International Journal of Medical and Health Research
ISSN: 2454-9142; Impact Factor: RJIF 5.54
Received: 28-03-2019; Accepted: 30-04-2019
www.medicalsciencejournal.com
Volume 5; Issue 5; May 2019; Page No. 136-139

Clinical evaluation of septicemia patients identified with candida species in Bihar population

Dr. Ahsan Hamidi[1], Dr. Shamim Ahmad[2*], Dr. Shiv Nandan Singh[3]
[1] Assistant Professor, Department of Microbiology, Government medical college, Bettiah, Bihar, India
[2] Tutor, Department of Microbiology, Government medical college, Bettiah, Bihar, India
[3] Professor, Department of Microbiology, Government medical college, Bettiah, Bihar, India
[*] Corresponding Author: Dr. Shamim Ahmad

Abstract
Infections leading to sepsis are usually bacterial, but may be fungal or viral. Gram-positive bacteria was the predominant cause of sepsis before the introduction of antibiotics. Over the past year, we noticed an increase in the isolation rate of nonalbicans Candida species from cases of neonatal septicemia, which prompted us to undertake the present study; to analyse and evaluate the change in the species distribution of Candida species in neonatal septicemia and determine their in vitro antifungal susceptibility and the risk factors associated with their acquisition.
The data from the 125 cases were collected and presented as below. Infection with unusual organisms is an increasing problem. Due to advances in medical and surgical management, an increase in nosocomial fungal infection rate has been observed. Candidemia is an emerging problem in healthcare settings. Knowledge of the epidemiology of candidemia can help to salvage patients, who are in the productive age group, with few with underlying medical condition.
The changing epidemiology of candidemia highlights the need for close monitoring of Candida species distribution and susceptibility to optimize treatment and outcome. It is apparent from the results of the present study that routine identification of Candida isolates to the species level, and the detection of resistant strains by antifungal susceptibility test is essential. Furthermore, there is a continued need for surveillance of candidemia to monitor changes in the epidemiological features and antifungal susceptibility and also to develop and evaluate prevention strategies.

Keywords: Septicemia, sepsis, candida, Gram-positive bacteria, etc

Introduction
Septicemia, or sepsis, is the clinical name for blood poisoning by bacteria. It is the body's most extreme response to an infection. Sepsis that progresses to septic shock has a death rate as high as 50%, depending on the type of organism involved. Sepsis is a medical emergency and needs urgent medical treatment. Without treatment, sepsis can quickly lead to tissue damage, organ failure, and death. Septicemia, formerly called blood poisoning, infection resulting from the presence of bacteria in the blood (bacteremia). The onset of septicemia is signaled by a high fever, chills, weakness, and excessive sweating, followed by a decrease in blood pressure. The typical microorganisms that produce septicemia, usually gram-negative bacteria, release toxic products that trigger immune responses and widespread blood clotting (coagulation) within the blood vessels, thus reducing the flow of blood to tissues and organs.
The development of septicemia following surgery or after the patient has contracted an infectious disease indicates that the infectious process has escaped the control of the body's immune system and requires immediate medical intervention. Septicemia has increased in both severity and incidence, especially in hospitalized patients, because of both the more invasive technology employed and the increased prevalence of antibiotic-resistant bacteria in the hospital environment. Septicemia often cannot be traced to a single microorganism but results from multiple infections, so that broad-spectrum antibiotic therapy may be required. If not treated promptly with appropriate antibiotics and surgical drainage of any detectable foci of infection, septicemia is followed by septic shock, in which the mortality rate exceeds 50 percent [1].
Sepsis is a life-threatening condition that arises when the body's response to infection causes injury to its own tissues and organs. Common signs and symptoms include fever, increased heart rate, increased breathing rate, and confusion. There may also be symptoms related to a specific infection, such as a cough with pneumonia, or painful urination with a kidney infection. In the very young, old, and people with a weakened immune system, there may be no symptoms of a specific infection and the body temperature may be low or normal, rather than high. Severe sepsis is sepsis causing poor organ function or insufficient blood flow. Insufficient blood flow may be evident by low blood pressure, high blood lactate, or low urine output. Septic shock is low blood pressure due to sepsis that does not improve after fluid replacement [2].
Sepsis is caused by an inflammatory immune response triggered by an infection. Most commonly, the infection is bacterial, but it may also be fungal, viral, or protozoan. Common locations for the primary infection include the lungs, brain, urinary tract, skin, and abdominal organs. Risk factors include very young age, older age, a weakened immune system from conditions such as cancer or diabetes, major trauma, or burns. An older method of diagnosis was based on meeting at least two systemic inflammatory response syndrome (SIRS) criteria due to a presumed

infection. In 2016, SIRS was replaced with a shortened sequential organ failure assessment score (SOFA score) known as the quick SOFA score (qSOFA) which is two of the following three: increased breathing rate, change in level of consciousness, and low blood pressure. Blood cultures are recommended preferably before antibiotics are started, however, infection of the blood is not required for the diagnosis. Medical imaging should be used to look for the possible location of infection. Other potential causes of similar signs and symptoms include anaphylaxis, adrenal insufficiency, low blood volume, heart failure, and pulmonary embolism [3].

Sepsis is usually treated with intravenous fluids and antibiotics. Typically, antibiotics are given as soon as possible. Often, ongoing care is performed in an intensive care unit. If fluid replacement is not enough to maintain blood pressure, medications that raise blood pressure may be used. Mechanical ventilation and dialysis may be needed to support the function of the lungs and kidneys, respectively. To guide treatment, a central venous catheter and an arterial catheter may be placed for access to the bloodstream. Other measurements such as cardiac output and superior vena cava oxygen saturation may be used. People with sepsis need preventive measures for deep vein thrombosis, stress ulcers and pressure ulcers, unless other conditions prevent such interventions. Some might benefit from tight control of blood sugar levels with insulin [8]. The use of corticosteroids is controversial. Drotrecogin alfa, originally marketed for severe sepsis, has not been found to be helpful, and was withdrawn from sale in 2011 [4].

Disease severity partly determines the outcome. The risk of death from sepsis is as high as 30%, from severe sepsis as high as 50%, and from septic shock as high as 80%. The number of cases worldwide is unknown as there is little data from the developing world. Estimates suggest sepsis affects millions of people a year. In the developed world approximately 0.2 to 3 people per 1000 are affected by sepsis yearly, resulting in about a million cases per year in the United States. Rates of disease have been increasing. Sepsis is more common among males than females. The medical condition has been described since the time of Hippocrates. The terms "septicemia" and "blood poisoning" have been used in various ways and are no longer recommended [5].

In addition to symptoms related to the actual cause, sepsis is frequently associated with the following – fever, low body temperature, rapid breathing, a fast heart rate, confusion, and edema. Early signs include a rapid heart rate, decreased urination, and high blood sugar. Signs of established sepsis include confusion, metabolic acidosis (which may be accompanied by a faster breathing rate that leads to respiratory alkalosis), low blood pressure due to decreased systemic vascular resistance, higher cardiac output, and disorders in blood-clotting that may lead to organ failure. The drop in blood pressure seen in sepsis can cause lightheadedness and is part of the criteria for septic shock [6].

Infections leading to sepsis are usually bacterial, but may be fungal or viral. Gram-positive bacteria was the predominant cause of sepsis before the introduction of antibiotics in the 1950s. After the introduction of antibiotics, gram-negative bacteria became the predominant cause of sepsis from the 1960s to the 1980s. After the 1980s, gram-positive bacteria, most commonly staphylococci, are thought to cause more than 50% of cases of sepsis. Other commonly implicated bacteria include Streptococcus pyogenes, Escherichia coli, Pseudomonas aeruginosa, and Klebsiella species. Fungal sepsis accounts for approximately 5% of severe sepsis and septic shock cases; the most common cause of fungal sepsis is infection by Candida species of yeast [7]. a frequent hospital-acquired infection.

The most common sites of infection resulting in severe sepsis are the lungs, the abdomen, and the urinary tract [16]. Typically, 50% of all sepsis cases start as an infection in the lungs. No definitive source is found in one third to one half of cases [8].

Over the past year, we noticed an increase in the isolation rate of nonalbicans Candida species from cases of neonatal septicemia, which prompted us to undertake the present study; to analyze and evaluate the change in the species distribution of Candida species in neonatal septicemia and determine their in vitro antifungal susceptibility and the risk factors associated with their acquisition.

Methodology

The present study was planned in the Department of Microbiology in Government Medical College, Bettiah, Bihar. Total 125 patients were referred to the department were enrolled in the present study. All patients diagnosed as having candidemia were included in the study. Candidemia was defined as the presence of at least one positive blood culture containing pure growth of Candida species with supportive clinical features.

Blood samples for cultures were collected (on clinical suspicion of septicemia) into Bactec Peds plus/f culture vials of an automated blood culture system (Bactec 9120, Becton Dickinson, USA). Any growth indicated was subcultured on 5% sheep blood agar, Mac Conkey agar and Sabouraud's dextrose agar (SDA) with chloramphenicol (0.05%) and incubated at 37°C. The Candida species isolated were identified as per standard mycological techniques. The preliminary identification was done by colony morphology on SDA, chromogenic media (HiChrome, Himedia, Pvt., Ltd.), growth at 45°C, germ tube test and was confirmed by carbohydrate fermentation and assimilation tests [9].

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Results & Discussion

The data from the 125 cases were collected and presented as below. Infection with unusual organisms is an increasing problem. Due to advances in medical and surgical management, an increase in nosocomial fungal infection rate has been observed. Candidemia is an emerging problem in healthcare settings. Knowledge of the epidemiology of candidemia can help to salvage patients, who are in the productive age group, with few with underlying medical condition.

Infection represents a frequent complication among the patients admitted to tertiary care hospitals. Candida spp. infections have increased in the last few decades, particularly those caused by the NAC, indicating the importance of laboratory diagnosis for the correct identification of species involved and initiation of timely and adequate treatment [10].

Table 1: Age & Sex Details

Age in years	No. of Cases
0 – 1 years	11
1 – 5 years	8
5 – 12 years	21
12 – 18 years	7
18 – 30 years	23
31 – 40 years	39
40 – 50 years	10
50 years and above	6
Total	125

Table 2: Distribution of microorganisms isolated

Type of Microbes	No. of Isolates
Candida species isolated	40
Candida tropicalis	17
Candida albicans	8
Candida krusei	6
Candida parapsilosis	3
Candida guilliermondii	3
Candida dubliniensis	3
Gram-negative bacilli	50
Gram-positive bacilli	35
Total	125

Table 3: Risk Factors

Risk factors	No. of Cases
Risk factors in Adults	
Indwelling central line	12
Malignancy	16
Total parenteral nutrition	9
Chemotherapy	13
Abdominal surgery	7
Sepsis	5
Abdominal diseases	6
Malnutrition	10
Total	78
Risk factors in Childrens	
Total parenteral nutrition	14
Indwelling central line	10
Low birth weight	9
Preterm	11
Maternal complication	3
Total	47

Colonization is the precursor for clinical infection and the risk for nosocomial infection is as high as 38% with colonization by Candida [11]. Studies have demonstrated that a significant reduction in Candida colonization and invasive Candida infections was observed in NICU when antifungal prophylaxis was used [12, 13]. Various investigators have suggested that preventive strategies in ICUs should be targeted to populations with a baseline rate of candidemia ≥10%, however, long term use of prophylactic antifungals was associated with drug resistance [14-15]. Ideally, using the lowest effective dose for the shortest length of time may be most desirable as it may limit the development of resistance. Currently, our center does not have a trend of prophylactic antifungal administration and we suggest the use of same in high risk neonates.

Use of multiple invasive devices such as catheters, endotracheal tubes or surgery causes break in the integrity of skin/mucosa and predisposes these sites for colonization and infection by Candida spp. Studies suggest that clearance of fungemia occurs more quickly when catheters are removed and failure to remove catheter as soon as candidemia is detected is a risk factor for death [16].

The trends in BSI caused by yeasts have been changing in the past few decades and many new species of Candida have been isolated from patients with candidemia in the last few years. More than 17 species of Candida have been implicated in human infections till date and the list of reported species continues to grow. The emergence of new species of Candida as potential pathogens is a reflection of the changing scenario in medicine since the 1960s.

More than 90% of the invasive infections due to Candida are attributed to five species-C. Albicans, C. Glabrata, C. Parapsilosis, C. Tropicalis and C. Krusei. However, the list of new species of Candida isolated from clinical specimens continues to grow every year [17]. This is due to the fact that clinical microbiology laboratories worldwide are using commercially available identification methods to supplement the conventional methods of identification. Besides, the increasing isolation of previously "nonpathogenic" yeasts could also be due to the increased number of immunocompromised patients worldwide in view of the Human Immunodeficiency virus (HIV) epidemic and the increasing number of organ transplantations.

Antibiotics promote fungal overgrowth at the expense of normal bacterial flora and encourage translocation of yeast across the intact mucosa. The risk of candidemia is also known to increase exponentially with each class of antimicrobial used [18]. Recent reports have suggested that the use of third generation cephalosporins was strongly associated with candidemia [19]. In our center, an empiric antibiotic regime is initiated based on high perinatal risk factors for early onset sepsis. The current hospital antibiotic policy recommends initial empiric use of ampicillin-gentamicin for neonates born within the facility and cefotaxime-amikacin for neonates referred from elsewhere. Probably, the long-term use of these broad spectrum antibiotics must have created a negative pressure and a favorable environment for Candida species to flourish. This further substantiates the need of prophylactic antifungals to be used in a set up where continuous upsurge in the incidence of candidemia is seen. Anecdotally, NICUs have observed decreasing rates of candidemia by implementing wise antimicrobial stewardship strategies and improving infection control practices [20].

In patients with candidemia, other bacteria were isolated from various sites like blood, pus, urine and sputum in our study. The most common bacteria are, Coagulase negative staphylococci and Pseudomonas aeruginosa in blood, Pseudomonas aeruginosa and Klebsiella pneumoniae in pus and E coli and Pseudomonas aeruginosa in urine. This suggest that Pseudomonas aeruginosa is the predominant bacteria isolated from majority of the sample which is similar to a study conducted in AIIMS, New Delhi.1

Conclusion

The changing epidemiology of candidemia highlights the need for close monitoring of Candida species distribution and susceptibility to optimize treatment and outcome. It is apparent from the results of the present study that routine identification of Candida isolates to the species level, and

the detection of resistant strains by antifungal susceptibility test is essential. Furthermore, there is a continued need for surveillance of candidemia to monitor changes in the epidemiological features and antifungal susceptibility and also to develop and evaluate prevention strategies.

References

1. https://www.britannica.com/science/septicemia
2. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM *et al*. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012 (PDF). Critical Care Medicine. 2013; 41(2):580-637.
3. Jui Jonathan *et al*. (American College of Emergency Physicians) Ch. 146: Septic Shock. In Tintinalli, Judith E, Stapczynski J, Stephan Ma O. John; Cline, David M.; Cydulka, Rita K.; Meckler, Garth D. Tintinalli's Emergency Medicine: A Comprehensive Study Guide (7th ed.). New York: McGraw-Hill, 2011, pp. 1003-14.
4. Martí-Carvajal AJ, Solà I, Gluud C, Lathyris D, Cardona AF. Human recombinant protein C for severe sepsis and septic shock in adult and paediatric patients The Cochrane Database of Systematic Reviews. 2012' 12:CD004388.
5. Angus DC, van der Poll T. Severe sepsis and septic shock. The New England Journal of Medicine. 2013; 369(9):840-51.
6. MedlinePlus Encyclopedia Sepsis. Retrieved 29 November, 2014.
7. Delaloye J, Calandra T. Invasive candidiasis as a cause of sepsis in the critically ill patient. Virulence. 2014; 5(1):161-9. DOI:10.4161/viru.26187. PMC 3916370.
8. Munford RS, Suffredini AF. Ch. 75: Sepsis, Severe Sepsis and Septic Shock". In Bennett JE, Dolin R, Blaser MJ. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases (8th ed.). Philadelphia: Elsevier Health Sciences, 2014, 914-34.
9. McGinnis MR. Yeast identification. In: Laboratory Handbook of Medical Mycology. New York: Academic Press, 1980, 337-73.
10. Colombo AL, Guimarães T. Epidemiologia das infecções hematogênicas por Candida spp. Rev Soc Bras Med Trop. 2003; 36:599-607.
11. Saiman L, Ludington E, Dawson JD, Patterson JE, Rangel-Frausto S, Wiblin RT, *et al*. Risk factors for Candida species colonization of neonatal intensive care unit patients. Pediatr Infect Dis J. 2001; 20:1119-24.
12. Ozturk MA, Gunes T, Koklu E, Cetin N, Koc N. Oral nystatin prophylaxis to prevent invasive candidiasis in neonatal intensive care unit. Mycoses. 2006; 49:484-92.
13. Ganesan K, Harigopal S, Neal T, Yoxall CW. Prophylactic oral nystatin for preterm babies under 33 weeks' gestation decreases fungal colonisation and invasive fungaemia. Arch Dis Child Fetal Neonatal Ed. 2009; 94:F275-8.
14. Zaoutis TE, Prasad PA, Localio AR, Coffin SE, Bell LM, Walsh TJ, *et al*. Risk factors and predictors for candidemia in pediatric intensive care unit patients: Implications for prevention. Clin Infect Dis. 2010; 51:e38-45.
15. Sarvikivi E, Lyytikäinen O, Soll DR, Pujol C, Pfaller MA, Richardson M, *et al*. Emergence of fluconazole resistance in a Candida parapsilosis strain that caused infections in a neonatal intensive care unit. J Clin Microbiol. 2005; 43:2729-35.
16. Benjamin DK Jr, Stoll BJ, Fanaroff AA, McDonald SA, Oh W, Higgins RD *et al*. Neonatal candidiasis among extremely low birth weight infants: Risk factors, mortality rates, and neurodevelopmental outcomes at 18 to 22 months. Pediatrics. 2006; 117:84-92.
17. Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: A persistent public health problem. Clin Microbiol Rev. 2007; 20:133-63.
18. Juyal D, Adekhandi S, Negi V, Sharma N. An outbreak of neonatal candidemia due to non-albicans Candida species in a resource constrained setting of Uttarakhand State, India. J Clin Neonatol. 2013; 2:183-6.
19. Hartung de Capriles C, Mata-Essayag S, Azpiróz A, Ponente A, Magaldi S, Pérez C, *et al*. Neonatal candidiasis in Venezuela: Clinical and epidemiological aspects. Rev Latinoam Microbiol. 2005; 47:11-20.
20. Zaoutis TE, Prasad PA, Localio AR, Coffin SE, Bell LM, Walsh TJ, *et al*. Risk factors and predictors for candidemia in pediatric intensive care unit patients: Implications for prevention. Clin Infect Dis. 2010; 51:e38-45.