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Emergence of Non- Albicans Candida Species in Neonatal Candidemia in A Tertiary Care Hospital in Meerut City

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Abstract
Background: *Candidemia is a significant cause of nosocomial mortality and morbidity in neonates. The changing pattern in the isolation of Candida species from C. albicans to non-albicans Candida (NAC) species has resulted in the emergence of resistance to antifungal drugs.*
Aims & Objectives:*i) To study the frequency of neonatal candidemia in our tertiary care hospital ii) To identify the Candida isolates upto species level. iii) To determine the risk factors and correlate the data clinically.*
Methods: *Blood samples collected from clinically suspected cases of neonatal septicaemia were inoculated into automated BacT/Alert 3D system (bioMerieux). Any growth indicated was sub-cultured on 5% sheep blood agar and Sabouraud's dextrose agar (SDA) with chloramphenicol and incubated at 37°C for 24 hours. Candida species isolated was identified upto species level as per standard mycological techniques and by automated Vitek 2 YST identification card (bioMerieux).*
Result: *The frequency of neonatal candidemia was 37.5% (117/312). Out of the total of 117 cases of neonatal candidemia,non –albicansCandida (NAC) species were isolated in 82.06% cases and in the remaining 17.94% cases C. albicans was isolated. The predominant isolate was C. tropicalis (43.58%), followed by C.albicans (17.94%), C. parapsilosis(17.09%), C. glabrata (8.54%) and C. krusei (5.12%).Candidemia was most commonly associated with prematurity (76.92%), followed by low birth weight (64.10%), prolonged antibiotic usage (48.71%), steroid therapy (13.67%) and ventilatory support (11.11%). The most common clinical presentation was feed intolerance, followed by abdominal distension, lethargy and failure to gain weight.*
Conclusions: *Isolation of NAC species definitely indicates a changing trend and the emergence of antifungal drug resistance. Strict infection control strategies and a restrictive policy of antibiotic use should be implemented*
Keywords: *Neonates, candidemia, Non-albicans Candida, Candida albicans*

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I. Introduction

The *Candida* species are one of the most common causes of blood stream infections (BSIs).[1,2,3] As per initial records, *C. albicans* has been considered as the frequent fungal isolate causing neonatal candidemia, but in the recent years there has been a mycological shift towards non-albicans *Candida* (NAC) species.[4,5,6,7,8]. Various factors such as broad spectrum antibiotics, low birth weight (LBW), prematurity, total parental nutrition, artificial ventilation, and /or history of fungal colonization contribute to the risk of candidal sepsis.[3,8,9]*Candida* can also spread through vertical transmission from maternal flora or via horizontal transmission from hands of healthcare workers (HCW),[10,11]The important concern associated with isolation of NAC species is the increased resistance to antifungal drugs, thus contributing to morbidity and mortality.[1,2,8]

II. Materials And Method

The prospective study was carried out in the Post Graduate Department of Microbiology, Subharti Medical College and associated ChhatrapatiShivajiSubharti Hospital, Meerut, from May 2017 to April 2018. The study group included the neonates admitted in NICU with the clinical diagnosis of septicaemia.

Ethics approval: Approval by the institutional ethics committee was taken before conducting the study.
Sample Processing: -A total of 440 neonates with the clinical diagnosis septicemia were enrolled in the present study. Blood samples collected from clinically suspected cases of neonatal septicaemia were inoculated into paediatric automated culture bottle (BacT/Alert 3D system, bioMerieux). Any growth indicated was sub-cultured on 5% sheep blood agar and Sabouraud's dextrose agar (SDA) containing chloramphenicol and incubated at 37°C for 24 hours.[1,2]The isolates were identified up to species level using 1) conventional method as per standard mycological techniques,[1,2,12] using Gram stain, germ tube test, microscopic characteristics on Corn Meal Agar, culture characteristics on Chrom agar, carbohydrate fermentation and sugar assimilation
2) Automated Vitek 2 YST identification card (bioMerieux, France) as manufacturer's instructions.

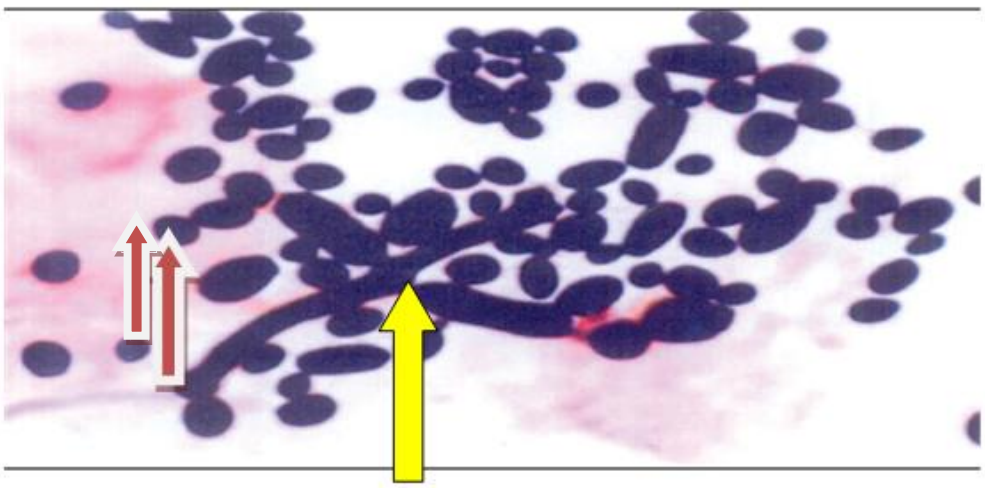

Figure 1: Gram stained smear showing Gram positive oval budding yeast cell (thin arrow) with pseudohyphae(thick arrow)

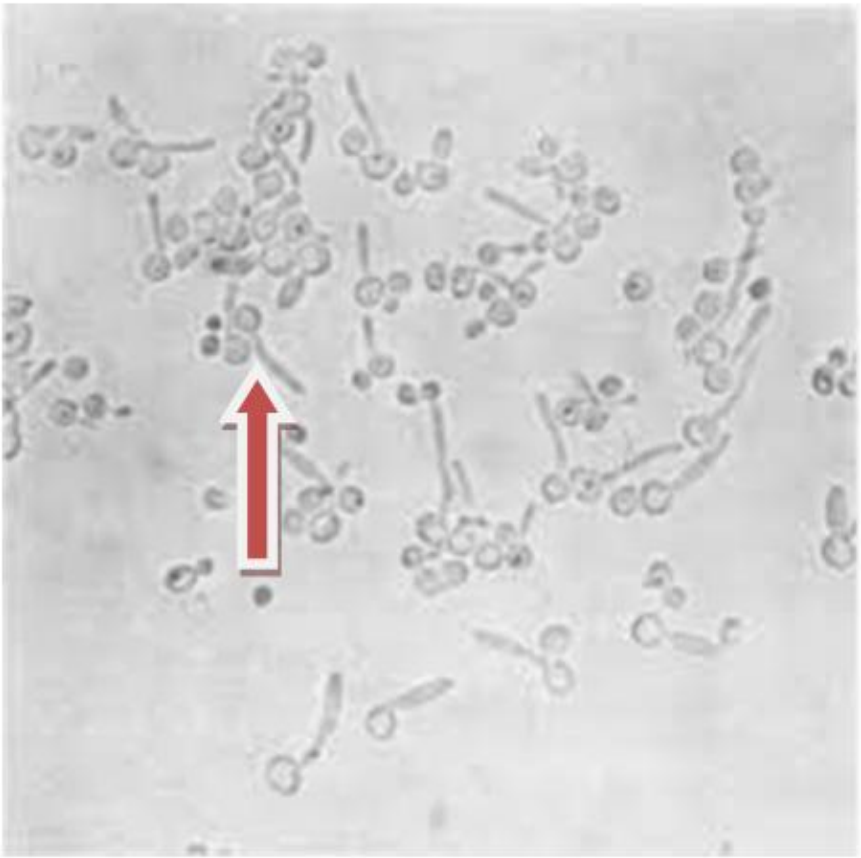

Figure 2: *Candida albicans* showing germ tube formation (arrow)

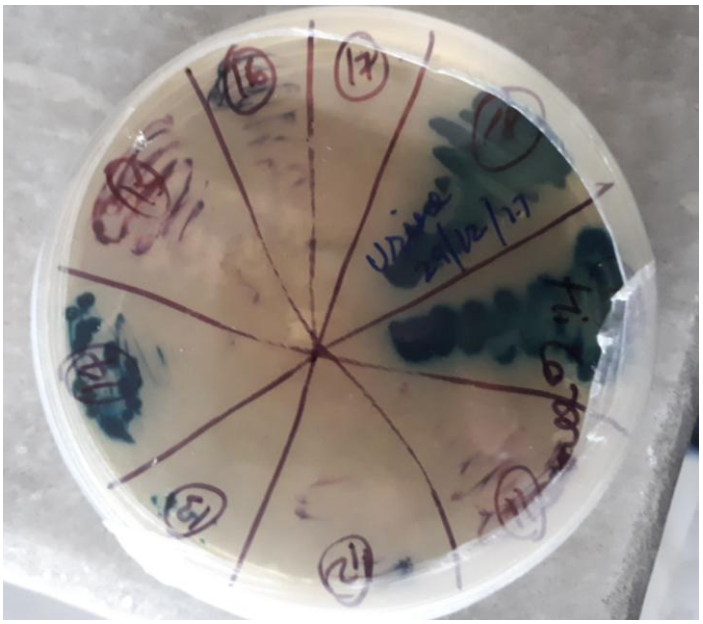

Figure 3: Colony colour of *Candida* species on Chrom agar

Figure 4: Carbohydrate fermentation test

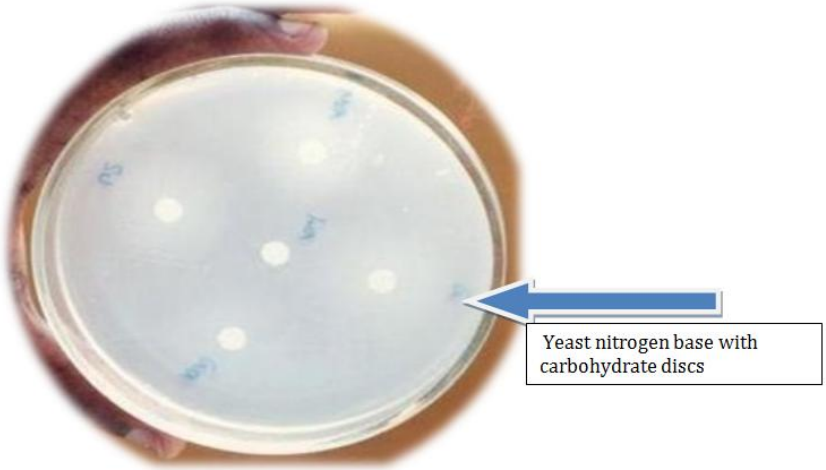

Figure 5: **Sugar Assimilation**

Figure 6: Vitek 2 yeast identification card

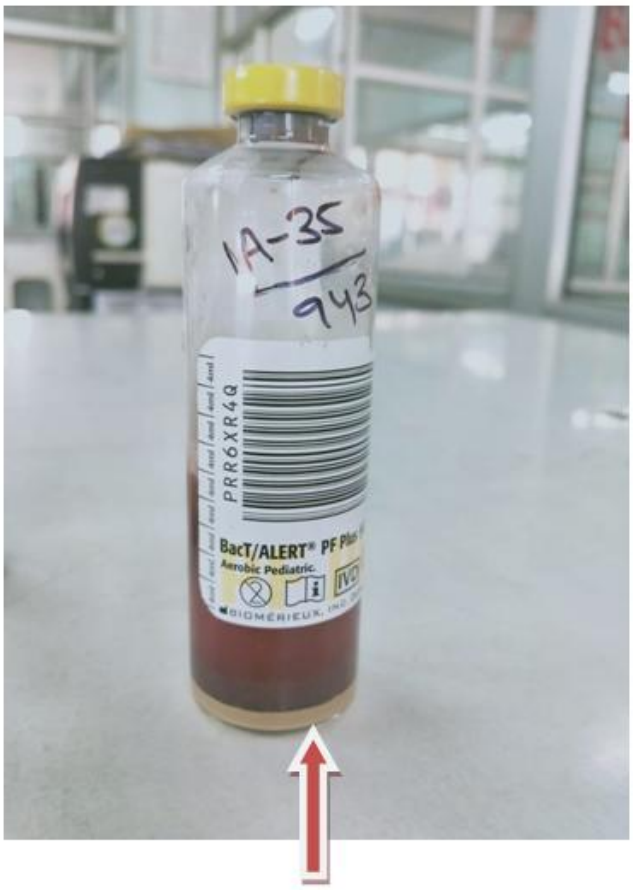

Figure 7: Bact/Alert 3D pediatric blood culture bottle positive for growth (arrow)

III. Results

Out of total of 440neonates clinically suspected of septicemia, 312 (70.9%) cases were blood culture positive and the remaining 128(29.1%) cases were blood culture negative. Out of culture positive cases, pure growth of *Candida* was isolated from 37. 5% (117/312), pure growth of bacteria from 53.8% (168/312) and mixed growth of bacteria and yeast from 8.6%(27/312) cases. Second blood sample was collected from 90 neonates out of 117,and both the sets of blood culture showed growth of *Candida* with same speciation,but in the remaining 27 neonates , even though the second sample could not be collected but these neonates were CRP positive. Thus,the frequency of neonatal candidemia in our set up was 37.5% (117/ 440).Out of the total of 117 cases of neonatal candidemia,NAC species were isolated in 96 (82.06%)cases and in the remaining 21

(17.94%)cases,*C. albicans* was isolated.(Figure 8).In the present study,*C. tropicalis* (43.58%), was thepredominant isolate, followed by *C.albicans* (17.94%),*C. parapsilosis*(17.09%), *C. glabrata* (8.54%) and *C. krusei* (5.12%) [Table1].Among the risk factors, prematurity (76.92%) was the commonest followed by LBW (64.10%), prolonged antibiotic usage (48.71%), steroid therapy(13.67%) and ventilator support (11.11%).[Table 3].The most common clinical presentation was feed intolerance (76.06%),, followed by abdominal distension (64.95%), lethargy(60.68%)and failure to gain weight.(Table 3).

Figure 8: *Candida albicans* versus non-albicans *Candida* in cases of neonatal candidemia (n=117)

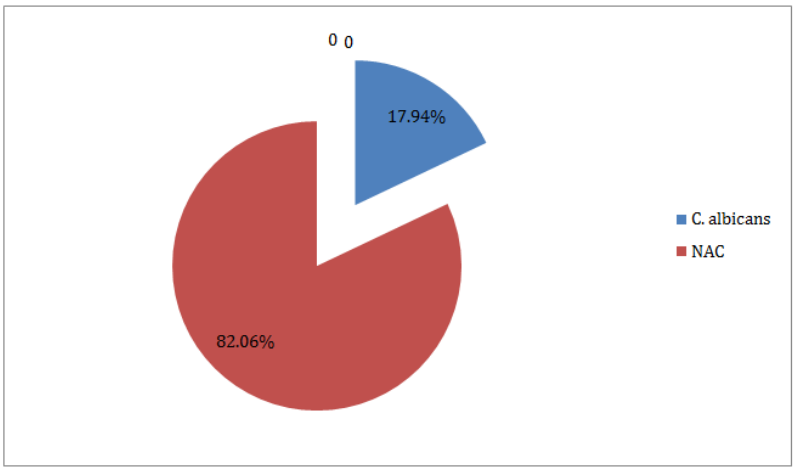

Table 1: Identification of *Candida* species isolated from the cases of neonatal candidemia (n = 117)

Organism	No of isolates	%
C. tropicalis	51	43.58%
C, *albicans*	21	17.94%
C.parapsilosis	20	17.09%
C. glabrata	10	8.54%
C. krusei	6	5.12%
C. glilliermondii	4	3.41%
C. famata	2	1.7%
C. lusitaniae	2	1,7%
C.rugose	1	0.85%

Table 2: Risk factors associated with cases of neonatalcandidemia (n-117)

Risk factors	No of cases	Percentage
Prematurity	90	76.92%
Low birth weight	75	64.10%
Prolonged antibiotic usage	57	48.71%
Steroid therapy	16	13.67%
Ventilator support	13	11.11%

Table 3: Clinical presentationsin neonates withcandidemia(n- 117)

Clinical sign/ symptom	No. of cases	%
Feed intolerance	89	76.06%
Abdomen distension	76	64.95%
Lathagary	71	60.68%
Failure to gain weight	40	34.18%
Hypothermia	33	28.20%
Poor perfusion	21	17.94%
Respiratory distress	15	12.82%

IV. Discussion

Reporting of fungal blood stream infection and spectrum of species involved are essential measures in any intensive care unit in order to implement appropriate preventive and therapeutic strategies. The incidence of candidemia in neonates has increased substantially, due to multiple risk factors.

In our tertiary care hospital, the frequency of neonatal candidemia was 37.5%. In 2018, Shettigar CG*etal.*[13] reported the frequency of candidal sepsis in 9.59% of neonates in Mangalore. Rani *et al.*[14]found candidemia in 34.7% of neonates in New Delhi, which is comparable to our study. A study by Roy *et al.*[15]found

candidemia in 20.9%culture proven cases of neonatal septicemia from Kolkata. However, Agarwal J *etal.*[16] reported isolation of *Candida* species from blood in 13.6%cases of neonatal septicemia from Lucknow.

In the present study, NAC species accounted for 82.06% of the cases of neonatal candidemia, whereas *C.albicans*was responsible for 17.94% of cases. In 2018, Fu J *et al.*[17]found that 56.5% cases of neonatal candidemia were caused by NAC species in Western China. The predominance of NAC species in candidal sepsis have been observed by various other authors.[[4,18,19,20,21]].

In the present study, *C. tropicalis* (43.58%), was the predominant isolate, followed by *C.albicans* (17.94%), *C. parapsilosis*(17.09%), *C. glabrata* (8.54%) and *C. krusei* (5.12%) A study done by Geol S *et al.*[6] in Rohtak, have reported *C. tropicalis*as most common(43%) species isolated from neonates with candidemia, followed by *C.albicans*(41%)and *C. krusei*(9%).Our findings were similar to the study carried out by Gunjan*et al.*[22] who had reported the isolation of *C. tropicalis* (44%) as the most common cause of neonatal candidemia. A study done by Sardana V *et al.*[4] found *C. glabrata* as most common cause of candidemia in neonates (39%), followed by*C. tropicalis* (26.4%) and *C. parapsilosis*(14.5%).A study from Hyderabad by Sirinivas Rao MS *et al.*[23]found *C.tropicalis*as most common cause of candidemia in neonates (36.53%), followed by*C. albicans* (26.92%) and *C. glabrata*(19.23%). Similar observations of change in trend of candidemia in NICU were also made by many other authors.[17,24,25]The emergence of NAC species has posed a serious issue leading to increased resistance to antifungal drugs, which has become a great therapeutic concern. *C. glabrata* and *C. krusei* are innately resistant to azoles. The change in the pattern might be due to widespread use of prophylactic or empiric antifungal therapy.[1,2,4,8]

In the present study, among the risk factors associated with candidemia, prematurity and LBW were more common followed by prolonged antibiotic usage, steroid therapy and ventilator support .

A study by Juyal D *etal.*[8] observed that prematurity(73.49%) and LBW(67.42%) were the common risk factors which is almost similar to our study. Narang A *et al.*[26] and Romeo *et al.*[27]found that prematurity was associated with 94% and 85% cases of neonatal candidiasis respectively.

In our setup, feed intolerance was the most common clinical presentation, followed by abdominal distension, lethargy and failure to gain weight. Shettigar CG *et al.*[13] in a study from Mangalore have also reported feed intolerance(77.78%), abdominal distension(64.81%) and lethargy(61.11%) as the common clinical symptoms. Sardana V *et al.*[4] found respiratory distress as prominent clinical symptom (74.55%) followed by lethargy(64.55%) and feed intolerance (60.91%).

LIMITATION OF THE STUDY

Due to unavailability of resources, antifungal susceptibility testing of the *Candida* isolates could not be done.

V. Conclusion

A mycological shift towards the isolation of non-albicans *Candida* species in neonatal candidal sepsis definitely indicates a changing trend and the emergence of antifungal drug resistance. Strict infection control strategies and a restrictive policy of antibiotic use should be implemented to reduce the morbidity and mortality associated with candidiasis.

Preventive measures such as use of filters for parenteral nutrition, prophylactic antifungal use, and a restrictive policy of antibiotic use to decrease *Candida* infection rates should be implemented

References

[1]. Chander J, *Texbook of Medical Mycology*, 4th editionJaypee Brothers Medical publisher:2017.

[2]. Winn W, Allen S, Janda W, Koneman E, Procop G, Schreckenberger P. *et* al(eds.) *Koneman's Color Atlas and Textbook of Diagnostic Microbiology*. 6thedition. Philadelphia: Lippincott Williams &Wilkins;2006.

[3]. Caggiano G., Lovero G., De Giglio, OBarbuti, G., Montagna, O., Laforgia, N., &Montagna, M. T. (2017). Candidemia in the Neonatal Intensive Care Unit: A Retrospective, Observational Survey and Analysis of Literature Data. *BioMed research international*, *2017*, 7901763. doi:10.1155/2017/7901763

[4]. Sardana V, Pandey A, Madan M, Goel S P, Asthana AK Neonatal candidemia: A changing trend. Indian J PatholMicrobiol 2012;55:132-3

[5]. Benjamin DK, Jr. Stoll BJ, fanaroff AA, McDonald SA, Oh W, Higgins RD,et al. National Institute of Child Health and Human Development Neonatla Network. Neonatlal candidiasis among extremely low birth weight infants: Risk factors, mortality rates, and neuro develpmental outcomes at 18 to 22 months. Pediatrics. 2006; 117:87-92.

[6]. Goel N, RajanPk, Aggarwal R, Chaudhary U, Sanjeev N. Emergence of non albicans candida in neonatal septicaemia and antifugal susceptibility: Experience from a tertiary care center. J Lab physicians. 2009; 1: 53-5.

[7]. Oberoi JK, Wattal C, Goel N, Raveendran R, Datta S, Prasad K. Non – albicanscandida species in blood stream infections in a tertiary care hospital at New Delhi, India. Indian J Med Res. 2012;136:997-1003.

[8]. Juyal D, Adekhandi S, Negi V, Sharma N. An Outbreak Of NeonatalCandidemia Due To Non-Albicans *Candida* Species In A Resource Constrained Setting Of Uttarakhand State, India. J. Clin.Neonatal.2013 2(4):183-6

[9]. Singhi S, Rao DS, Chakrabarti A. Candida colonization and candidemia in a pediatric intensive care unit. PediatrCrit Care Med. 2008;9:91–5.

[10]. Ariff S, Saleem AF, Soofi SB, Sajjad R. Clinical spectrum and outcomes of neonatal candidiasis in a tertiary care hospital in Karachi, Pakistan. J Infect Dev Ctries. 2011;5:216–23.

[11]. Adib SM, Bared EE, Fanous R, Kyriacos S. Practices of Lebanese gynecologists regarding treatment of recurrent vulvovaginal candidiasis. N Am J Med Sci. 2011;3:406–10.
[12]. McGinnis MR. Laboratory Handbook of Medical Mycology. New York: Academic Press; 1980. Yeast Identification; pp. 337–73.
[13]. Shettigar CG, Shettigar S. Non albicansCandidemia: an emerging menace in neonatal intensive care unit. Int J ContempPediatr 2018;5:436-41
[14]. Rani R, Mohapatra NP, Mehta G, Randhawa VS, Changing species in neonatal septicemia in a tertiary North Indian hospital. Ind J Med Mirobiol 2002;20:424
[15]. Roy A, Maiti PK, Adhya S *etal*. Neonatal candidemia . Indian J Pediatr. 1993;60:799-801
[16]. Agarwal J,Bansal S, Malik GK ,Jain A. Trend in neonatal septicemia; Emergence of non albicans Candida . Indian Pediatr 2004;41;712-5.
[17]. Fu J, Ding Y, Jiang Y, Mo S, Xu S, Qin P. Persistent candidemia in very low birth weight neonates: risk factors and clinical significance. *BMC Infect Dis*. 2018;18(1):558. Published 2018 Nov 12. doi:10.1186/s12879-018-3487-9
[18]. Baradkar VP, Mathur M, Kumar S, Rathi M. Candida glabrata emerging pathogen in neonatal sepsis. Ann Trop Med Pub Health. 2008;1:5–8.
[19]. Kothari A, Sagar V. Epidemiology of *Candida* bloodstream infections in a tertiary care institute in India. Indian J Med Microbiol. 2009;27:171–2.
[20]. Juyal D, Sharma M, Pal S, Rathaur VK, Sharma N. Emergence of non-albicans Candida species in neonatal candidemia. *N Am J Med Sci*. 2013;5(9):541–545. doi:10.4103/1947-2714.118919
[21]. Roilides E, Farmaki E, Evdoridou J, Francesconi A, Kasai M, Filioti J, et al. *Candida tropicalis* in a neonatal intensive care unit: Epidemiologic and molecular analysis of an outbreak of infection with an uncommon neonatal pathogen. J ClinMicrobiol. 2003;41:735–41.
[22]. Shrivastava G, Bajpai T, Bhatambare GS, Chitnis V, Deshmukh AB. Neonatal candidemia: Clinical importance of species identification. Sifa Med J 2015;2:37-40
[23]. Srinivas Rao MS, Surendranath M, Sandeepthi M. Prevalence of neonatal candidemia in a tertiary care institution in Hyderabad, South India. Int J Res Med Sci. 2014;2:1016-9.
[24]. Caggiano G, Lovero G, Giglio O De, Barbuti G, Montagna O, Laforgia N, et al. Candidemia in the neonatal intensive care unit: a retrospective, observational survey and analysis of literature data. Bio Med Res Int. 2017;2017:Article ID 7901763.
[25]. Lovero G, Giglio O De, Montagan O, Diella G, Divenuto F, Lopezzo M, et al. Epidemiology of candidemia in neonatal intensive care unit: a persistent public health problem. Ann Ig. 2016;28:282-7
[26]. Narang A, Agrwal PB. Chakrabarti A, Kumar P. Epidermiology of systemic candidiasisin a tertiary care neonatal unit .J Trop Ped998;44:45-8
[27]. Romeo Reyes MC, Fernandez Gutierrez F, Poyato Dominguez JL. Neonatal systemic candidiasis in the nineties . An Esp Pediatr.1996;26:642-5

Vandanasardana. "Emergence of Non- Albicans Candida Species in Neonatal Candidemiain A Tertiary Care Hospital in Meerut City." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 4, 2019, pp 42-48.