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Enterococcus faecalis: A Mini-Review

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المكورات المعوية البرازية: مراجعة مصغرة

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ABSTRACT

Background:

Enterococcus faecalis is one of the most pathogenic bacteria that causes severe infections and antibiotic resistance diseases that are related to many animals such as reptiles, insects, birds, mammals and humans. Enterococcus faecalis is considered a cytolysin bacteria that has ability to lysis blood, as it was isolated from many pathological samples such as teeth caries and intestinal samples that include urine and feces. In this article, we discuss many general characteristics of bacteria such as phenotypic and microscopic characteristics, genetic structure, virulence factors, pathogenicity, transmission, and immunity against bacteria..

Conclusion:

Diseases related to intestinal infections are very important because of their impact on human health and that enterococci are part of the gut microbiome. Researchers and doctors have found that patients with ulcerative colitis and Crohn's disease have more enterococci in their intestines compared to healthy people, where researchers have suggested that the reason as changes occur in the gut wall that enable bacteria to access and obtain food, which in turn encourages them to grow properly. The rapid development of E. faecalis strains, which made them more resistant to antibiotics, confirms the need to making several studies that help in understanding the morphological, biochemical and physiological characteristics of these bacteria. in addition to its development and classification throughout history.

Key words:

Enterococcus faecalis, pathogenicity , virulence factor, cytolysin.

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الخلاصة

مقدمة:

تعد المكورات المعوية البرازية من أكثر أنواع البكتيريا المسببة للأمراض التي تسبب العدوى الشديدة وأمراض مقاومة المضادات الحيوية التي تصيب العديد من الحيوانات مثل الزواحف والحشرات والطيور والثدييات والإنسان. تعتبر Enterococcus faecalis من cytolysin bacteria وهذا يعني ان لها القدرة على تحلل الدم، حيث تم عزلها من العديد من العينات المرضية مثل تسوس الأسنان وعينات الأمعاء التي تشمل الادرار والبراز. في هذه المقالة، نناقش العديد من الخصائص العامة للبكتيريا مثل الخصائص المظهرية والمجهرية والتركيب الجيني ، وعوامل الفوعة ، والإمراض، والانتقال، والمناعة ضد البكتيريا.

الاستنتاجات:

تعتبر الأمراض المتعلقة بالعدوى المعوية مهمة للغاية بسبب تأثيرها على صحة الإنسان وأن المكورات المعوية هي جزء من الميكروبات التي تعيش في الأمعاء. وجد الباحثون والأطباء أن مرضى التهاب القولون التقرحي ومرض كرون لديهم المزيد من المكورات المعوية في أمعائهم مقارنة بالأشخاص الأصحاء، حيث اقترح الباحثون أن السبب هو حدوث تغيرات في جدار الأمعاء تمكن البكتيريا من الوصول والحصول على الطعام، وهذا بدوره يشجعهم على النمو بشكل صحيح. إن التطور السريع لسلالات E. faecalis، يؤكد الحاجة إلى إجراء العديد من الدراسات التي تساعد في فهم الخصائص المورفولوجية والكيميائية الحيوية والفسيولوجية لهذه البكتيريا بالإضافة إلى تطورها وتصنيفها عبر التاريخ مما جعلها أكثر مقاومة للمضادات الحيوية .لا يزال أصل المكورات المعوية غير معروف، لذا فإن الارتباط بينها وبين المكورات المعوية مهم للغاية. تعيش المكورات المعوية في مواطن كثيرة، وتوجد بشكل أساسي في مياه الصرف الصحي والتربة والجهاز الهضمي للإنسان والحيوان. تحتوي المكورات المعوية على العديد من عوامل الضراوة، حيث إنها قادرة على إنتاج السيتولايسين، والتي تقضي على البكتيريا المنافسة أو تشكل معقدات، وتساعدها على غزو مضيفها ، فضلاً عن قدرتها على تطوير قدرتها على مقاومة المضادات الحيوية ونقلها وانتشارها على نطاق واسع. إن قدرة الكائنات الحية الدقيقة، بما في ذلك البكتيريا، على مقاومة المضادات الحيوية ليست جديدة. لقد كان موجودًا منذ فترة طويلة، لكنه زاد مؤخرًا بسبب الاستخدام الخاطئ المتكرر للمضادات الحيوية، مما أدى إلى ظهور سلالات شديدة المقاومة للعديد من المضادات الحيوية، مثل السيفالوسبورين والستربتوجينات والأمينوغليكوزيدات وبيتا لاكتام.

الكلمات المفتاحية:

المكورات المعوية البرازية، الإمراضية، عامل الضراوة، السيتولايسين.

INTRODUCTION

Enterococcus faecalis is a facultative anaerobic bacteria with low levels of GC and G-+ and is one of the three most common pathogens isolated to healthcare and MDR hospitals worldwide [1] . These bacteria are Gram-positive commensal member of symbiotic bacteria that found in the intestines of a wide range of organisms and because of the wrong use of antibiotics, which led to the occurrence of many mutations in the beneficial bacteria symbiotic in the intestines that made them resistant to antibiotics, including Enterococcus faecalis [2]. This bacteria is characterized as an opportunistic pathogen that contributes to intestinal infections such as infective endocarditis and it has the ability to secrete an exogenous toxin that lysis bacteria and eukaryotic cells called cytolysin[3]. These bacteria are endemic to the human digestive system and the genitourinary tract, and some strains of these bacteria are relatively stable, so they are used as a probiotic because have

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ability to produce some vitamins and elements of important interest during the digestive process in the intestines [4] .

Morphology

Microscopically these bacteria have a circular or oval shape arranged in different lengths or in the form of chains or pairs, and they are not have ability to forming spores or capsules and some of them moving by flagella, such as Enterococcus casselifavus and Enterococcus gallinarum [5], While on blood agar these bacteria are looks milky white or yellow for some colonies that produce carotenoid pigment [6] , These characteristics are illustrated in Figure 1.

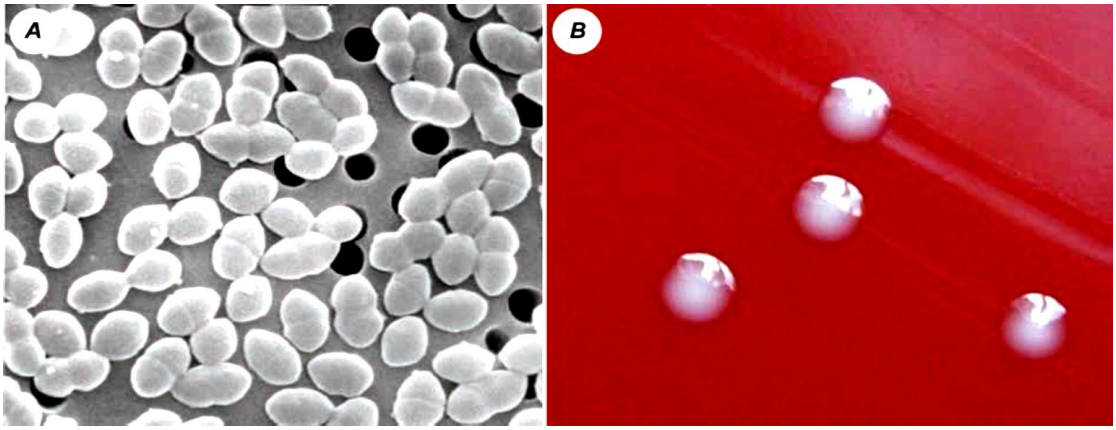

Figure 1: Enterococci faecalis. , A- microscopic form of bacteria. B- Enterococcus faecalis colonies after 24 hours cultivation 37°C on blood agar [7].

Biochemical and Physiological features

This bacteria belongs to the Enterococci group that contains teichoic acid in their cell wall as the main surface antigen while does not contain proteins or lipids. E. faecalis, belongs to Enterococci which contains lysine-alanin type of peptidoglycan while other species of this genus have lysine-D-asparagin type [8].These bacteria grow in a wide range of temperatures ranging between 10-45 °C, and the optimum temperature for their growth is between 35-37 °, which is the same as the body temperature of mammals. In addition, these bacteria have the ability to grow and adaptation at a salt concentration of up to 6.5% NaCl, 22% ethanol or higher concentration of bile and sodium dodecyl sulfate , these features allows them to grow at different temperatures and able to live easily in environments with unsuitable conditions such as dry environment and hospital environment [9].

Enterococcus faecalis are not able to produce catalase enzyme but are able to grows on complex media that contains chemical organic substance or on blood agar because have lysine enzyme in addition this bacteria are able to grow in aerobic or anaerobic facultative conditions with preference to anaerobic environments Because it has the ability to produce superoxide dismutase enzyme , which converts superoxide (toxic) into (less toxic) peroxide resulting in the formation of oxygen [10].

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Taxonomy

Enterococcus faecalis belong to the phylum Firmicutes, Lactobacillales classand Enterococcaceae family [11].There are 36 different types of enterococci, 30 of which are known at present. By phylogenetic similarity, they are divided into five groups: E. faecalis, E. faecium, E. avium, E. gallinarum a E. cecorum. Table 1 shows the genera of this family

Table 1: Division of phylogenetically similar species of the Enterococcus genus [12],

E. faecium	*E. avium*	*E. faecalis*
“”E. faecium, E. canis,””	*“”E. avium, E. devriesei “”*	*“” E. faecalis, E. caccae “”*
“”E. durans, E. hirae “”	*“”E. gilvus, E. malodoratu “”,*	*“” E. haemoperoxidus“*
“”E. mundtii, E. ratti “”	*“” E. pseudoavium “”*	*“” E. moraviensis “”*
“”E. villorum, E. asini “”	*“”E. raffinosus, E. pallens“”*	*“” E. silesiacus “”*
“”E. phoeniculicola “”	*“” E. hermanniensis“”*	*“”E. termitis“”*
“”E. canintestini “”	*“” E. vikkiensis“”*	
“” E. thailandicus“”		
E. cecorum	*E. gallinarum*	*Non-classified species*
“”E. cecoru “”	*“”E. gallinarum “”*	*“”E. aquimarinus, E. dispar “”*
“” E. columbae “”	*“”E. casseliflavus“”*	*“”E. saccharolyticus “”*
		“” E. sulfureus, E. italicus “”

Pathogenicity and virulence factors

The pathogenicity is described by the ability of microorganisms to cause disease in many host organisms in addition the transmissibility, toxicity and invasion of microorganisms are the main factors that determine this ability. While the virulence is one of the pathogenicity factor. The pathogenicity factors was encoded by both chromosomal and plasmid genes which increases the virulence and the transmission of these genes between strains makes them more pathological [13]. Enterococcus faecalis that live in the environment are less pathogenicity from than those live inside

of the bodies of organisms but they may acquire some virulence genes such as plasmids and transposons that change them from nonpathogenic to pathogenic strain, and one of the most important pathogenic factors they acquire is resistance to antibiotics such as (cephalosporin's, Clindamycin, aminoglycosides and vancomycin), in addition to some other pathogenic factors such as the ability to invade different types of living organisms and live in different environments [14].

The first step in the pathogenesis process is the entry of bacteria into the cells of the host through contact between their receptors ,then the bacteria secrete one of the factors that make colonization of the host easy such as cytolysin or enterosin enzymes, then they begin to adapt better to the environment of host cell including lack of nutrients, high oxidative potential, and host defense mechanisms .These virulence factors and another factors help bacteria to invade the body cells and move between cells and organs to causes disease in addition it also contribute to the aggregation of bacteria to biofilim formation that preventing the process of phagocytosis [8].

Enterococcus faecalis have the ability to acquire virulence genes through conjugation between bacteria of the same species or plasmid transmission or extrachromosomal elements that help bacteria colonize the body, compete with other organisms, resist the host's defense mechanisms, and cause pathological changes. It can also produce enzymes or substances that contribute to increasing the intensity of the biofilm layer to form calcified biofilm, which is highly resistant to the host's immune defense mechanisms[15]. Enterococcus faecalis are part of the normal intestinal flora but when any disturbance occur in the intestine by any pathological infection such as bacteria, parasites, viruses and tumors that weaken the body's immunity, These bacteria can transmitted through the lining of the intestine and travel through the blood to cause systemic infection or transmission and multiplies abundantly in the intestinal tract to invade the dentinal tubes that lead to causes urinary tract infections (UTIs) [16]. Also, these bacteria have the ability to cause many infections such as septicemia , bacteremia, root canal inflammation and meningitis [17]. Some studies also indicated that the transmission of this bacteria from the mother to the newly born child through the birth canal is responsible for about 20% of cases of bacterial endocarditis in newborns and may cause infections in the heart, abdomen and pelvis, and in some cases may cause meningitis [18, 19].

Transmission and Host Factors that are Predisposed to Colonization

Enterococcus faecalis are present symbiotically in the digestive system of humans and animals, especially in the mouth, intestines and vaginal tract. They usually do not cause any pathological problems, but they may turn into pathogenic at the earliest opportunity in the event that appropriate conditions such as less immunity or killing of beneficial bacteria by excessive use of antibiotics , So it can travel across the mucosal barrier to cause systemic infections [20]. Studies have indicated that the increased transmission of these bacteria to humans and causing diseases was from animal sources or from animal fecese. where these bacteria are found in huge numbers in the intestines of animals, which were transmitted to humans through contamination of food and drink sources with the waste of these animals [21].

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Previous studies that makes on human and mice demonstrated that Enterococcus faecalis possess selectively colonizes on colon tissues and reduces the healing process by interfering with the activity of the collagen matrix. It also inhibits the activation of human plasminogen protein, which was found in normal colon tissues in a higher concentrations [19] . The transmission of these bacteria to the blood is most likely from the genitourinary system, since these bacteria have the ability to colonize the mucosal surfaces of the intestinal wall by means of cytolysin enzymes that considered an external poison and also resistance to antibodies through its virulence factors, then may pass through the blood to the liver and cause damage to its tissues and functions [22].

Epidemiology

Most epidemiological cases of enterococci are related to nosocomial infections, although there is such a great diversity of enterococci in the environment. Enterococcus faecalis and E. faecium are the most pathogenic among other species belonging to Enterococcaceae family . In the past, E. faecalis was less pathogenic, but nowadays it has become more pathogenic, due to the excessive use of antibiotics which also made competition between bacteria Gram-positive , negative bacteria and other symbiotic organisms slightly, which provide an opportunity for the growth and reproduction of these bacteria [23]. In addition, as a result of the increased infection with this bacteria, Enterococcus faecalis is considered one of the most common types in hospitals and a long-term bacteria in hospitalization because of its highly resistance to antibiotics, like vancomycin, which affects the operations that take place inside these hospital, such as affected organs, or bone marrow transplantation [24].

The spread of these bacteria, especially pathological strains in some hospitals, leads to their transmission to the soft tissues of the body, which can lead to abscesses, and can also cause urinary tract infections and endocarditis . This bacteria is usually associated with urinary tract infections and abscesses, since Enterococcus faecalis is a facultative anaerobic bacteria, so it is present with other types of non-pathological anaerobic bacteria that do not cause infection automatically. Therefore, antibiotics that have a good effect on these bacteria can be used to inhibition the infection with Enterococcus faecalis [25].

Enterococcus faecalis and its role in cancerous diseases

The types of beneficial bacteria (symbiosis bacteria) that are present in the intestines of animals and humans play an important role in many vital metabolic processes, especially the production of vitamins and aid in digestion, and most of them are known as opportunistic pathogens that can cause disease in the case of excessive intake of antibiotics incorrectly or decreased immunity, but most research indicates that the role of E. faecalis as pathogenic is greater than its beneficial role, which has changed a lot because the mutations in their genes. In addition, E. faecalis can live and develop in the tissues of the pancreas causing chronic disease and cytolytic infiltrates which in turn leads to pancreatic cell heterogeneity [26].

Infection of host cells with Enterococcus faecalis and their proliferation within cells leads to the production of many free radicals that have a role in destroying cells and triggering immune diseases. It also affects many biological processes such as cellular signaling and aging, so the exacerbation of infection with these bacteria leads to increased production Reactive oxygen

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compounds are cytotoxic and carcinogenic ,Oxidative phosphorylation by mitochondria is low after infection, indicating that ROS production is primarily generated in an oxphos-independent manner within infected cells [27]. Studies have shown the presence of many colonies of Enterococcus faecalis within some colon cancer cells, which had a role in activating Gelatinase and autolysin activities responsible for the formation of biofilms, which contribute to the activation of pathways related to tumor invasion and cancer metastasis. This was shown by the growth of this bacteria on human T84 cancer cell lines [28].

E. faecalis resistance mechanism of the immune system

Enterococcus faecalis has the ability to resist the host's immunity through the formation of biofilms and the secretion of lysin-stimulating enzymes, which preventing the process of phagocytosis and stay a live inside macrophages ,neutrophils for long periods [29] These bacteria possess many virulence factors making them more pathogenic compared to other pathogenic bacteria such as Pseudomonas aeruginosa and Proteus mirabilis. among these factors aggregation substance (AS), gelatinase, and TcpF) [20].

Enterococcus faecalis is characterized by its ability to adapt to live in different environments and in different parts of the body of the organism, such as the heart and blood, epithelium ,digestive system, and urinary tract due to its ability to enter from different places and cause infection because it has ability to metabolize quickly , it also have many mechanism to resist the innate and adaptive immunity in the host such as resistance to the process of phagocytosis and evasion of immune cells [30].

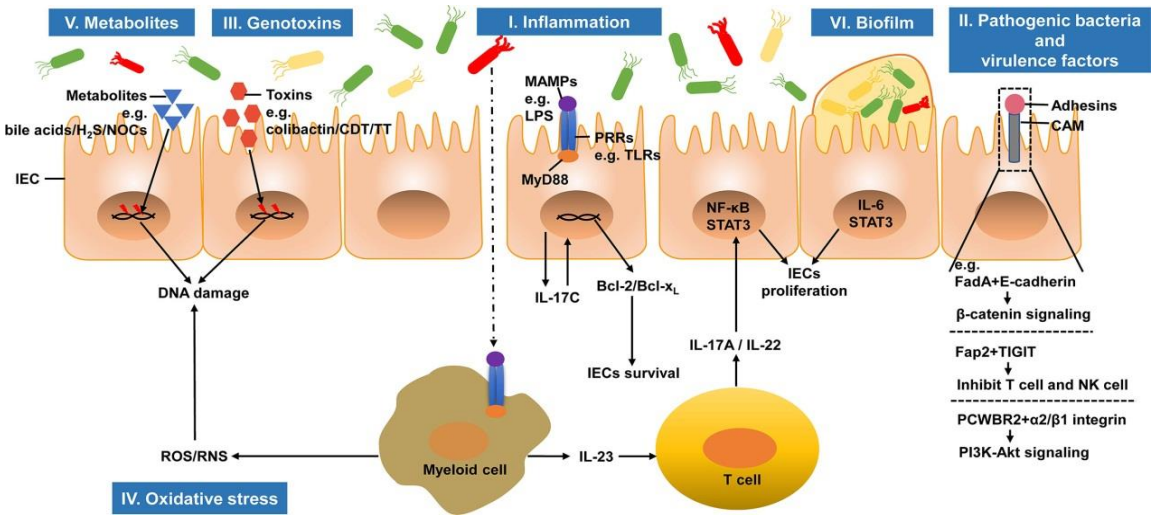

Figure 2: E.faecalis resistance mechanism of the immune system [30].

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Treatment

Enterococcus faecalis has some genes that make its cell wall resistant to the entry of antibiotics such as β-Lactam. this makes it difficult to treat with these antibiotics or other antibiotics belonging to this family, such as ampicillin , also some strains of this bacteria are resistant to other antibiotics such as penicillin G and vancomycin . This prompted researchers to find alternative antibiotics to kill or inhibition the spread of these bacteria by either using synergistic antibiotics with each other or using other new treatments (22). The higher development in the strains of Enterococcus faecalis, which made them resistant to many antibiotics, made treatment options with current antibiotics difficult, and other alternatives must be searched for, and also made the bacteria more prevalent and a threat to public health (31).

Results and Discussion

Diseases related to intestinal infections are very important due to their impact on human health and that enterococci are part of the gut microbiome. Researchers and doctors have found that patients with ulcerative colitis and Crohn's disease have more enterococci in their intestines compared to healthy people, where researchers have suggested that the reason is changes occur in the gut wall that enable bacteria to access and obtain food, which in turn encourages them to grow properly. The rapid development of E. faecalis strains, which made them more resistant to antibiotics, confirms the need to making several studies that help in understanding the morphological, biochemical and physiological characteristics of these bacteria. in addition to its development and classification throughout history.

The origin of enterococci is still unknown, so the association between it and enterococci is very important. There are many habitats for enterococci, and they are mainly found in the sewage, soil, and digestive systems of humans and animals. Enterococci contain many virulence factors, as they are able to produce cytolysin, which them to eliminate competing bacteria or form complexes, and help them invade their host, as well as their ability to develop their ability to resist antibiotics, transport and spread widely. The ability of microorganisms, including bacteria, to resist antibiotics is not new. It has been around for a long time, but it has recently increased due to the frequent wrong use of antibiotics, which has led to the emergence of strains that are highly resistant to many antibiotics, such as cephalosporin's, streptogens, Aminoglycosides and beta-lactams .

Conflict of interests.

There are non-conflicts of interest.

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