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Review Article

Candida-An emerging and re-emerging pathogen

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ABSTRACT

Candida contains a wide range of organisms, and more than 17 different Candida species have been linked to human infections. Newer species are emerging and Candida albicans and other Species are re-emerging. Isolated strains showing increased antifungal resistance, which necessitates the need for new antifungal drugs. Candida Spp can cause a wide range of mycoses, including invasive candidiasis, which can be deep, widespread, and extremely painful. The majority of the time, it spreads by endogenous Candidaemia. They adhere to host tissues and medical equipment, form biofilms, and release enzymes that break down proteins. Conventional techniques and molecular techniques have made laboratory diagnosis of Candida easy. However, Candida infections are more common in immunocmpromised and hospitalised patients.

1. Introduction

Invasive fungal infections have increased since the 1980s. This is especially true for the large number of people who have weakened immune systems or are being treated in hospitals for serious diseases. Candida species are naturally present in the oral mucosa, gastrointestinal tract, and vaginal mucosa. They can cause a wide range of symptoms, including mucocutaneous overgrowth and bloodstream infections.[1] These yeasts are common in healthy people, but because they are so adept at adapting to different host niches, they can cause systemic infections in people with compromised immune systems. The genus contains a wide range of organisms, and more than 17 different Candida species have been linked to human infections. Over 90% of infections that spread to other parts of the body are caused by Candida albicans, Candida glabrata, Candida parapsilosis, Candida tropicalis, and Candida krusei.[2] Immunocompromised patients are increasingly likely to require intravenous catheters, total parenteral nutrition, invasive surgery, broad-spectrum antibiotics, cytotoxic chemotherapies, and transplants. Candida species are harmful because they are able to evade the body's defenses, adhere to the body, create biofilms (both on the body and on medical equipment), and produce enzymes that degrade tissue, such as proteases, phospholipases, and haemolysin.[3] Antifungal drug resistance is increasing globally. This indicates that in vitro lab testing could aid doctors in selecting the appropriate medication. The ability of Candida species to form drug-resistant biofilms contributes significantly to their potential to make humans sick.[4] As with virtually all microbial biofilms, C. albicans has cells that are stuck together. Antimicrobials are less likely to kill Candida albicans biofilms than planktonic cells. The spread of drug-resistant Candida biofilms has been linked to a quicker maturation process. Some research has also found that Candida biofilms grow slowly in the presence of a small amount of matrix and are just as resistant to drugs (fluconazole and amphotericin B) as cells grown in a shaker with a large amount of matrix. Because the

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number of strains that cannot be destroyed by antifungals is increasing, researchers must look for new targets for new antifungals. The new Candida auris strain, which is resistant to many drugs, aggravates the problems caused by other infections around the world.[5] This causes Candida infections in people in intensive care units and other critical care areas.

2. Pathogenicity of Candida Species

Candidasis, also known as candidosis, is a yeast infection caused by Candida. These fungi can cause a wide range of mycoses, including invasive candidiasis, which can be deep, widespread, and extremely painful. The majority of the time, it spreads by endogenous candidaemia, which occurs when Candida species located in the microbiota of various anatomical sites serve as pathogens when the host is weak.[6] Exogenous transmission is another method by which the fungus spreads from person to person. This is most common when health care workers come into contact with patients. Infections can also spread via medical devices such as contaminated catheters and intravenous solutions. Candida species are harmful pathogens because they may alter and dwell in different regions of the body. People used to believe that yeasts were merely bystanders in the pathogenesis process, which is how fungal infections begin. As a result, it was thought that an opportunistic infection could only occur if the host was physically or mentally weak. Since then, this notion has evolved. Most specialists think that these organisms actively participate in disease pathogenesis via mechanisms known as "virulence factors".

Candida species are opportunistic eukaryotic pathogens that thrive on the mucosa of the digestive tract, as well as the mouth, esophagus, and vaginal regions. Despite the fact that this organism normally lives on mucosal surfaces without causing any problems, it has the potential to become one of the most important causes of a crippling and fatal infection. Fungi became one of the leading causes of nosocomial infections in the early 1980s, primarily affecting people with weakened immune systems or those who had been in the hospital for an extended period of time due to serious diseases. Candida species exist in the environment and are part of the microbiota of healthy people. Most people are thought to have one strain of Candida in various parts of their bodies for an extended period of time. However, some people have multiple strains or species at the same time, and this is common in hospitalized patients. However, the Candida species has the potential to be harmful. This is something that all medical professionals should always keep in mind. The ability of these organisms to live as commensals in different parts of the body, each with its own set of environmental stresses, is an important aspect of their adaptability. Despite the fact that different varieties of Candida can infect different sections of the body, there is evidence that the immune system protects each kind differently.[7] Furthermore, cutaneous candidiasis and vaginal infections are more likely to be associated with a phagocytic response including neutrophils and mononuclear phagocytes. The urinary tract is the body part where hospitalized patients are most likely to get infections, but this is still a problem of unknown significance. Although bacteria cause the majority of these infections, it is estimated that at least 10% are caused by fungi, with Candida species being the most common. Candida species were found in approximately 22% of urine samples from patients in the intensive care unit. Candida species frequently colonize the lungs of people who have been on mechanical ventilation for more than two days. When colonies from the mouth or stomach enter the bloodstream or are breathed into the lungs, this occurs. Long stays in the ICU or hospital are also important. Candida is hazardous due to a variety of virulence factors. The most essential are those that let bacteria adhere to host tissues and medical equipment, form biofilms, and release enzymes that break down proteins.

Furthermore, while significant research has been conducted to determine what makes fungus, particularly Candida albicans, harmful, little is known about fungi that are not Candida albicans. Because C. albicans and other pathogens can recognize their hosts, they are dangerous. This enables them to attach to their hosts' cells and proteins.[8] In addition, enzymes that break down things play an important role in virulence. The transition from yeast cell growth to filamentous growth aids fungi in spreading more than yeast growth alone. Fungi enter human tissues primarily through adhesion to host surfaces. This process is initiated by several cell-signaling cascades both inside and outside the fungus. Candida species can also form biofilms on medical equipment. At first, Candida cells stick together because of things like static electricity and the fact that they don't like water. Then, on the surface of fungal cells, particular adhesins that identify ligands such as proteins, fibrinogen, and fibronectin are identified. They aid in the adhesion of cells. Adhesion is caused by adhesins, which are proteins on the surface of cells that bind to amino acids and sugars on the surfaces of other cells or help cells stick to nonliving surfaces. Because Candida species are part of the human microbiota, they are frequently detected on biomaterials, implants, and many types of catheters. Biofilms are a medical concern because they limit the efficacy of antifungal medications. The process by which biofilms develop resistance to antimicrobial medicines is not entirely understood. According to one idea, the existence of the matrix inhibits drug dissemination by forming a diffusion barrier, allowing only the top layers to come into touch with fatal dosages of antibiotics.[9,10] Extracellular hydrolytic enzymes appear to play an important role in adhesion, tissue penetration, invasion, and host tissue destruction. The most important water-breaking enzymes

are proteases and phospholipases. Because it has ten aspartic proteinase (Sap) isoenzymes, Candida albicans functions as a proteinase. These proteins, which range in size from 35 to 50 kDa, are encoded by the SAP1-10 genes. The SAP1-6 genes are implicated in adhesion, tissue injury, and immune response alterations. Although nothing is known about how SAP7 functions, Sap9 and Sap10 are not thought to be secreted proteinases. Instead, they are likely to be utilised to maintain yeast cells' regulatory surfaces intact. Sap proteins have also been examined in C. tropicalis, C. parapsilosis, and C. gullermondii. Many investigations have found a relationship between increased extracellular hydrolytic enzyme synthesis and activity and increased pathogenic potential of yeasts, which leads to clinical indications of severe candidiasis. Microbial extracellular lipases may degrade lipids to obtain nutrients, adhere to host cells and tissues, initiate inflammation without being particular by influencing immune cells, and defend themselves by eliminating rival microflora. Lipase inhibitors have been found in studies to significantly minimize damage to reconstituted human tissues when infected. Lipase-negative C. parapsilosis mutants did not form biofilms and grew at a much slower rate on lipid-rich media. Lipase-negative mutants were also substantially less hazardous in infection scenarios. In addition, haemolysin production is an essential component of virulence. This protein is essential for life and has something to do with iron absorption. Haemolysins, proteins that destroy red blood cells, are produced by microorganisms. Iron is an inorganic element required for the growth of microorganisms such as yeasts, and the ability to obtain this element is required for the infectious process to begin. Seven phospholipase genes have been discovered (PLA, PLB1, PLB2, PLC1, PLC2, PLC3, and PLD1), however it is still unknown what these enzymes accomplish. In animal models of candidiasis, PLB1 has been claimed to play a role in how deadly the infection is. Plb1p is an 84 kDa glycoprotein discovered at hyphae tips when the fungus invades tissue. It is a lysophospholipase-transacylase and a hydrolase. C. albicans can transition from single yeast cells to pseudohyphal or hyphal development. This is known as morphogenesis (creating a transition between unicellular yeast cells and a filamentous growth form). Both Candida albicans and Candida dubliniensis grow filamentously, which implies they can grow isotopically (yeast) or apically (pseudohyphal). The formation of pseudohyphae is an important aspect of tissue invasion and resistance to phagocytosis as a virulence mechanism. To treat candidosis, you must identify and address the factors that make the host susceptible to infection. Recently, the world has been paying more attention to new species because they are already resistant to several medications. Non-albicans species such as Candida glabrata, Candida parapsilosis, and Candida tropicalis are becoming more widespread and resistant to antifungal medications. This, together with the species' unacceptably high morbidity and mortality rates, indicates that we need to learn more about their virulence and resistance mechanisms.[11] Emerging non-albicans strains and re-emerging C.albicans strains make it hard to treat and manage, especially in hospitals where there is multidrug resistance and not as many options. Candida is one of the most common diseases that affect new borns, pregnant women, people with diabetes, and people whose immune systems don't work well. Health care workers worry about high resistance to antifungal drugs.[12] Current developments in genomic and postgenomic research, such as genome sequencing and gene expression data, have given us a better understanding of how harmful Candida yeast is.

3. Antifungal Susceptibility Testing and Drug Resistance

The disc diffusion method and the broth microdilution method from the Clinical and Laboratory Standard Institute (CLSI) were used to analyze the antifungal susceptibility pattern of Candida isolates identified to the species level. MIC values can also be determined using automated technologies such as the Vitek 2. Antifungal testing is necessary since Candida albicans and other kinds of Candida have developed resistance to numerous antifungals. Most of the time, antifungal susceptibility testing assists clinicians in selecting the most effective antifungal drug to treat fungal infections. In MIC detection, fluconazole, variconazole, amphotericin B, itraconazole, and ketoconazole are evaluated for susceptibility and breakpoints. Antifungal resistance based on various mechanisms is rising and evolving, making it even more critical to identify novel approaches to treat Candida infections.[13]Candida that is drug-resistant is difficult to treat, thus species-level identification should be performed, and antifungals should be developed based on the species and severity of sickness.[14]C. auris possesses biofilm forming genes, proteinases, lipases, phospholipases, adhesins, secreted aspartyl proteases, and azole resistance transporters.[15]Before we can start treating these resistant new strains, we need to know what the MIC is. Drug resistance is a major issue since C. auris bloodstream infections are associated with high rates of fluconazole resistance, mortality, and treatment costs.[16] C.auris is the only drug-resistant Candida strain prevalent in the majority of the world.

Fungal bloodstream infections are a major concern in infants due to their high mortality rate and abundance of resistant organisms.[17] To protect newborns from having blood stream infections and to discover and test for antifungal susceptibility, all hospitals that care for newborns must follow strict infection control criteria. All healthcare personnel will be required to participate in a program known as "antibiotic and antifungal stewardship".[18]

4. Laboratory Diagnosis of Candida Spp.

Candida species are identified using long-established techniques. Because they are specific and sensitive enough, these approaches are adequate for detecting non albicans candida (NAC) species. Mycologists picked the method of diagnosis based on the sample and diagnostic assays available in their lab. Urine, burn tissue, intravascular catheter tips, and bronchoalveolar lavage specimens may benefit from quantitative or semiquantitative cultures. If some samples are stained with immunofluorescence, they may be easier to diagnose.[19] Molecular approaches have made it easier for labs to diagnose and treat Candidiasis due to higher sensitivity and specificity thresholds.[20] PCR and sequencing are used in modern mycology facilities.

5. Conclusions

Candida species-caused systemic fungal infections are becoming more common in hospitalized patients. This is a major cause of illness and mortality all across the world, particularly among the very sick. Biofilms play an important role in the propagation of many illnesses, especially because they can adhere to various medical instruments. People are getting more interested in adopting natural goods as medication, even if they are linked to other treatments. Because nanoparticles, antibodies, and, more recently, photodynamic inactivation have the potential to be successful treatments, much research has been conducted on their application to treat fungal infections. Because of the negative side effects of current antifungal treatments, the increasing number of strains resistant to traditional antifungal medications, and the creation of biofilms in medical devices and tissues, it is critical to discover novel antifungal agents that work.

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7. Conflicts of interest

There are no conflicts of interest.

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