



Study of Anaerobic Bacterial Infections in Iran, Are They Important?

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ANAEROBIC bacteria can either alone or in association with other microorganisms lead to various diseases such as oral infection; anaerobic bacteria do not perform oxidative phosphorylation. Air-tolerant organisms have only non-oxidative metabolism but are resistant to oxygen for reasons such as the presence of these enzymes. *Clostridium difficile* is caused by bacteremia. Recovery from the infections caused by anaerobic bacteria requires prompt and proper management and treatment. The isolation, identification, and eradication of anaerobic bacteria can become complicated, challenging, time-consuming, labor-intensive, and expensive. A few studies have addressed anaerobic bacterial associated-infections (ABAI), but recently this idea has acquired attention in Iran. So, in this study, we reviewed various aspects of ABAs addressed in Iran. Anaerobic bacteria can either alone or in association with other microorganisms lead to various diseases such as oral infections, *C. difficile* infection, and bacteremia. Recovery from the infections caused by anaerobic bacteria requires prompt and proper management and treatment. The isolation, identification, and eradication of anaerobic bacteria can become complicated, challenging, time-consuming, labor-intensive, and expensive. A few studies have addressed ABAs, but recently this idea has acquired attention in Iran. So, in this study, we reviewed various aspects of ABAs addressed in Iran.

Keywords: Anaerobic bacteria, *Clostridium difficile* infection, Bacteremia, Oral infections.

Introduction

ABAs are relatively common but undoubtedly among the most overlooked bacterial infections. As they dominate the diagnostic flora, anaerobic bacteria are particularly important and frequently associated with a range of infections, from severe to even lethal. Some anaerobic bacteria may cause infections all by themselves, but mixed infections mediated by anaerobic and aerobic bacteria are challenging. In such cases, anaerobes can be completely overlooked unless culturing is performed carefully to recover all types of infection-causing bacteria [1, 2]. Recovery from the infections caused by anaerobic bacteria relies on immediate and effective management [2] that

can be warranted by a variety of actions such as suppressing their proliferation and spread to other body tissues and inhibiting the toxins produced by them [3]. Therapeutic options for mixed (anaerobic and aerobic) bacterial infections are limited, and there are even more challenges with drug-resistant infections among these groups of organisms. In fact, several antimicrobials have been shown to present poor or no activity against some anaerobic bacteria. Also, the failure of anti-bacterial agents to eradicate anaerobes in mixed aerobic-anaerobic infections can cause failure in obtaining a therapeutic response, which may result in death. The therapeutic approach in anaerobic bacterial infections involves the modification of the local environment to confine bacterial growth

and the use of appropriate antibacterial agents. So, there is a need to pay more attention to ABAs, especially in terms of diagnostic challenges by taking special precautions in collecting and transporting specimens. The identification, isolation, and eradication of anaerobic bacteria can be expensive, labor-intensive, time-consuming, and challenging [2-4]. Although ABAs have not been under attention for many years, recently, they are coming out of the shadows. In many Asian countries, particularly Iran, there is no space for characterizing ABAs, and even best-equipped laboratories are not able to isolate these bacteria. In the present mini-review, we provided a brief story on the topics related to ABAs in Iran. The most common infections caused by anaerobic bacteria include *C. difficile* infection (CDI), periodontal infections, bacteremia, vaginitis, endometritis, and post-abortion infection. A brief description on these infections in Iran has been provided below.

Clostridium difficile Infection

Clostridium difficile is a toxin-producing anaerobic Gram-positive and spore-forming bacterium, as well as a prominent nosocomial pathogen causing pseudomembranous colitis and antibiotic-associated diarrhea (AAD). Inadequate data is available regarding the true prevalence and *C. difficile* role in diarrheic-related hospitalization in Iran, leading to uncertainty in estimations on the prevalence of this condition in the country [5, 6]. Unfortunately, it has been estimated that the incidence of CDI is relatively high in most of Asian countries due to the absence of surveillance programs for antibiotic usage [7, 8]. As a life-threatening condition, there is an urgent necessity to control the spread of this infection in hospitals. Recently, more attention has been directed towards CDI in Iran. Previous studies on the prevalence of CDI in Iran, they expressed concern about the spread of the disease [9, 10]. There are concerns about the emergence of hyper virulent strains involved in the outbreaks of this infection in hospitals, so to better understand the epidemiology of various *C. difficile* genotypes, there is a need to conduct further epidemiological studies to ascertain the prevalence of CDI in Iran and restrict its propagation [5, 11].

Oral Infections

Anaerobic bacteria are among the most prevalent bacterial communities in the oral flora that contains more than 500 taxa of microorganisms. Hence, many of these bacteria have been reported

to contribute to the development of oral cavity infections [1]. The anaerobic bacteria present in dental plaques can facilitate the destruction of periodontal tissues, and their effective control is the most appropriate way to prevent the progression of periodontal diseases [12]. Dental caries and periodontal diseases are common causes for oral infections in humans. Oral anaerobic bacterial species such as *Streptococcus sobrinus*, *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans*, *Fusobacterium sp.*, *Prevotella sp.*, *Bacteroides sp.*, *Capnocytophaga sp.*, *spirochetes*, *Peptostreptococcus micros*, and *Eubacterium sp.*, along with their metabolites are important contributors in triggering and facilitating the progression of periodontal infections. However, there are some other bacteria in the oral cavity that their possible role in the development of periodontal infections remains to be disclosed. In Iran, studies on the role of anaerobic bacteria in the development of oral infections are scarce [13-15]. In a study conducted on 203 patients with chronic periodontitis, the most frequent anaerobic bacteria were *A. actinomycetemcomitans* (26.8%) and *P. gingivalis* (21.9%) as determined by conditional biochemical methods and a commercial rapid test system [15].

Bacteremia

The role of anaerobic bacteria as etiologies for bacteremia in adults and sepsis in newborns has been shown [2-4, 16]. These bacteria proliferate in the infant's body after delivery and have been identified as causative agents in a number of neonatal infections such as cellulite at the site of fetal monitoring, neonatal botulism, omphalitis, conjunctivitis, bacteremia, and neonatal aspiration pneumonia. Ineffective and insufficient therapy against these bacteria can result in treatment failure. The Gram-negative and Gram-positive anaerobic bacteria associated with bacteremia and sepsis include *Peptococcus*, *Peptostreptococcus*, *microaerophilic streptococci*, *Clostridium sp.*, *Propionibacterium*, *Bacteroid fragilis*, *Fusobacterium*, *Veillonella*, *Prevotella melaninogenicus*, and *Eubacterium*. The mortality associated with anaerobic bacteria bacteremia was reported to range from 4% to 38% [2-4]. A study on the risk factors of neonatal anaerobic infections in 35 infants with a positive aerobic culture suggested that pneumonia and abdominal distention in the neonatal period were significantly associated with anaerobic bacterial infections, indicating that prescribing antibiotics with anaerobic coverage for neonates with abdominal

distention or antibiotic-resistant pneumonia may be helpful [17]. Additionally, Tabib *et al.* in Iran assessed the prevalence of anaerobic and aerobic bacteria in 402 neonates suspected of having early onset (during 72 hours of age) septicemia. Totally, early onset neonatal sepsis was seen in 27 neonates [i.e., the incidence rate per 1000 live births of 15.66 (11.6 aerobe + 4 anaerobe)]. Of these, 26 samples rendered positive blood cultures for anaerobic bacteria with *Peptostreptococcus* and *Propionibacterium* being the most frequently isolated organisms [18].

Vaginitis

Vaginitis, which can be infectious or non-infectious, is a frequently encountered problem in clinical practice. While the normal flora of the vagina is dominated by lactobacilli, in bacterial vaginosis (BV), a combination of anaerobic bacteria (either facultative anaerobes or obligate anaerobes bacteria) including *Mobiluncus sp.*, *Peptostreptococcus*, *Bacteroides sp.*, *Gardnerella vaginalis*, *Prevotella*, *Porphyromonas*, *Fusobacterium*, *Eubacterium*, *Propionibacterium spp.*, and *Atropobium vaginae*, which are normally found in low quantities in the vagina, constitutes the majority of bacterial populations [19, 20]. In terms of microbiology, BV is not a detailed mono-bacterial infection, but a synergic mixture of CO₂-dependent, microaerophilic, and anaerobic species. Although in many healthy asymptomatic females, these bacteria are detected in low quantities, they dominate the flora in patients with vaginosis. It is not clear if bacterial metabolic interactions and communications contribute to BV pathogenesis by generating excessive secretions and active products. For example, it has been reported that the amino acids and pyruvate produced by *G. vaginalis* can be converted to amines via decarboxylation by anaerobic bacteria such as *Bacteroides sp.*, as the most recently detected organism associated with BV [21]. Recently, researchers have suggested that BV, as a common genital tract infection, to be linked with low birth weight, premature birth, as well as HIV risk [19]. The prevalence of BV infection in the community depends on many factors such as racial, geographic, and clinical characteristics of the study population [22]. A case-control prospective study on 540 women with genital infections, conducted in a teaching hospital affiliated with Hamedan University of Medical Sciences, Iran, reported a prevalence of 28.5% for BV in the case group [19].

Conclusions

Anaerobic bacteria cause a wide range of infections. It is sufficient to note that approximately 30% of bacterial infections are caused by anaerobic bacteria, so these organisms should be equally isolated from clinical samples. However, these bacteria are out of order for daily diagnosis in practice. It is expected that in the coming years, the look of ABAs will change in Iran. Thus, more studies to develop more accurate risk stratification and large-scale screening/surveillance modalities for ABAs are necessary prerequisites in this area.

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Conflict of interest

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