species of Brucella, showing favorites for numerous hosts, have been identified [36]. Utmost human brucellosis cases are related to *B. melitensis*, *B. canis B. abortus* and *B. suis* [37]. These have isolated from ungulate, predominantly livestock, as chief cause of human infection [38]. Exactly, *B. suis* infects pigs, *B. abortus* infects cattle, *B. melitensis* infects sheep and goats, and *B. canis* infects dogs [39] (Bukhari, 2018).

Diagnosis

In cases of miscarriage, there are often a major challenge because of nonspecific nature of its clinical symptoms that easily complicated with other public complication in pregnancy or febrile infections[40]. Serological tests may yield false negative results in initial stages of infection or in individuals with immunocompromised, requiring a multimodal diagnostic test comprising method of culture and molecular test for definitive diagnosis [41]. Diagnostic test is necessary joining clinical suspicion, serological tests such as the Rose Bengal test and aggregation test beside molecular methods like PCR that given intracellular nature of organism and its predilection to chronic infection [42].

Gold diagnosis remains bacterial culture still its sensitivity is often limited by slow growth of Brucella spp. [43,44] . Novel molecular test are real-time PCR that proposal-improved sensitivity and specificity for direct finding of bacteria incapacitating restrictions of culture method and specified faster results [45].

Treatment

Treatment is complicated by need to balance maternal treatment efficiency with fetal safety that uttering careful selection of antibiotics to escape teratogenic properties [46]. As a result, treatment regimens typically exclude tetracyclines and aminoglycosides, instead opting for combinations of drugs such as rifampicin and trimethoprim-sulfamethoxazole, mainly throughout second and third trimesters of pregnancy owing to their known safety profiles during pregnancy [15].

The ideal duration of treatment for pregnant women residues a subject of ongoing research, although most recommendations propose extended courses to reduce the risk of relapse and improve maternal and fetal outcomes [47]. Administration of sulfamethoxazole and antipyretics to pregnant patient that resulted in miscarriage even with treatment [5]. Managing Brucella infection in pregnancy and underlines urgent need for early diagnosis and suitable and safe treatment interventions to evade adverse consequences [48,49].

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Immune response in *brucella*

Innate immune system, encompassing anatomical barriers, secretory molecules, and cellular populations similar phagocytes and innate lymphocyte subsets, forms initial defense against *Brucella* infection [50] . Later, adaptive immune system, comprising T and B-lymphocytes, is activate, targeting pathogen via humoral responses and cell-mediated[51] . Whereas brucellosis is mainly identifyd as a zoonotic disease, usually transmitted via contact with infected animal or consumption of unpasteurized dairy products, its expression in pregnant women offerings sole challenges due to possible vertical transmission[52].

The clinical complications of brucellosis in pregnant women are diverse and nonspecific, and include symptoms for instance fatigue, fever, and joint pain often leading to misdiagnosis[53 54] .

Besides, disease can considerably affect pregnancy consequences, with rates of spontaneous abortion and stillbirth alternating from 31% to 53% [55]. In addition to direct fetal loss, Brucella infection during pregnancy is allied with augmented risk of preterm birth, intrauterine growth restriction and neonatal sepsis [53] .

Maternal bacteremia, disseminated intravascular coagulation, toxin production, and acute febrile reactions are thought to contribute to these opposing pregnancy results, predominantly impulsive abortion and intrauterine fetal death [56] .

In fact, laboratory studies have exposed which *Brucella* can replicate inside human trophoblasts, subsequently interfering with the invasive ability of trophoblast-like cell outside the villus and inducing proinflammatory responses, wholly of which likely donate to these pregnancy complications[53] .

This ability to replicate intracellularly in placental tissue highlights a critical mechanism by which Brucella can directly influence fetal viability and maternal health during pregnancy[57] .

Notwithstanding the serious values detected in animals, where reproductive failure is a symbol of brucellosis, spontaneous abortions in humans owing to brucellosis are fewer frequent, perhaps because of lack of erythritol in human placenta and anti-*brucella* activity in amniotic fluid of human [54] .

Nevertheless, this does not disprove significant risk stood by Brucella infection throughout human pregnancy, as demonstrated by information of miscarriages consequence from Brucella melitensis [55].

Specific case study things to see second-trimester spontaneous abortions credited to Brucella melitensis, highlighting direct role of pathogen in adverse pregnancy consequences [55].

These points to the urgent need to strengthen surveillance and diagnostic strategies for brucellosis in pregnancy, particularly in endemic areas to ease risk of maternal and fetal complications[55] .

The occurrence of brucellosis among pregnant women, especially in agro-pastoral communities, features the need for complete screening and treatment rules to defend maternal and fetal health [56].

Pathogens such as cytomegalovirus, herpes simplex virus, Plasmodium falciparum ,Toxoplasma gondii and Listeria monocytogenes are known to cross maternal-fetal barrier then leading to opposing fetal consequences, importance broader challenge in handling infectious diseases throughout pregnancy [58] .

Considerate mechanism of infectious agents' development during pregnancy is serious for developing real vaccination strategies and realizing immunization protocols that guard pregnant women, their fetuses and newborns [59] . Infection throughout pregnancy postures an important threat to reproductive health and can cause preterm birth, stillbirth, or congenital infection via vertical transmission[60] .

Conclusions

Brucella infection remains persistent zoonotic threat with profound inferences for maternal and fetal health mainly in endemic areas. However, role Brucella in miscarriage in animals is well recognized that growing indication proposes a comparable link in pregnant women, when Brucella infection can upset function of placenta and threaten fetal existence.

Diagnosis tests that result from lack of specific clinical presentation and confines of conventional test, often interval timely diagnosis and treatment, increase risk of adverse consequences. Treatment during pregnancy entails a subtle balance between efficacy of maternal and safety of fetal, demanding cautious selection of antibiotic procedures.

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Author's Declaration

- We have obtained ethical clearance for our study from the local ethical committee at [Al-Nahrain University/College of Biotechnology]. This approval underscores our commitment to ethical research practices and the well-being of our participants.

Author's Contribution Statement

First Author and Second]: Contributed to the conception and rearrangement and drafted the manuscript.]

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