CORRELATION OF RISK FACTORS ASSOCIATED WITH FUNGAL SEPSIS IN NEONATES ADMITTED TO NEONATAL INTENSIVE CARE UNIT. A ONE YEAR HOSPITAL BASED OBSERVATIONAL STUDY

By
REGISTRATION NO: BM0120007

Dissertation

Submitted to

KAHER, Belagavi, Karnataka

In partial fulfilment

of the requirements for the degree of

M.D.

IN

PAEDIATRICS

DEPARTMENT OF PAEDIATRICS

JAWAHARLAL NEHRU MEDICAL COLLEGE

BELAGAVI- 590010. KARNATAKA.

JUNE/JULY 2023

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH, BELAGAVI, KARNATAKA

Endorsement by the HOD/ Principal/ Head of the Institution

This is to certify that the dissertation entitled "**CORRELATION OF RISK FACTORS ASSOCIATED WITH FUNGAL SEPSIS IN NEONATES ADMITTED TO NEONATAL INTENSIVE CARE UNIT. A ONE YEAR HOSPITAL BASED OBSERVATIONAL STUDY"** is a bonafide research work done by **REG NO: BM0120007.**

Dr. TANMAYA METGUD
MD (PAEDIATRICS)
Professor and Head,
Department of Paediatrics,
J. N. Medical College,
Nehru Nagar, Belagavi – 10

Date: 2/1/2023
Place: Belagavi

Dr.(Mrs.) N.S. MAHANTSHETTI
MD (PAEDIATRICS)
Principal
J. N. Medical College,
Nehru Nagar, Belagavi – 10

PRINCIPAL
J.N. Medical College,
BELAGAVI-590 010

Date: 2/1/2023
Place: Belagavi

KAHER BELAGAVI J.N. MEDICAL COLLEGE

ii

UNDERTAKING

I, **Reg. No. BM0120007,** hereby declare that the information and the data mentioned in my dissertation entitled **"CORRELATION OF RISK FACTORS ASSOCIATED WITH FUNGAL SEPSIS IN NEONATES ADMITTED TO NEONATAL INTENSIVE CARE UNIT. A ONE YEAR HOSPITAL BASED OBSERVATIONAL STUDY"** belongs to me and is original. I am aware of the definition of plagiarism as detailed below.

- An act or instance of using or closely imitating the language and thoughts of another author without authorization and the representation of that author's work as one's own, as by not crediting the original author.
- A piece of writing or other work reflecting such unauthorized use or imitation.
- The deliberate or reckless representation of another's words, thoughts or ideas as one's own without attribution in connection with submission of academic work, whether graded or otherwise.

I hereby declare that the dissertation prepared by me is original-one and does not involve plagiarism anywhere. In case at a later stage, it is found that I have indulged in plagiarism, then I am solely responsible for the same and the institution is at liberty to take any disciplinary action against me including cancellation of dissertation or any other penalties imposed by the University.

Date: 2/1/2023

Place: Belagavi

PLAGIARISM CERTIFICATE

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH

JAWAHARLAL NEHRU MEDICAL COLLEGE

(Recognized by Medical Council of India, New Delhi)

Accredited 'A+' Grade by NAAC (3rd Cycle) **Placed in Category 'A' by MHRD (GoI)**

Nehru Nagar, Belagavi- 590 010, Karnataka, INDIA

0831 - 2471350 0831 - 2470759 www.jnmc.edu principal@jnmc.edu

Ref No: MDC/PG/ Date: 21-12-2022.

ACCEPTANCE LETTER

The softcopy of thesis entitled: **"CORRELATION OF RISK FACTORS ASSOCIATED WITH FUNGAL SEPSIS IN NEONATES ADMITTED TO NEONATAL INTENSIVE CARE UNIT- A ONE YEAR HOSPITAL BASED OBSERVATIONAL STUDY"** has been submitted for Anti-Plagiarism check through Turnitin software. The scan has been carried out and the scanned output reveals a match percentage of **07%** which is within the acceptable limits of **10%** as per the guidelines given by UGC.

Guide.

PRINCIPAL
J.N. Medical College,
BELAGAVI- 590 010

KAHER BELAGAVI J.N. MEDICAL COLLEGE

Dr. (Mrs.) N.S. Mahantashetti.
Chairperson-Antiplagiarism Committee &
Principal,
J. N. Medical College, Belagavi.

PRINCIPAL
J.N. Medical College,
BELAGAVI- 590 010

To,
Reg. No. BM0120007,
Postgraduate Student,
2020-21 Batch,
Department of Paediatrics,
J. N. Medical College, Belagavi.

INSTITUTIONAL ETHICAL CLEARANCE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 165 **Date: 25/01/2021**

To,

PG student in Paediatrics,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"CORRELATION OF RISK FACTORS ASSOCIATED WITH FUNGAL SEPSIS IN NEONATES ADMITTED TO NEONATAL INTENSIVE CARE UNIT. A ONE YEAR HOSPITAL BASED OBSERVATIONAL STUDY",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Smita Sonoli)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Harsha Hegde)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

ABSTRACT

Introduction: Systemic fungal infections, occurs in 5% of low birth weight babies admitted to NICU. Candida species commonly causes Neonatal nosocomial bloodstream infections, especially in premature infants. The mortality is as high as 50% for fungal sepsis and the disability due to neurodevelopmental impairment poses a significant burden. Hence the early identification and appropriate empirical therapy specific to the regional prevalence, among the high-risk neonates is essential.

Objectives:

I. **Primary Objective:** To assess the correlation of risk factors associated with fungal sepsis in neonates admitted to NICU.

II. **Secondary Objectives:** To assess the prevalence of candida subspecies. To compare clinical outcome of albicans and non-albicans candida species. To study the antifungal sensitivity pattern

Methodology: This is a Prospective Observational study, among 70 New-borns (<28 days old) with proven candidial sepsis, admitted to neonatal intensive care unit, under the KLEH DR. Prabhakar Kore Charitable Hospital, Department of Paediatrics, Jawaharlal Nehru Medical College, Belagavi. Data regarding probable risk factors, clinical outcome of neonates with fungal sepsis, and species of the fungal organism isolates were collected.

Results: Neonatal risk factors observed in newborn with fungal sepsis in our study were newborns with Preterm(67.1%), LBW(77.1%), respiratory distress(82.9%), birth asphyxia(18.57%), NEC(25.7%), Neonatal seizures(22.9%), associated bacterial sepsis with shock(35.7%) , DIC(31.4%), MIS-N(18.6%), thrombocytopenia(85.7%),

hypocalcemia(65.7%), deranged coagulation profile(31.4%), and interventions like use of broad spectrum antibiotics mainly third generation cephalosporin(100%), use of steroids(27.1%), iv fluids(97.1%), non invasive oxygen support(78.6%), long line insertion(70%) and mechanical ventilation(24.3%). Important predictors of mortality in newborns with fungal sepsis in our study were complications like apnoea(p=0.043), NEC(p=0.009), neonatal seizures(p=0.006), associated bacterial sepsis with shock(p=0.001), DIC(p=0.001), MIS-N(p=0.014) and presence of hypoglycemia(p=0.034), anemia(p=0.002), deranged coagulation profile(p=0.001) and interventions like invasive ventilation(p=0.001), use of steroids(p=0.009) and ionotropes(p=0.001) .

The most common organism isolated were C. non albicans (74.29%) of which C. glabrata(73%) was common , followed by C. albicans (25.71%). The mortality rate was found to be 14.29%, with prematurity (80%) being the most common cause of death. C. non albicans was associated with high mortality, of which Candida parapsilosis had higher proportion of deaths with 33.33% (6 out of 70) followed by Candida glabarta (13.15%).

CONCLUSION: we found that the risk factors associated with mortality were prematurity being most common followed by NICU complications such as apnoea, NEC, neonatal seizures, bacterial sepsis with shock, DIC, MIS-N. Presence of hypoglycemia, anemia, deranged coagulation profile and use of steroids, ionotropes and prolonged invasive ventilation were high predictors for mortality as they were statistically significant. Majority of fungal isolates showed sensitivity to Caspofungin (58 of 70) followed by Fluconazole(29 out 70),hence we suggest fluconazole should be the first line of antifungal to be used empirically in newborns having risk factors

for fungal sepsis. and subsequently use of other anti fungal drugs should be based on culture & sensitivity reports.

KEYWORDS: Fungal sepsis, Risk factors, mortality in neonates with fungal sepsis

LIST OF ABBREVIATIONS USED

NICU	-	Neonatal intensive care unit
SIRS	-	Systemic inflammatory response syndrome
MODS	-	Multiple organ dysfunction syndrome
LBW	-	Low birth weight
VLBW	-	Very low birth weight
ELBW	-	Extremely low birth weight
ET	-	Endotracheal tube
GBS	-	Group- B streptococcus
PCR	-	Polymerase chain reaction
LSCS	-	Lower(uterine) segment caesarean section
NVD	-	Normal vaginal delivery
UTI	-	Urinary tract infection
GDM	-	Gestational diabetes mellitus
PV leak	-	Leak per vagina
DIC	-	Disseminated intravascular coagulation
NEC	-	Necrotising enterocolitis
MIS	-	**N-** Neonatal multisystem inflammatory syndrome
MAS	-	Meconium aspiration syndrome

PT	-	Prothrombin time
APTT	-	Activated partial thromboplastin clotting time
INR	-	International normalised ratio
HsCRP	-	High sensitivity C- reactive protein
NOGC	-	No growth cultured
TPN	-	Total parenteral nutrition

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Neonatal sepsis is one of the common cause of the death among neonates, causing nearly one million new-born deaths globally every year. [1,2] The incidence of neonatal sepsis varies between less than 1% to more than 35% of live births. On the basis of time of onset, neonatal sepsis can be early-onset sepsis (<72 hours after birth) or late-onset sepsis (≥72 hours after birth). [3,4]

Sepsis can occur at any age. But the incidence and mortality rates of sepsis are higher among the neonates, compared to other age groups.[5] The incidence and mortality rates of sepsis are even higher among the preterm neonates. [6,7] The outcome of infection is predicted by at least four major factors: the type of the pathogen, the pathogenic load, the site of infection, and the host response.[5]

A successful immune response is essential to face the infectious challenges and prevention of dissemination of the infection. When the inflammation gets generalized, it leads to systemic inflammatory response syndrome (SIRS). If the infection is not controlled, the spread of the pathogen leads to systemic endothelial activation and precipitate sepsis, severe sepsis, and septic shock. Sepsis can progress to shock leading to multiple organ dysfunction syndrome (MODS) and death.[5]

Neonatal infections can be transmitted from mother to foetus or community acquired or may be nosocomial. New-born infants are less capable of responding to infections and coexisting condition often complicate the diagnosis and management. The clinical manifestation is varying from subclinical to severe. There may be focal or systemic infection and rarely, congenital syndromes resulting from in utero infection. The etiologic agents are wide variety, including bacteria, viruses, fungi, protozoa and mycoplasma. Preterm, very low birth weight (VLBW) babies need a prolonged hospital stay which puts them at continuous risk for acquired infections. [8,9]

Systemic fungal infections, previously considered to be rare complication, occur in as many as 5% of low birth weight babies admitted to NICU.[10,11] Candida species commonly causes Neonatal nosocomial bloodstream infections, especially in premature infants. The mortality is as high as 50% and the disability due to neurodevelopmental impairment poses a significant burden. [12,13] C. albicans is the most common cause of the fungal sepsis in neonates, followed by C. parapsilosis, C. glabrataC. tropicalis, and C.krusei. [14,15]

Risk factors can be Maternal risk factors (like vaginal candida colonization through the route of delivery), Neonatal risk factors (like prematurity, low birth weight, co-morbidities such as Meconium aspiration syndrome, persistent pulmonary hypertension of new-born, intra-ventricular haemorrhage, necrotizing enterocolitis, respiratory distress syndrome, inborn errors of metabolism and cardiac anomalies), Intensive care procedures (like placement of naso gastric tubes, endo tracheal (ET) tubes, mechanical ventilation, peripherally inserted central catheter, lumbar puncture), and Concomitant use of medications like antibiotics, parenteral nutrition, intra lipids.[16–18]

Need for the study / Justification of the study:

Fungal infections especially Candida species exhibits varying levels of resistance to azoles and other anti-fungal agents. Hence the current data on neonatal fungal isolates and their antimicrobial susceptibility patterns to guide empiric anti-fungal therapy.[19–21] Some studies involving the prediction models to estimate the risk of neonatal fungal sepsis based on wide range of clinical features, risk factors and/or laboratory tests but due to lack of specificity and limitations these models are considered insignificant to predict the neonatal fungal sepsis.

There is paucity of literature in fungal sepsis among neonates, especially focussing on the risk factors of the incidence and the outcomes. Hence, this study would be beneficial so as to determine the risk factors associated with fungal sepsis and identify possible predictors of poor outcomes of fungal sepsis in our hospital set up. Therefore this study aims to study the, clinical outcomes, antifungal sensitivity pattern, and the correlation of risk factors associated with fungal sepsis in neonates admitted to NICU.

AIM AND OBJECTIVES

AIM:

To study the risk factors in newborns with fungal sepsis admitted to NICU and to assess the clinical outcomes, antifungal sensitivity pattern,

OBJECTIVES:

Primary Objectives: To assess the correlation of risk factors associated with fungal sepsis in neonates admitted to NICU.

Secondary Objectives: To compare clinical outcome of newborns with fungal sepsis. To study the antifungal sensitivity pattern.

REVIEW OF LITERATURE

Review of Literature of this study on fungal sepsis in neonates admitted to NICU, is discussed under the following heads:

a. Neonatal Sepsis
    i. Definitions
    ii. Aetiology
    iii. Systemic Inflammatory Response Syndrome (SIRS)
    iv. Diagnosis
    v. Complications
    vi. Pathophysiology
b. Fungal Sepsis in neonates
    i. Risk factors
    ii. Diagnosis
    iii. Treatment
c. Similar studies in the same topic

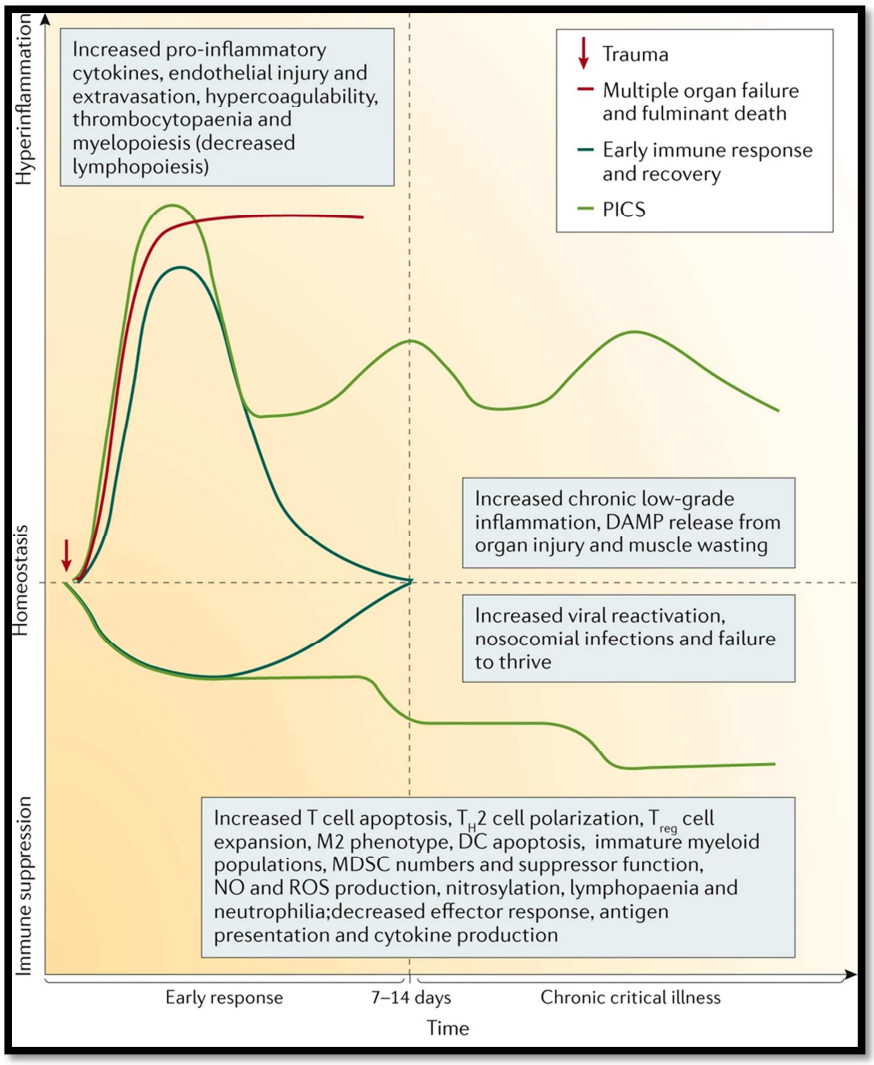
a. Neonatal Sepsis:

A successful immune response is essential to face the infectious challenges and prevention of dissemination of the infection. When the inflammation gets generalized, it leads to systemic inflammatory response syndrome (SIRS). If the infection is not controlled, the spread of the pathogen leads to systemic endothelial activation and precipitate sepsis, severe sepsis, and septic shock. Sepsis can progress to shock leading to multiple organ dysfunction syndrome (MODS) and death.(5)

Definitions:

- **Bacteraemia** - refers to presence of bacteria in blood stream.Bacteraemia itself is often a self-limiting process in otherwise healthy children. Approximately, 10 % of children with bacteraemia will develop serious bacterial infections.
- **Occult bacteraemia**- relatively asymptomatic(occurs in normal daily activities such as conducting oral hygiene and after minor medical procedures)
- **Sepsis** - accompanied by findings of serious bacterial infections.When immune response mechanisms fail or overwhelmed, bacteraemia develops into a bloodstream infection.
- Untreated and clinically significant bacteraemia progresses to sepsis, septic shock, systemic inflammatory response syndrome (SIRS), and multiple organ dysfunction syndrome (MODS).(22–24) The following figure represents the Current conceptual model of outcomes of sepsis,(25)

Figure 1.Current conceptual model of outcomes of sepsis.



Aetiology:

Identification of the primary source of infection is important in management of bacteraemia. Among the hospitalised patients, Common sources of bacteraemia is from the respiratory tract and indwelling catheters, specifically the central venous catheters.(26,27) Among the community-acquired bacteraemia, Urinary tract infections are common.(28–30)

Soft tissue and intraabdominal infections are common in the post-operative surgical setting, otherwise rare. Most common cause of gram-negative bacteraemia is Escherichia coli and the most common cause of gram positive bacteraemia is Staphylococcus aureus.(31–33) The following table represents the common microorganisms causing bacteraemia,(34)

Table 1.Common microorganisms causing bacteraemia

Gram-positive
Staphylococcus aureus
Coagulase-negative *Staphylococcus*
Streptococcus group A
Streptococcus pneumoniae
Enterococcus species
Streptococcus, other species
Listeria monocytogenes
Other bacilli
Gram-negative
Escherichia coli
Pseudomonas species
Salmonella species
Klebsiella species
Enterobacter species
Proteus species
Brucella species
Other Enterobacteriaceae
Other nonfermentative bacilli
Other cocci
Anaerobic
Bacteroides species
Clostridium species
Fungal
Candida species
Cryptococcus species
Mycobacterial
Mycobaterium tuberculosis
Mycobacterium avium complex

Group B streptococcus (GBS), Escherichia coli, coagulase-negative Staphylococcus, Haemophilus influenza, and Listeria monocytogenes are the common causative organism of early onset neonatal sepsis (<72 hours). Coagulase-negative staphylococcal species, especially Staphylococcus epidermis, (nearly 50%) is the leading cause of late onset neonatal sepsis (>72 hours).(35,36)

Systemic Inflammatory Response Syndrome (SIRS) :

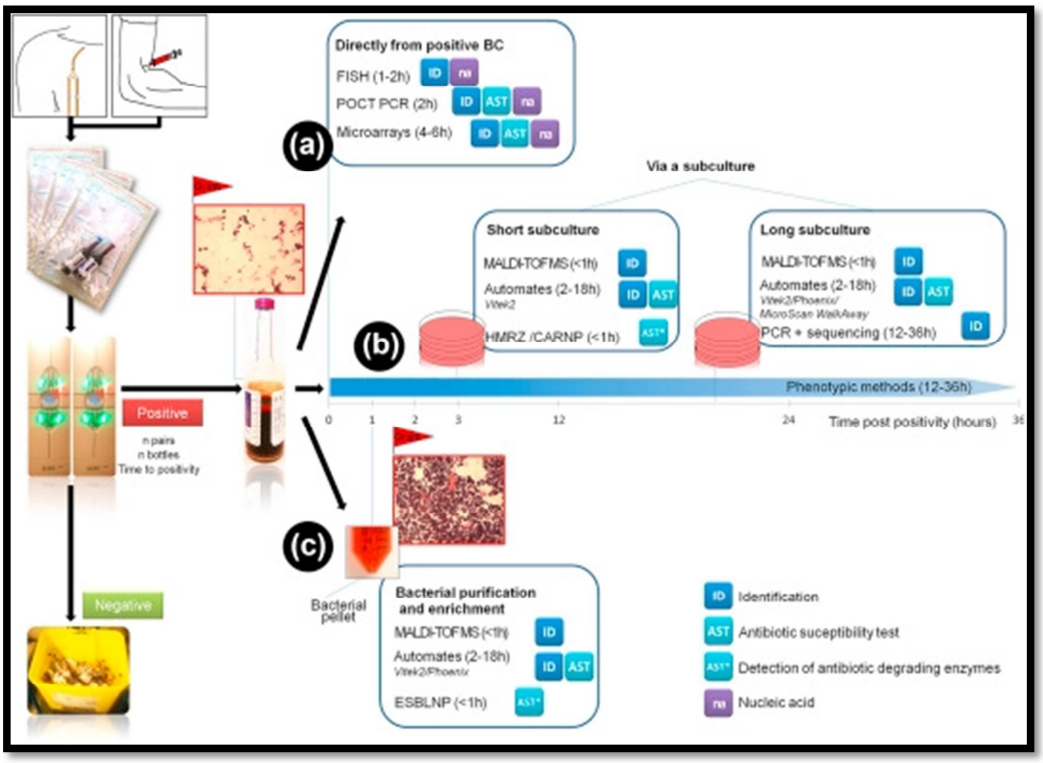
Criteria for diagnosing SIRS: 2 out of 4 criteria, 1 of which must be either abnormal temperature or abnormal leukocyte count.

i. core temperature >38.5 * c or <36 * c
ii. RR above normal for age or acute need-for mechanical ventilation.
iii. tachycardia for age in the absence of external stimuli or painful stimuli (or) unexplained persistent elevation over 0.5 -4 hours (or) in children <1yr , persistent bradycardia over 0.5 hours (in the absence of vagal stimuli, beta blockers, or congenital heart disease)
iv. leukocyte count elevated or reduced for age (not secondary to chemotherapy) or >10% immature neutrophils.(37–39)

Diagnosis:

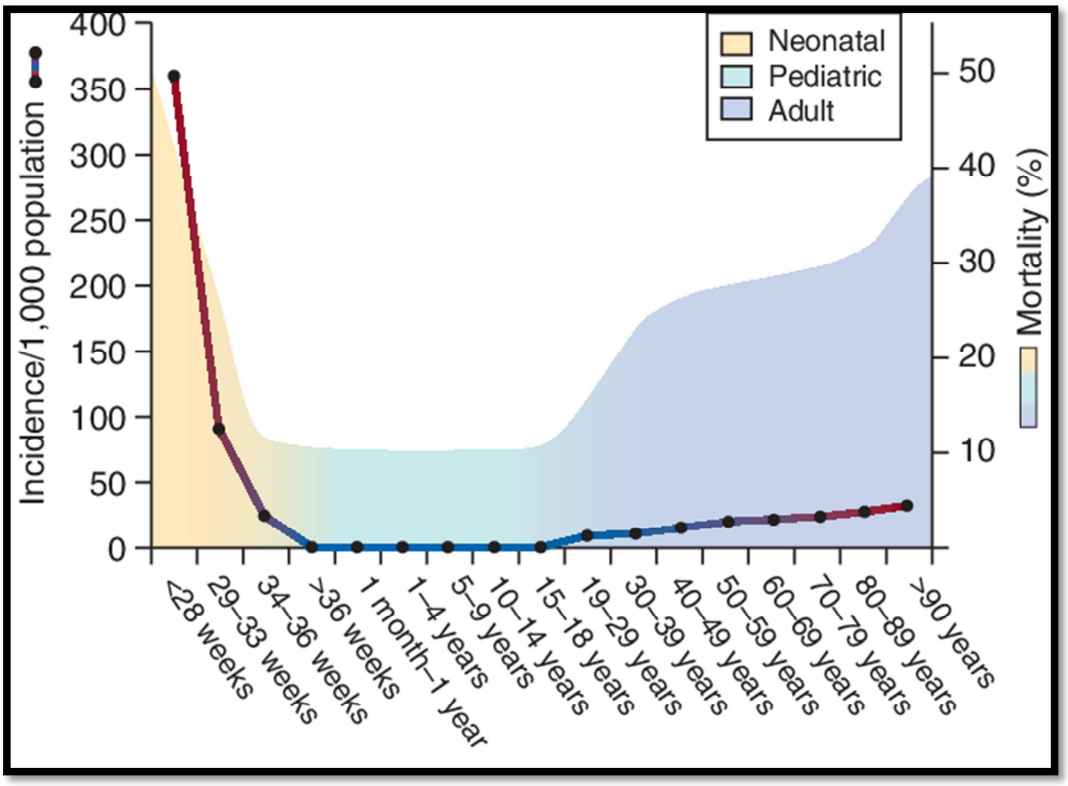
Blood culture remains the gold standard for diagnosing the bacteraemia.(27,40) The following figure represents the Methods to identify microorganisms from positive blood cultures,(41)

Figure 2.Methods to identify microorganisms from positive blood cultures



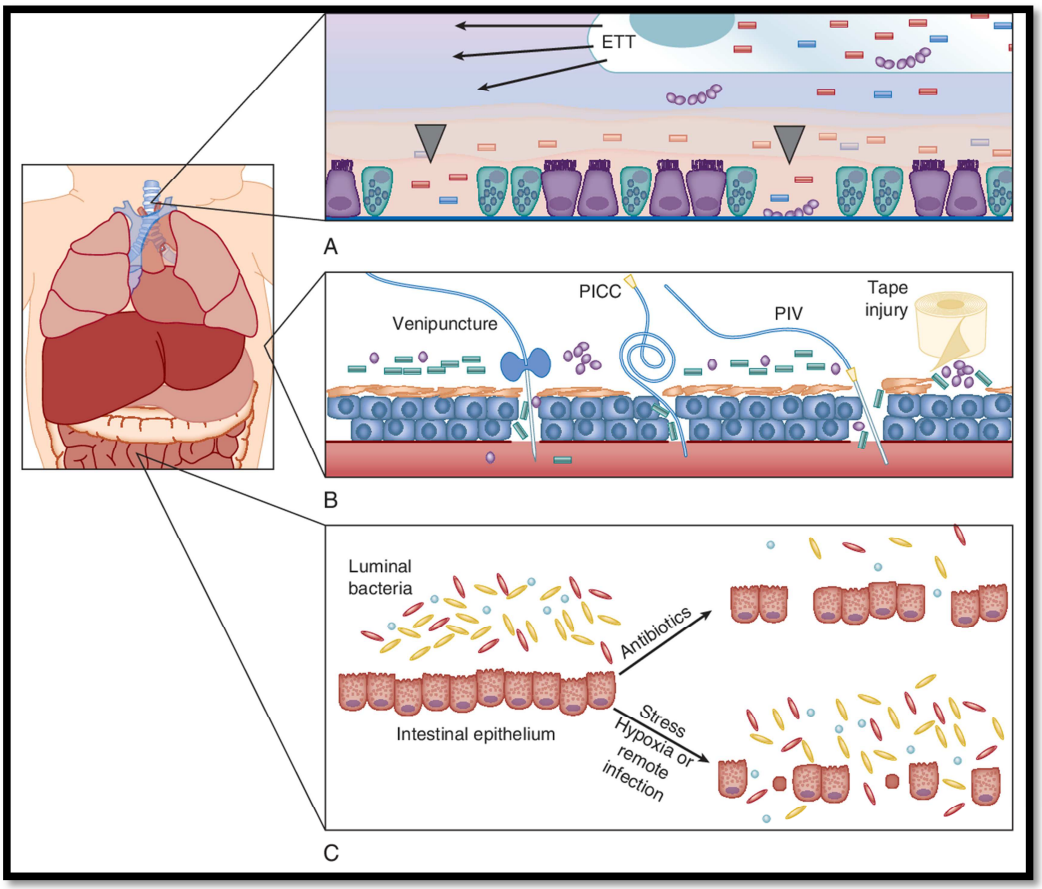
Sepsis can occur at any age. But the incidence and mortality rates of sepsis are higher among the neonates, compared to other age groups. The following chart explains the higher incidence and mortality rates of sepsis among the neonates,(5)

Figure 3.Incidence and mortality rates of sepsis among the neonates



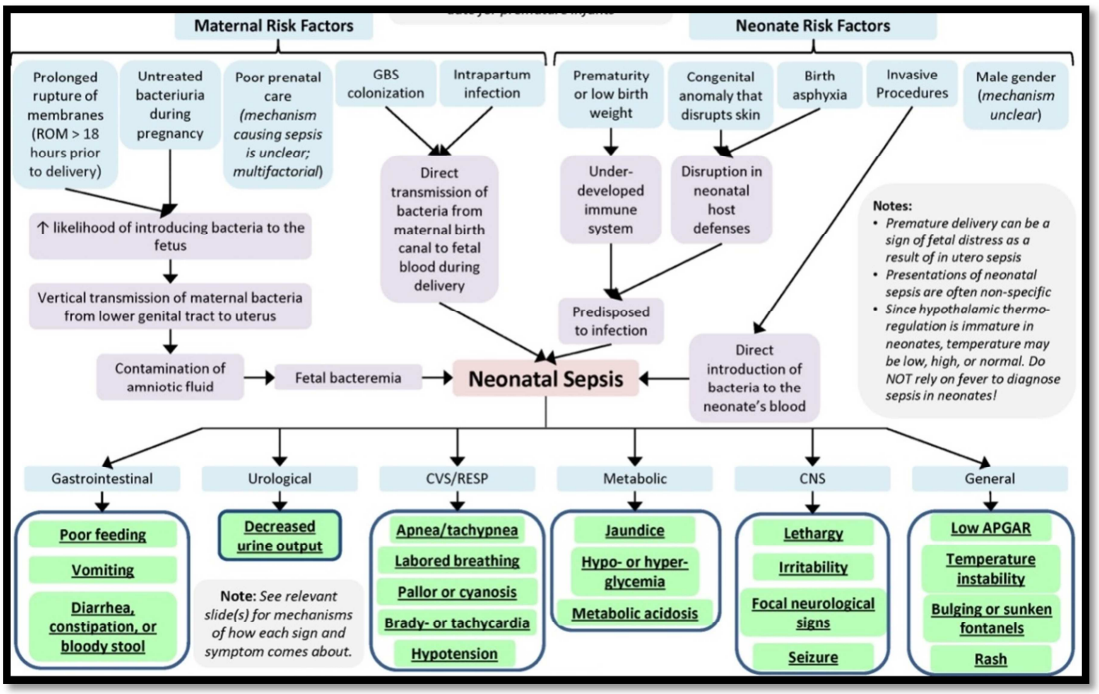
Respiratory mucosa, Skin and Gastrointestinal mucosa forms the Physical barriers to prevent the occurrence of neonatal sepsis. Any breach in this physical barrier due to multiple factors and causes, lead to neonatal sepsis. Presence of foreign body (like endotracheal tube) with or without positive pressure can create a breach in the respiratory epithelium. (A) Breach associated with trauma (like venepuncture or heel stick), can compromise the skin barrier. (B) The distribution interaction between intestinal bacteria and intestinal epithelium leads to loss of homeostasis and degradation of the Gastrointestinal mucosa. (C) The following image represents the Physical barriers to prevent the occurrence of neonatal sepsis, (5)

Figure 4.Physical barriers to prevent the occurrence of neonatal sepsis



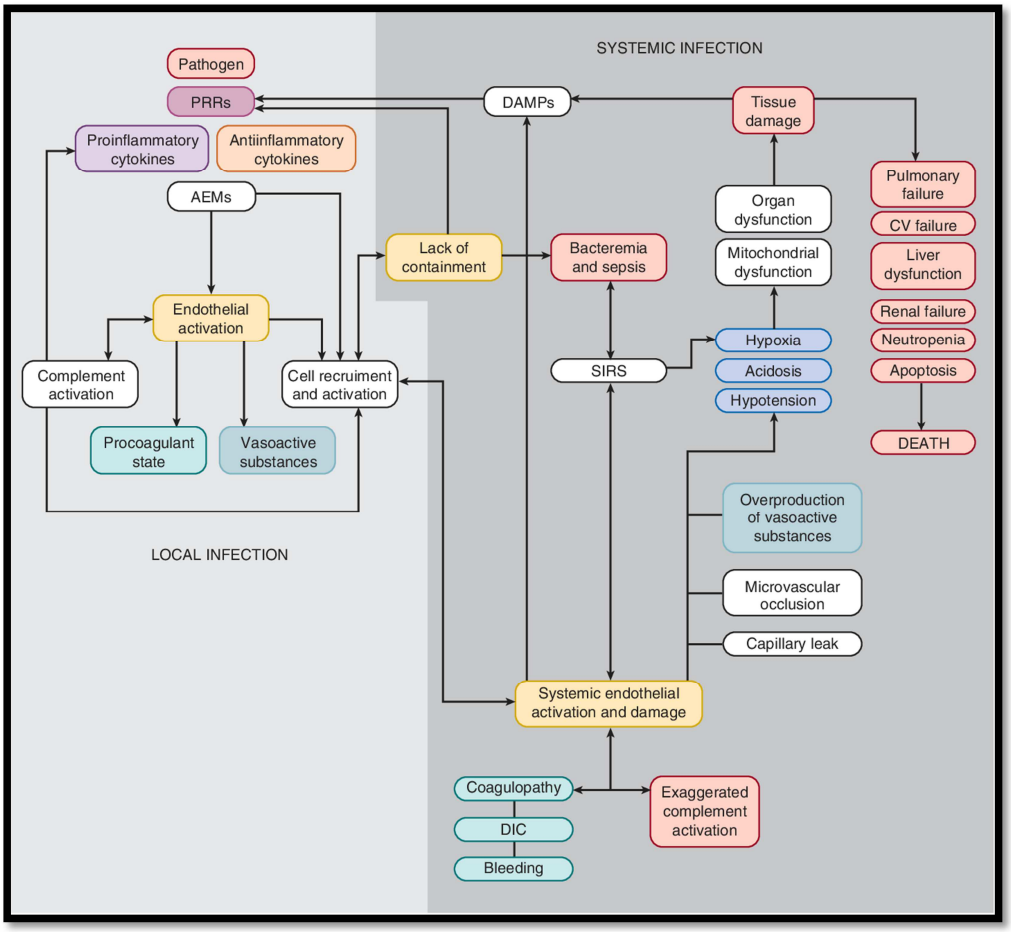
The following flowchart represents the risk factors, Pathogenesis and clinical overview of Neonatal sepsis, (42)

Figure 5.Pathogenesis and clinical overview of Neonatal sepsis



The following figure represents the pathophysiology of neonatal sepsis leading to septic shock due to systemic inflammatory response syndrome,(5)

Figure 6.Pathophysiology of neonatal sepsis leading to septic shock



Complications:

The outcome of infection is predicted by at least four major factors: the type of the pathogen, the pathogenic load, the site of infection, and the host response. The following list represents the complications of bacteraemia,

- Sepsis
- Meningitis
- Endocarditis
- Cellulitis
- Osteomyelitis
- Peritonitis.(43)

b. Fungal Sepsis in neonates:

Systemic fungal infections , previously considered to be rare complication, occur in as many as 5% of low birth weight babies admitted to NICU.(10,11) The mortality is as high as 50% and the disability due to neurodevelopmental impairment poses a significant burden. (12,13)

In present day practice, extremely low birth weight babies are surviving due to the neonatal care and invasive procedures. At the same time, incidence of fungal sepsis increases due to the inevitable effectsof such advancement. The timely clinicalsuspicion and administration of appropriate antifungal treatment, early identification of end organ damage, and follow-up can produce the outcomes favourable out of the fungal sepsis. Due to the extensive usage of azole antifungals for treatment and prophylaxis there is an epidemiological shift, Some ofthese non-albicans Candida species (e.g., C.glabrata andC.krusei) exhibit intrinsic resistance to routine triazole agents. (44)

Candida species commonly causes Neonatal nosocomial bloodstream infections, especially in premature infants, and present as late onset sepsis.C. albicans is the most common cause of the fungal sepsis in neonates, followed by C. parapsilosis, C. glabrataC.tropicalis, and C.krusei. (14,15)The following list of organisms are the causes of the fungal sepsis in neonates,

i. Candida albicans
ii. Candida parapsilosis
iii. Candida glabrata
iv. Candida tropicalis

v. Candida krusei

vi. Candida dubliniensis

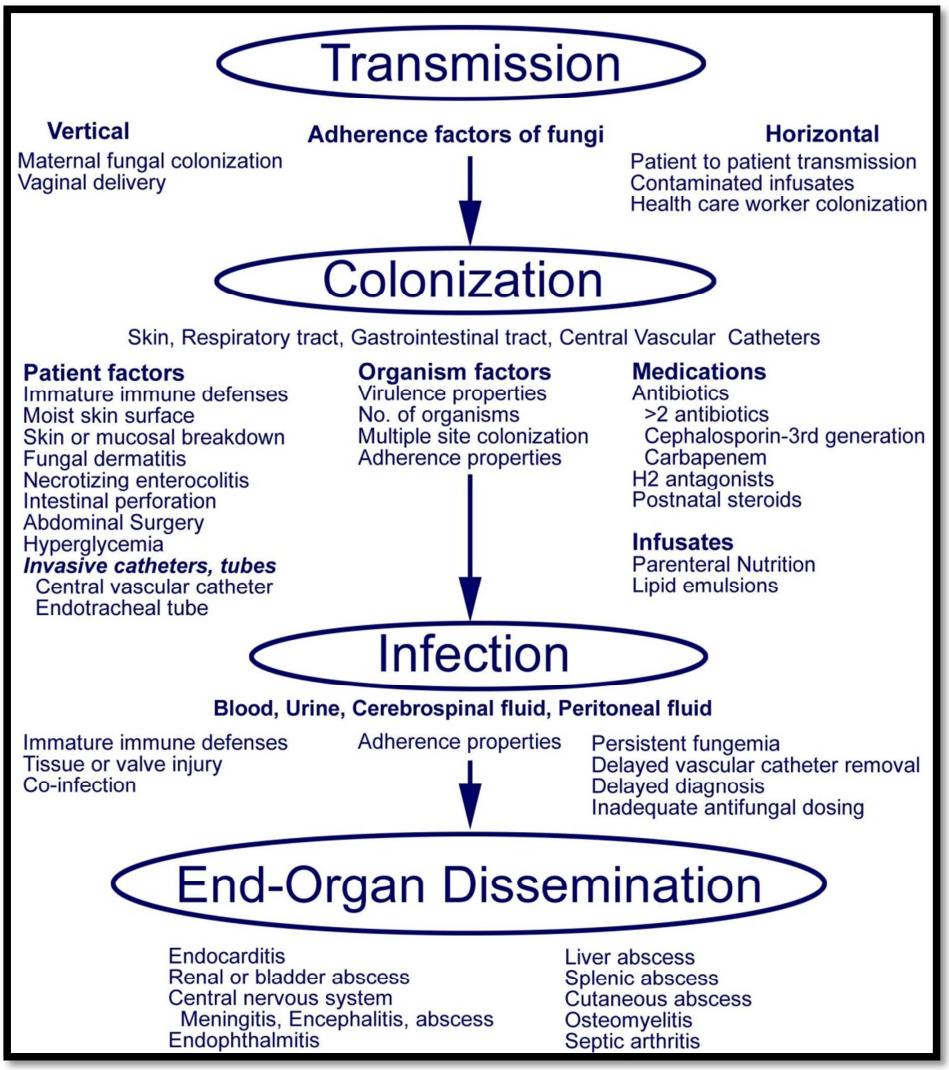
vii. Candida lusitaniae

viii. Hansenula polymorpha

ix. Saccharomyces cerevisiae. (45)

The following figure represents the Pathogenesis of fungal sepsis in neonates,(46)

Figure 7.Pathogenesis of fungal sepsis in neonates



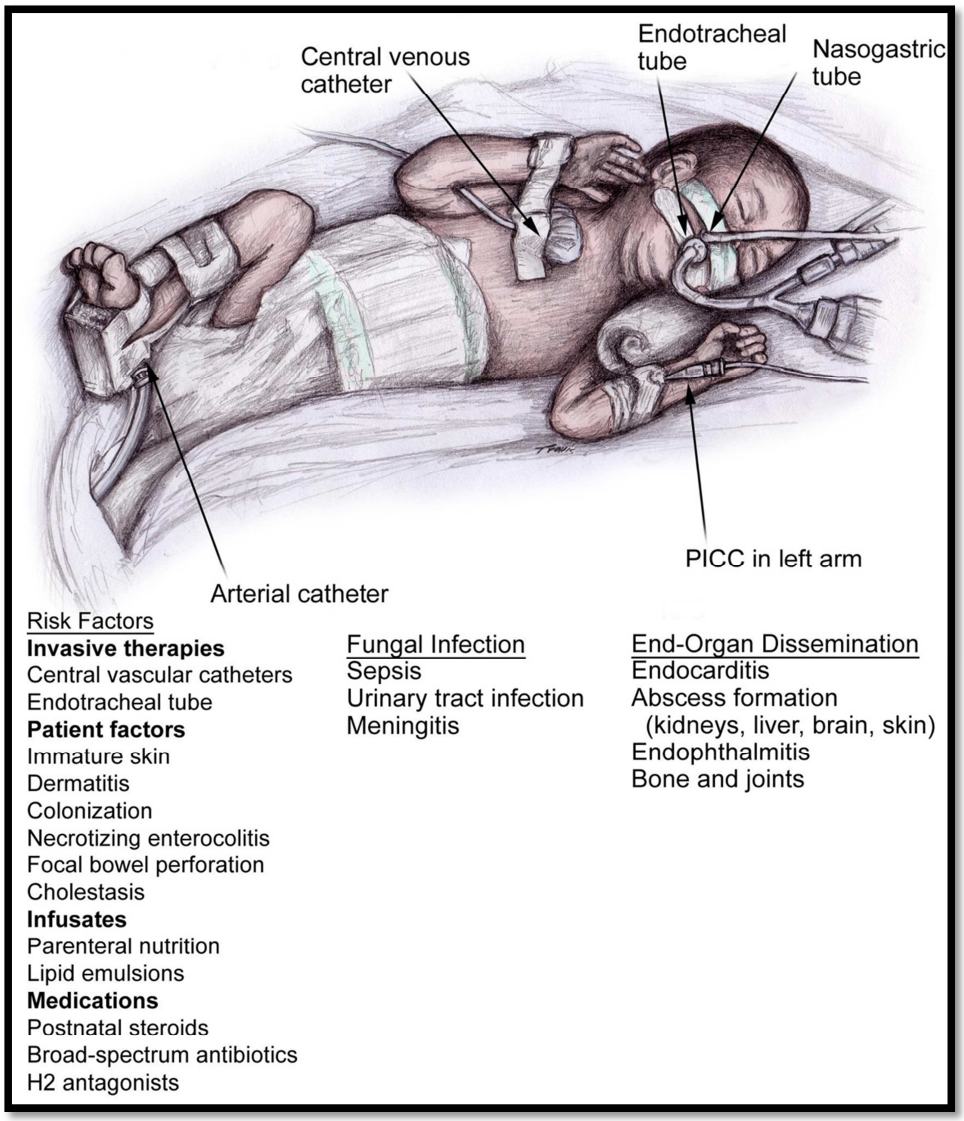
Risk factors:

Risk factors for the fungal sepsis in neonates include the following,

i. very low birth weight,
ii. gestational age <30 weeks,
iii. lack of antenatal care,
iv. use of central catheters,
v. endotracheal intubation,
vi. prolonged hospitalization,
vii. mechanical ventilation,
viii. intravenous hyperalimentation,
ix. exposure to H2 receptor antagonists,
x. use of broad-spectrum antibiotics/steroids
xi. previous colonization with Candida albicans. (47–49)

The following image summarises the risk factors for the neonatal fungal sepsis, (50)

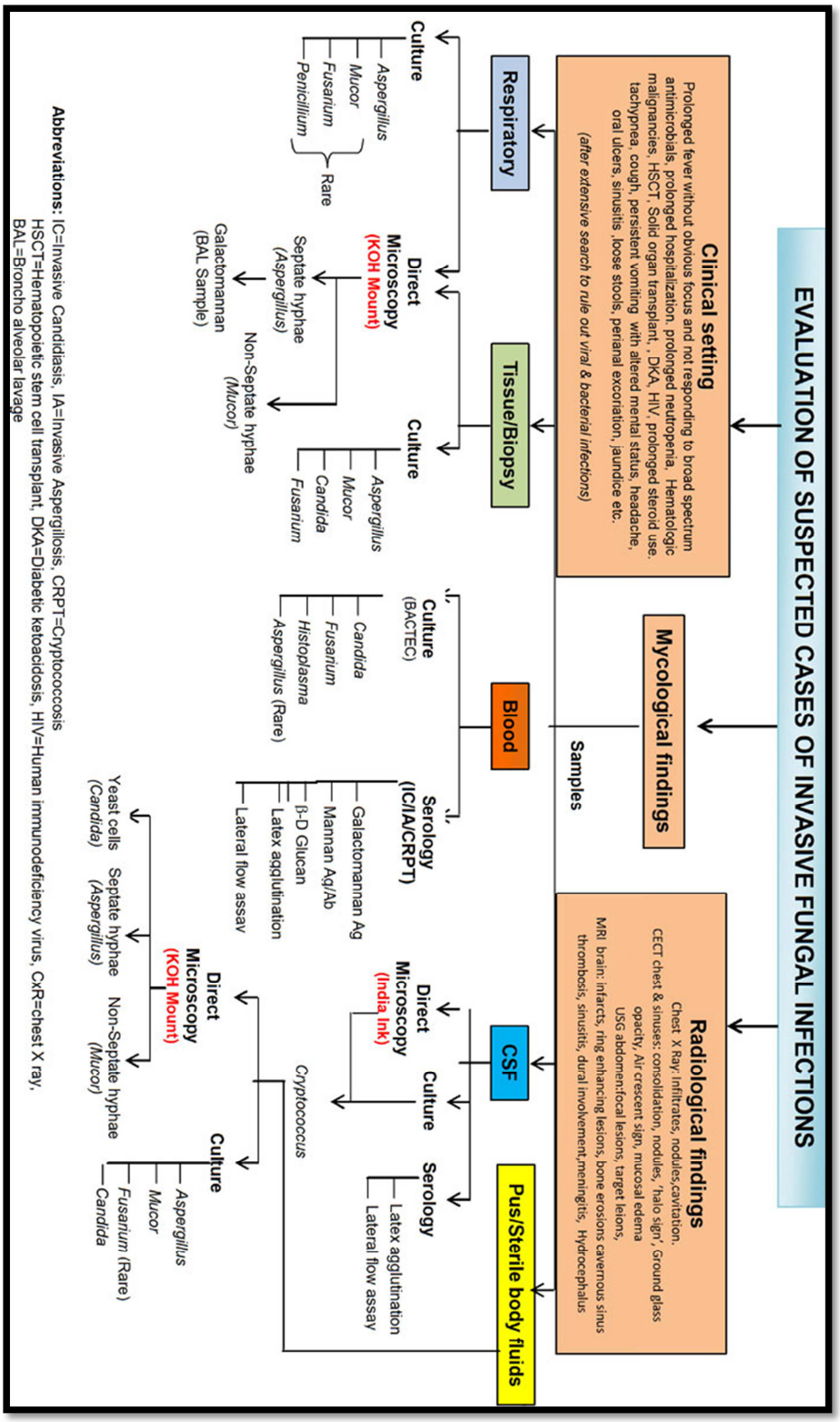
Figure 8.Risk factors for the neonatal fungal sepsis



Diagnosis:

Diagnosis of invasive fungal infection is challenging. Tissue diagnosis is the gold standard, while other tests like Galactomannan assay and PCR can help in diagnosis of invasive fungal infection in children. Role of radiology and Newer methods like T2 candida and lateral flow assay need validation. The following figure represents algorithm for approaching a suspected case of fungal infection, (51)

Figure 9.Algorithm for approaching a suspected case of fungal infection

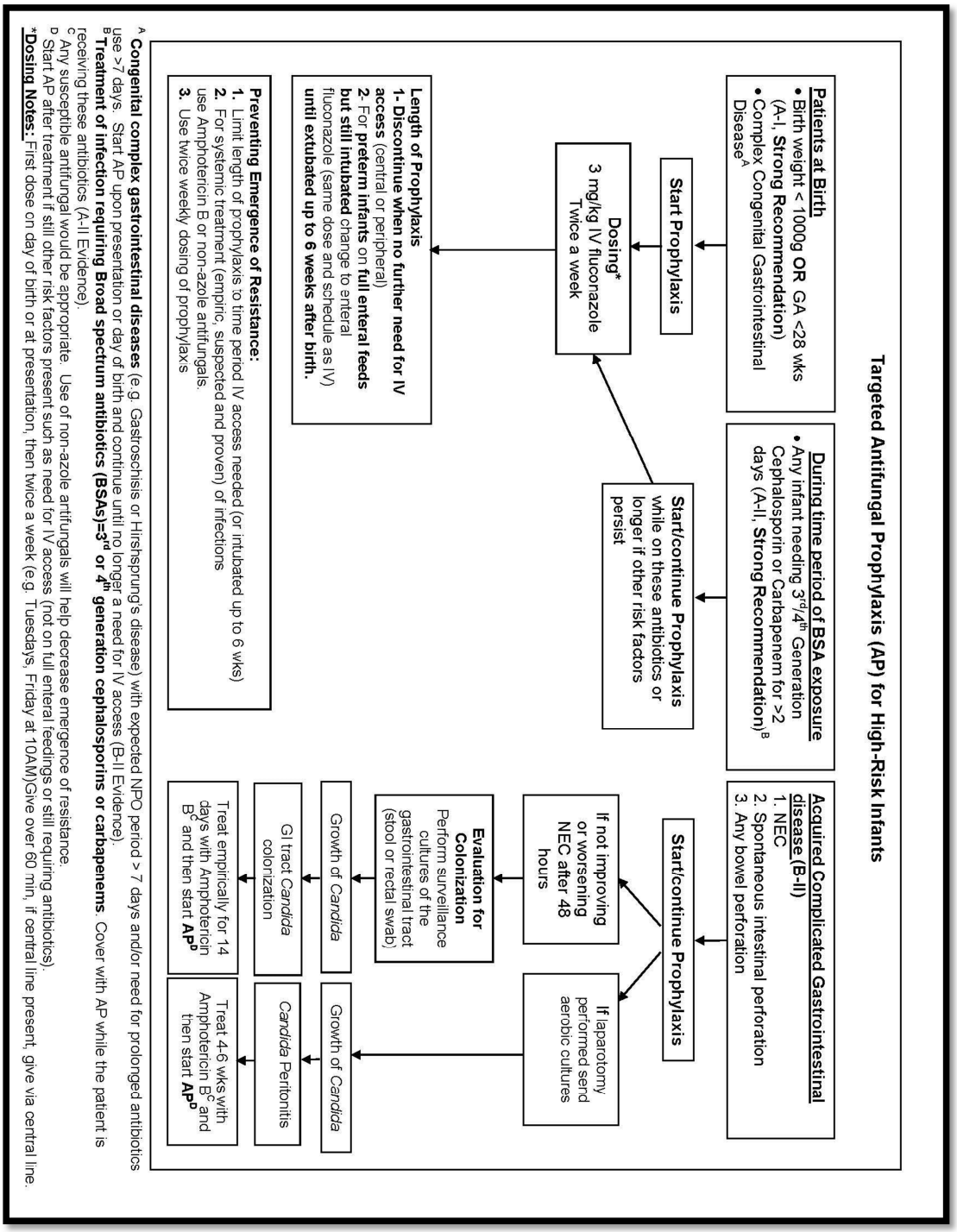


Treatment:

Early diagnosis and prompt treatment change the outcomes of the fungal sepsis. (52)Candida albicans (nearly 80%) is the predominant cause of neonatal fungal bloodstream infections and hence fluconazole can be used as empiric antifungal therapy.(53) As the isolation of fungus takes some time, empirical therapy is instituted, especially when the signs of suspected fungal sepsis like thrombocytopenia, glucose instability, lethargy, increasing ventilation requirements and apnoea were present.(53)

The following algorithm represents the Targeted antifungal prophylaxis for the high risk infants.(50)

Figure 10.Targeted antifungal prophylaxis.



[A] **Congenital complex gastrointestinal diseases** (e.g. Gastroschisis or Hirshsprung's disease) with expected NPO period > 7 days and/or need for prolonged antibiotics use >7 days. Start AP upon presentation or day of birth and continue until no longer a need for IV access (B-II Evidence).

[B] **Treatment of infection requiring Broad spectrum antibiotics (BSAs)=3rd or 4th generation cephalosporins or carbapenems**. Cover with AP while the patient is receiving these antibiotics (A-II Evidence).

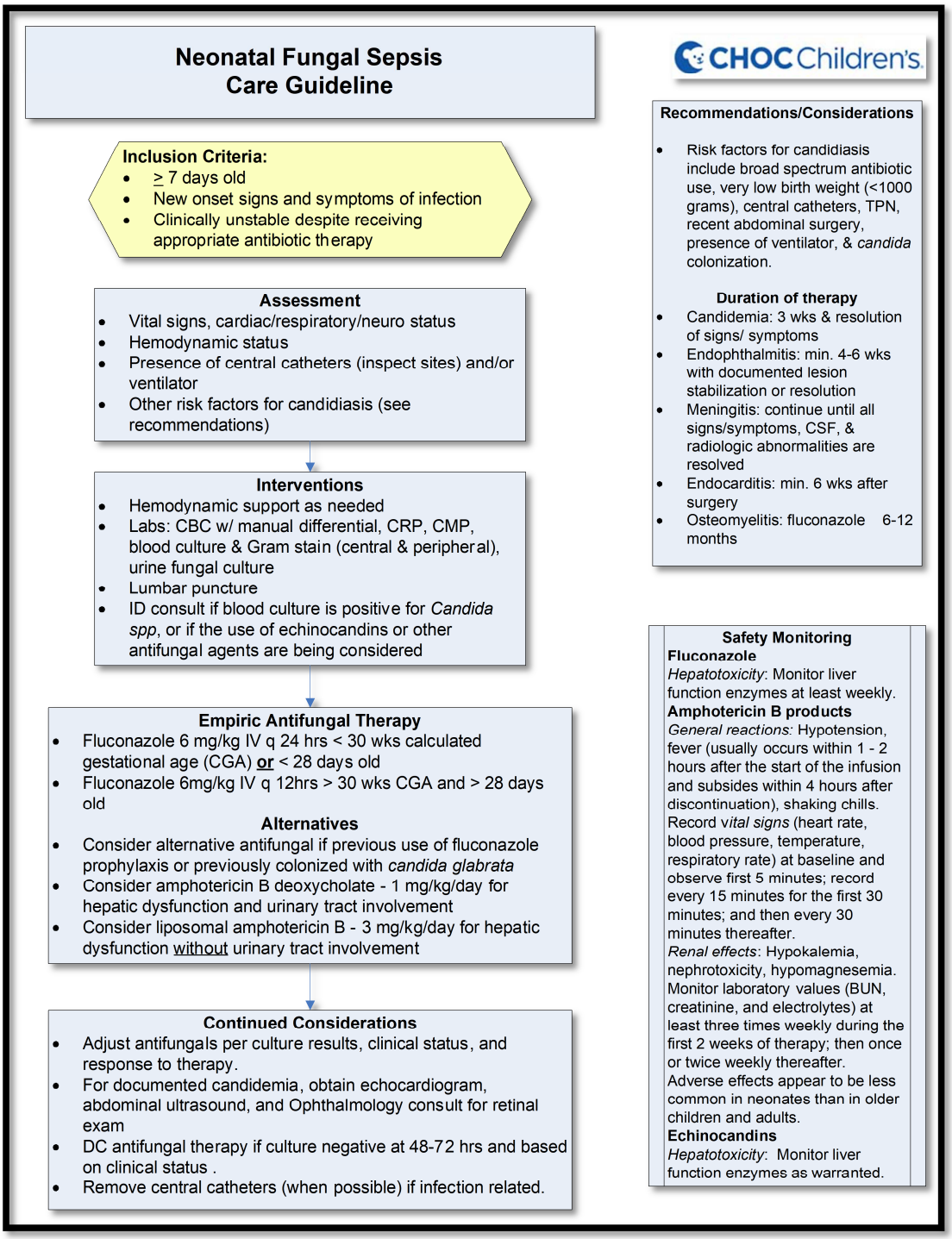
[C] Any susceptible antifungal would be appropriate. Use of non-azole antifungals will help decrease emergence of resistance.

[D] Start AP after treatment if still other risk factors present such as need for IV access (not on full enteral feedings or still requiring antibiotics).

***Dosing Notes:** First dose on day of birth or at presentation, then twice a week (e.g. Tuesdays, Friday at 10AM)Give over 60 min, if central line present, give via central line.

The following flowchart represents the Neonatal fungal sepsis care guideline by Children's Health of Orange County (CHOC), California,(54)

Figure 11.Neonatal fungal sepsis care guideline by CHOC



c. Similar studies in the same topic:

Yingfang Yu et al, from China, did a Clinical Analysis and studied the Risk Factors of Invasive Fungal Infection among the 5135 Neonatal Intensive Care Unit Patients over 7 years. They observed that the Candida parapsilosis was isolated in majority (33.3%) of the patients. The mortality rate was significantly higher among the case group was 8.9% vs 1.1% in controls ($p < 0.05$). Mechanical ventilation for more than 6 days, usage of peripherally inserted central venous catheter, use of third-generation cephalosporin, previous history of abdominal surgeries, and neutropenia during first week of life < 1500million cells/L were identified as a significantly associated risk factor with the presence of invasive fungal infection.(55)

Evangelia Farmakiet al, from Greece, studied the Risk Factors, Drug Susceptibility, and Association of Invasive Fungal Infection among the 593 Neonatal Intensive Care Unit Patients over 12 months. They observed that the Candida albicans was isolated in majority (42%) of the patients. They observed vaginal delivery was significantly associated with the fungal infection. Through multivariate regression, very low birth weight was identified as the single independent factor associated with the fungal infection. Most of the Candida albicans isolates were susceptible to azoles. (18)

Paolo Manzoniet al, from Italy, studied the Risk Factors of Invasive Fungal Infection among the 201 Neonatal Intensive Care Unit Patients over 7 years. They observed that the Central venous catheter colonization and multiple-site colonization are two independent risk factors and predictors of progression from colonisation to fungal sepsis among preterm very low birth weight neonates by Candida spp in the

NICU. They also observed that the Fluconazole prophylaxis was an independent protective factor for the prevention of fungal sepsis.(16)

Jyotsna Agarwal et al, from Lucknow, India, did a prospective analysis and included 660 neonates to study the trends in neonatal septicaemia and the emergence of non-albicans Candida. Of the 660 isolates, Candida was isolated from 90 neonates (isolation rate 13.6%), of which the Majority isolates were non-albicans Candida (76/90). They also observed that the Low birth weight was present in 73.3%. They also observed that the Crude mortality among the neonates were 52.6%.(45)

Daynia E. Ballot et al, from South Africa, studied the pattern of neonatal fungal blood stream infections between January 2007 and December 2011. They studied Fifty-nine patients with neonatal fungal blood stream infections. Majority of the isolates showed Candida parapsilosis (54.2%), followed by C. albicans (27.1%). Resistance to Fluconazole was significantly higher in 50% cases of C. parapsilosis vs 1/16 cases of C. albicans (P = 0.003). Mortality rate neonatal fungal blood stream infections was 45.8%. Mortality due to neonatal fungal blood stream infections was significantly associated with low birth weight (P= 0.046) and necrotizing enterocolitis (P= 0.034).(53)

Kheya Ghosh Uttam et al, from Kolkata, did a Cross-sectional Study, to study the Fungal Sepsis and its risk factors among 79 neonates, in a Tertiary Neonatal Intensive Care Unit. Majority isolates were non-albicans Candida, (97.3%) of which C. pelliculosa was found to be the common organism accounting (43%). C. tropicalis infections was having significantly higher mortality. Fluconazole and amphotericin resistance, was observed in 13% and 11% of the organisms respectively. 5% of the isolates were resistant to caspofungin and micafungin, None of the organisms were

resistant to voriconazole. Preterm, low-birthweight, need for mechanical-ventilation, parenteral-nutrition, and use of broad-spectrum antibiotics play a significant role as risk factors in morbidity and mortality associated with fungal sepsis. (56)

Deepti Chaurasiaet al, from Srinagar, J&K did a matched case control Study, to study the Fungal Sepsis and its risk factors among 30 neonates with fungal sepsis.Most of the candida isolates in their study were sensitive to Amphotericin-B (93%) followed by Fluconazole (80%) and Itraconazole (70%). Fluconazole resistance was observed in non- albicans Candida. They observed that the Risk factors identified were the duration of hospital stay > 7days, Mechanical ventilation, and previous use of antibiotic usage. They were unable to differentiate the candida sepsis from bacterial sepsis through the clinical features as it yielded a non-specific conclusion.(57)

Bashir Ahmad Charooet al, from Kolkata, did a 2-year observational study, to study the Systemic Candida infection and its risk factors among 304 preterm babiesneonates, in a Tertiary Neonatal Intensive Care Unit. 64 neonates were found positive for invasive Candida sepsis (11.6%). End-organ damage was noticed in 14% of patients. Mortality rate in their study was found to be 55%. The major complications encountered during the illness were found to be respiratory distress, shock, Necrotizing enterocolitis and disseminated intravascular coagulation, and thrombocytopenia.(58)

Neerul Panditaet al, (in 2015) from Dehradun, Uttarakhand, did a retrospective Study, to study the neonatal fungal blood stream infections and its risk factors among 360 neonates, in a Tertiary Neonatal Intensive Care Unit. Fungal sepsis was observed in 50/360 (13.6%) of neonates. Non Albicans candida species were

present in 88% of blood stream infections, of which Candida. glabrata (54%)as the most commonly isolated, followed by C.tropicalis (18%), C.albicans (12%), C.paraspinolosis (10%), C. Krusei (4%) and C. Kodo (2%). Amphotericin B had greater sensitivity to the isolates compared to the fluconazole. They observed that the Risk factors identified were the low birth weight, prematurity, broad spectrum antibiotic use, Mechanical ventilation, total parenteral nutrition and previous use of antibiotic usage.(59)

Rita Silva et al, from Portugal, did a 10-year retrospective analysis, to study the Fungal Sepsis and its risk factors among 3933 neonates, in a level III Neonatal Intensive Care Unit. In their study, they observed 15 (3.8 in every 1,000) had fungal sepsis. Of which, Candida albicans (n = 7, 43.8%) was common, followed by Candida parapsilosis (n = 9, 56.3%). They further observed that the Mortality rate among the 15 cases of fungal sepsis was 46.7% (n = 7).(60)

Okolo Mark Ojogbaet al, from Nigeria, did a Cross-sectional Study, to study the Fungal Sepsis and its risk factors among neonates, in a Tertiary Neonatal Intensive Care Unit.5.5% had fungal sepsis. Of which, C. albicans (n = 11/20) was common.They further observed that the resistance to the antifungal agents were not common except for the few cases of fungal sepsis reporting resistance to amphotericin from the Candida glabrata species.(61)

Zhang X et al, from China, did a Clinical Analysis and studied the Risk Factors of Invasive Fungal Infection among the Neonatal Intensive Care Unit Patients over 5 years. They observed that the incidence of neonatal fungal sepsis was 0.52% in neonates overall, it was 2.5% in very low birth weight neonates. Candida glabrata was the most common species in their study. All the isolates were sensitive to

amphotericin B, while they reported only one fluconazole resistance by Candida glabrata.(62)

S.H. Ahmedet al, from Egypt, did a Cross-sectional Survey, to study the Fungal Sepsis and its risk factors among 176 neonates, in a Tertiary Neonatal Intensive Care Unit. Of the 176 blood culture samples, 55 (31.3 %) samples was positive for pathogens of which fungi were isolated in 26 (14.8 %), including yeast (25 cases) and mould (1 case). The commonly isolated fungiin their study were Candida albicans, followed by Candida tropicalis, and Candida krusei. (63)

METHODOLOGY

Study Subjects: 70 New-borns (<28 days old) with proven candidial sepsis, admitted to neonatal intensive care unit, under the KLEH DR Prabhakar Kore Charitable Hospital, Department of Paediatrics, Jawaharlal Nehru Medical College, Belagavi.

Study Design: Prospective Observational study.

Study Period: Data collection – 1 year (2021January to 2021 December).

Study setting: KLE Academy of Higher Education and Research, Dr. Prabhakar Kore Charitable Hospital, Department of Paediatrics, Jawaharlal Nehru Medical College, Belagavi.

Sampling Procedure: Convenient Sampling.

Inclusion Criteria:

- New-borns <28 days old
- With proven candidial sepsis.
- Admitted to neonatal intensive care unit.

Exclusion criteria:

- Out born neonates.
- Neonates with frank bacterial sepsis.[If two simultaneous culture samples shows bacterial growth].
- Neonates with inborn errors of metabolism.
- Neonates with congenital cardiovascular anomalies.
- Neonates with congenital gastrointestinal anomalies.
- Neonates with clinically recognizable genetic syndromes.

Sample Size: According to Mamta Jajoo et al study,(64) considering the prevalence of Prevalence of fungal sepsis among neonates as 22.7% with a precision of 9.8% and 95% confidence interval, the sample size is calculated as

$$\mathbf{N = Z^2_{1-\alpha/2} * p * (1 - p) / d^2}$$

Z1-α/2 - two tailed probability for 95% confidence interval = 1.96

p (%) - prevalence of Prevalence of fungal sepsis among neonates = 0.227

d (%) - precision or allowable error for Prevalence of fungal sepsis among neonates = 0.098

N = 1.96^2 * 0.227 * (1 - 0.227) / 0.098^2

N = 70.19

Thus, the total sample size required for the study is 70

Ethical Consideration: Institutional Ethical Committee approval, from Jawaharlal Nehru Medical College, Belagavi, was obtained before the start of the study. Informed written consent was obtained from the parents.

Source of Funding: None declared

Conflict of Interest: None declared

Study procedure: After obtaining ethical clearance, Informed written consent was taken from the guardian prior to enrolment into the study. All inborn neonates<28 days with suspected sepsis were included in our study. All neonates with suspected sepsis on clinical grounds undergone septic work up which includes Complete blood count, CRP, Procalcitonin blood culture, urine culture. Blood cultures were collected in Colour cult culture vials [1ml of blood taken from peripheral vein under aseptic precaution] on the day of admission.

Neonates who showed candida growth in their blood culture, were included in our study. Simultaneously, urine samples were taken under aseptic precaution by catheterization and were sent to lab for routine, microscopy, culture and sensitivity and lumbar puncture was performed under asepsis and CSF samples were sent for Routine, Cytology , biochemistry and culture. Neonates received treatment as per NICU protocol or based on culture sensitivity report and neonates with positive blood culture for candidal growthanti-fungal were continued till cultures are negative.For neonates with fungal sepsis repeat cultures were done at 21 days and if required repeat cultures were done at 28 days. Enrolled neonates were followed till discharge or death.

We collected the data regarding maternal risk factors for sepsis, mode of delivery, vaginal candidal colonization, neonatal risk factors like preterm, low birth weight, Meconium aspiration syndrome, persistent pulmonary hypertension of new-born, intraventricular haemorrhage, necrotizing enterocolitis, respiratory distress syndrome, interventional procedures like naso-gastric tube, Long line insertion, total parenteral nutrition, days on mechanical ventilation, duration of hospitalization, any use of steroids , antibiotics and H2 blockers. Data regarding clinical outcome of neonates with fungal sepsis, fungal organism isolates and anti-fungal sensitivity pattern were also collected. For neonates with fungal sepsis repeat cultures were done at 21 days and if required repeat cultures were done at 28 days.

The following image represents the Paediatric culture vial,

Figure 1.Paediatric culture vial

1.11 **Budget:** Self. (No added investigation or intervention)

Statistical Methods:

I. Descriptive Statistics:

1. Numerical variables like Age, CBC values, Biochemical values, etc., are represented in mean, SD, median, and mode. Histograms are used wherever necessary.
2. Categorical variables like gender, Blood culture and sensitivity, etc., are represented in frequencies and percentages. Pie-charts and bar diagrams are used as appropriate.

3. Data was entered in MS excel sheet and analysed using SPSS software version 16.

II. Inferential Statistics:

1. When a Categorical Variable is compared with the presence of fungal sepsis, the variables are represented in both by tables and bar diagrams. For test of significance chi-square test is used.
2. When a Numerical variable is compared with the presence of fungal sepsis, independent t test is used.
3. P-values less than 0.05 were considered statistically significant.

.

RESULTS

RESULTS OF THE STUDY- CORRELATION OF RISK FACTORS ASSOCIATED WITH FUNGAL SEPSIS IN NEONATES ADMITTED TO NEONATAL INTENSIVE CARE UNIT- AN ONE YEAR HOSPITAL BASED OBSERVATIONAL STUDY.

A one year, hospital based observational study was conducted at KLES Dr. Prabhakar Kore hospital. All newborns with proven fungal sepsis were studied till their discharge or death.

We collected data regarding gender, gestational age, birth weight, mode of delivery, maternal risk factors, neonatal risk factors at birth and during their stay in NICU, duration of interventions and assessed biochemical and hematological parameters. Also, data regarding blood counts were collected and were compared with onset of fungal sepsis.

Data regarding Fungal isolates, trend in blood culture and sensitivity pattern were compared. All these risk factors, blood parameters, interventions were compared with outcome. The data obtained was tabulated into Microsoft Excel sheets and processed using SPSS software version 16.

The study included 70 newborns with proven fungal sepsis over a span of 1 year.

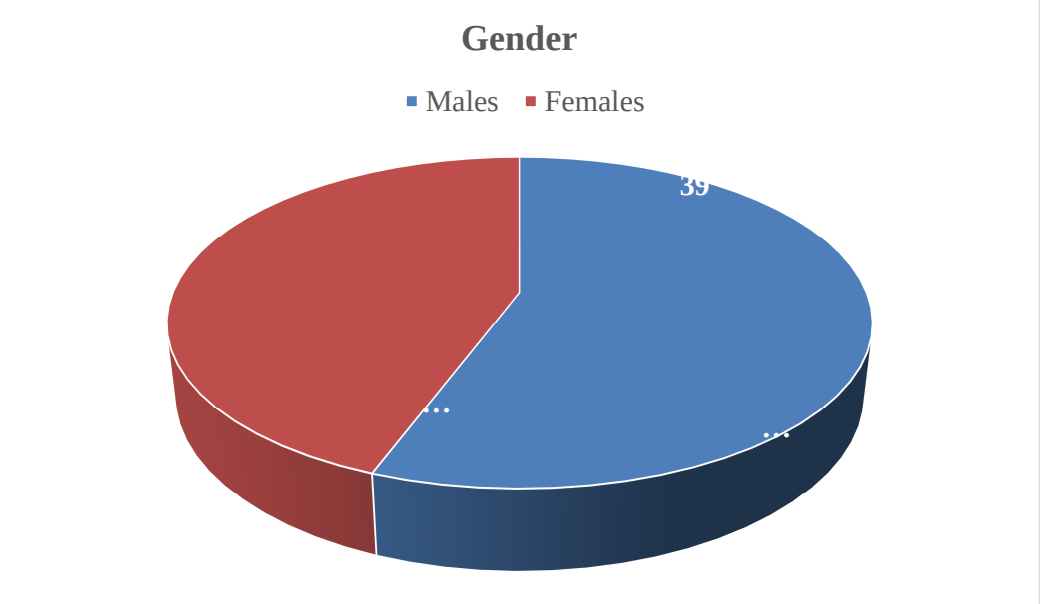
I. Gender

Out of 70 newborns, 39 (55.71%) were Males and 31 (44.29%) were Females

Table 2.Gender

Gender	Frequency	Percent
Males	39	55.71
Females	31	44.29
Total	70	100.00

Figure 1.Gender



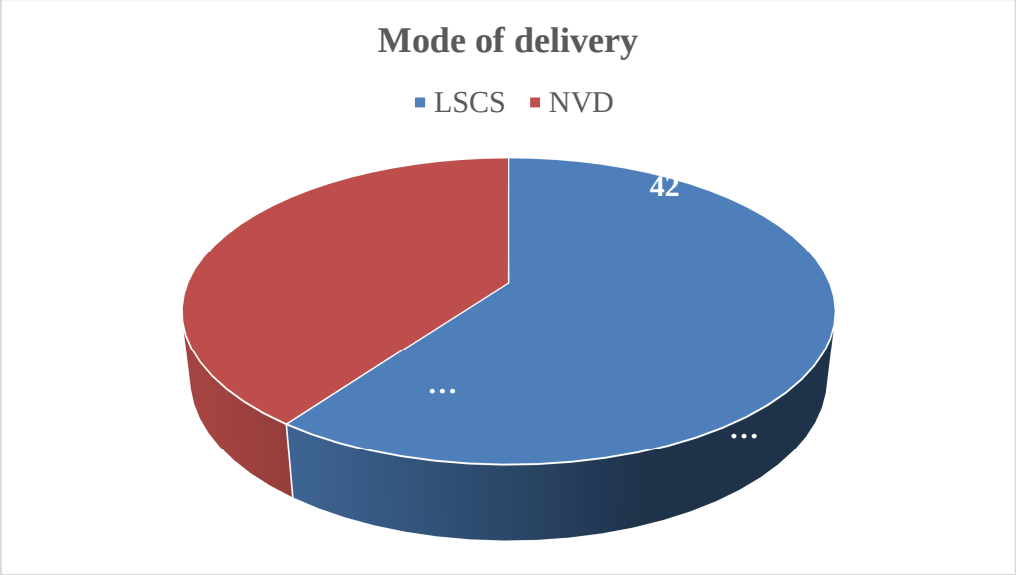
II.Mode of delivery

Among 70 newborns, 42 (60%) were delivered by LSCS and 28 (40%) were delivered by vaginal delivery.

Table 3.Mode of delivery

Mode of delivery	Frequency	Percent
LSCS	42	60.00
NVD	28	40.00
Total	70	100.00

Figure 14.Mode of delivery



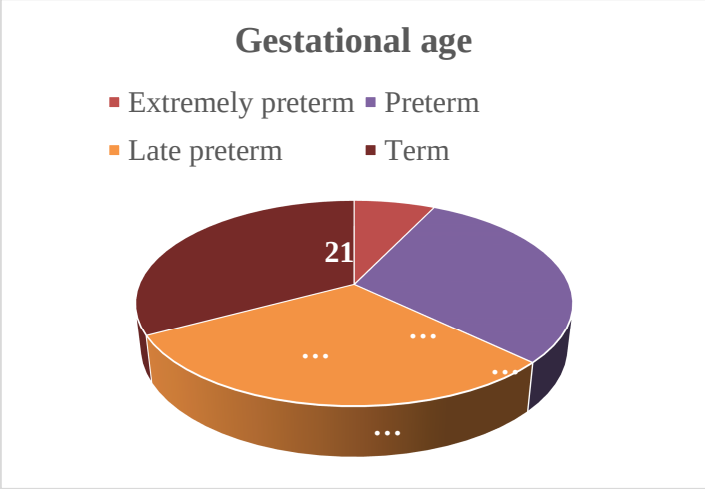
III.Gestational age

Among 70 newborns, 23 (32.86%) newborns were Term and 47(67.14%) newborns were Preterm, of which 21 (30%) newborns were late preterm, 21 (30%) newborns were preterm, 5 (7.14%) newborns were Extremely preterm

Table 4.Gestational age

Gestational age	Frequency	Percent
Extremely preterm	5	7.14
preterm	21	30.00
Late preterm	21	30.00
Term	23	32.86
Total	70	100.00

Figure 15.Gestational age



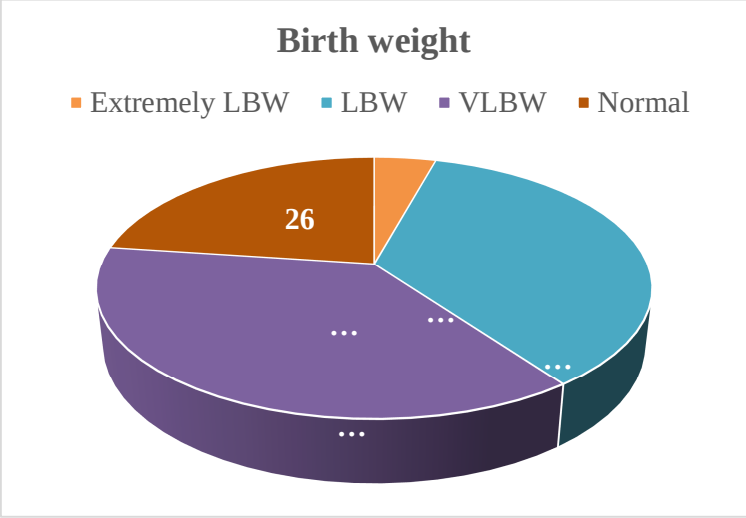
IV.Gestational Birth weight

Gestational birth weight of the newborns in the study showed that 26 (37.14%) newborns were VLBW, followed by 25 (35.71%) newborns who were LBW & 3 (4.29%) newborns were Extremely LBW. 16 (22.86%) newborns in our study had normal birth weight.

Table 5. Gestational birth weight

Birth weight	Frequency	Percent
Extremely LBW	3	4.29
LBW	25	35.71
VLBW	26	37.14
Normal	16	22.86
Total	70	100.00

Figure16.Gestational birth weight



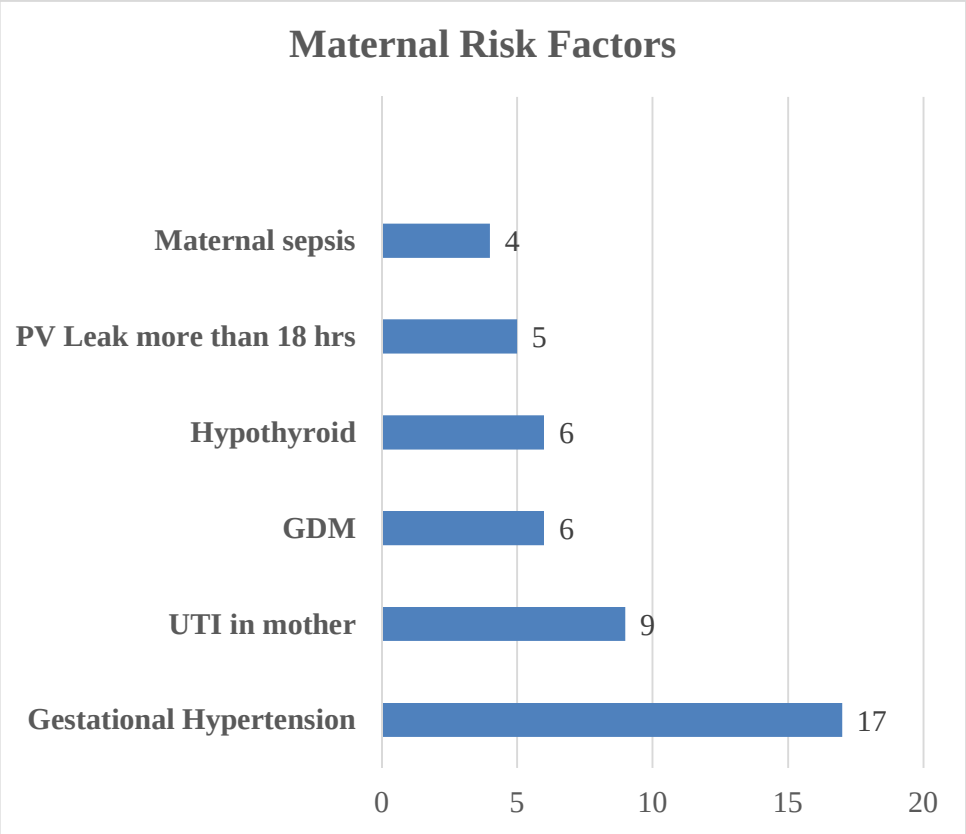
V. Maternal risk factors in newborns with fungal sepsis

Among the mothers, 17 (24.3%) mothers had Gestational Hypertension, 9 (12.9%) mothers had Urinary tract infection (UTI), 6 (8.6%) mothers had Gestational diabetes mellitus (GDM), 6 mothers (8.6%) had Hypothyroidism, 5 (7.14%) mothers had Per vaginal (PV) leak more than 18 hrs, 4 (5.7%) mothers were found to have Maternal sepsis.

Table 6. Maternal risk factors in newborns with fungal sepsis

	Frequency	**%**
Gestational Hypertension	17	24.29%
UTI in mother	9	12.86%
Hypothyroid	6	8.57%
GDM	6	8.57%
PV Leak more than 18 hrs	5	7.14%
Maternal sepsis	4	5.71%

Figure 17. Maternal risk factors in newborns with Fungal sepsis



VI. Neonatal Risk Factors in newborns with fungal sepsis

Out of 70 newborns, 58(82.86%) newborns were admitted for respiratory distress, 13(18.57%) newborns for Birth asphyxia, 47(67.1%) newborns were Preterm, 54 (77.1%) newborns were LBW.

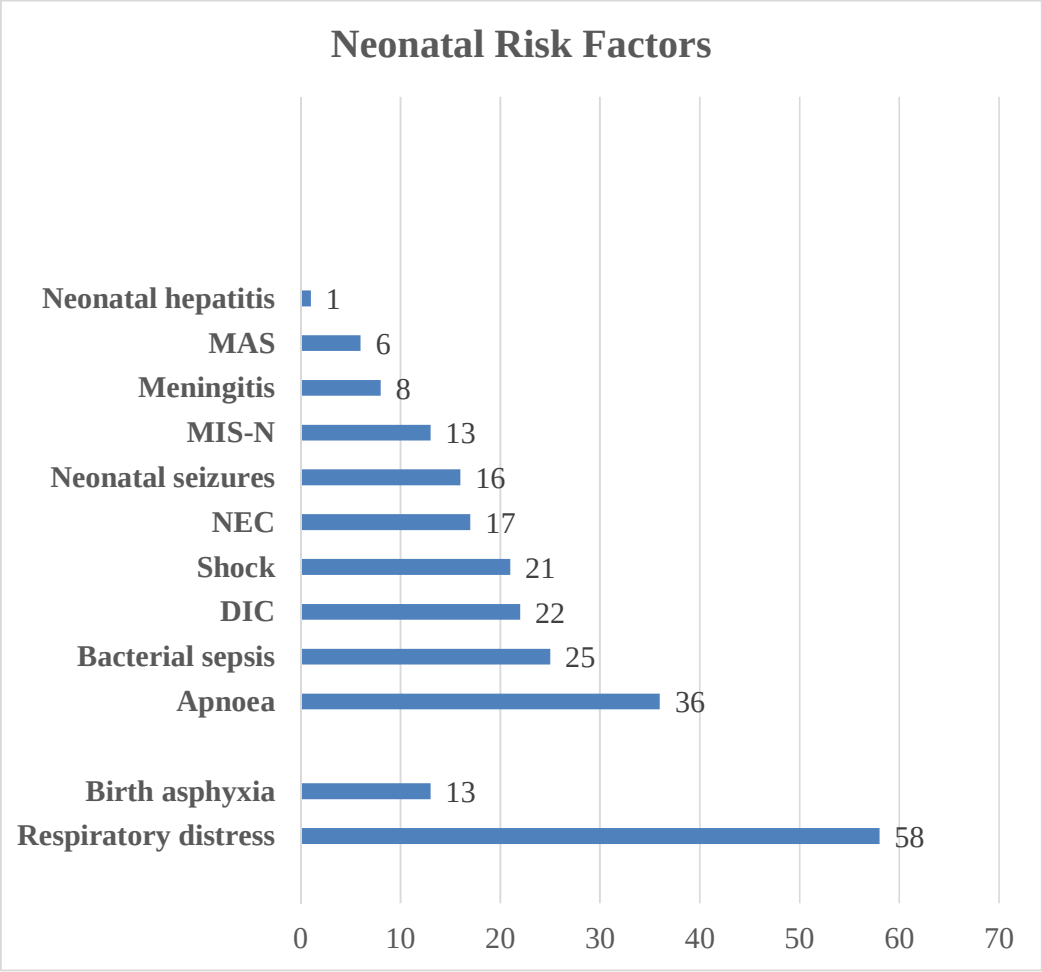
During NICU stay, 36 (51.43%) newborns developed apnoea, 25(35.71%) newborns had associated bacterial infection , 17(24.29%) newborns had Necrotising enterocolitis (NEC), 16(22.86%) newborns had neonatal seizures, 22(31.43%) newborns had Disseminated intravascular coagulation (DIC), 21(30%) newborns had shock, 13 (18.57%) newborns had Neonatal Multisystem inflammatory syndrome (MIS-N), 8 (11.43) newborns had suspicion of bacterial meningitis, 6(8.57%) newborns had Meconium aspiration syndrome (MAS), 1(1.43%) newborn had Neonatal hepatitis.

Table 7. Neonatal Risk Factors in newborns with fungal sepsis

At admission	Frequency	Percent
Preterm	47	67.1%
LBW	54	77.1%
Respiratory distress	58	82.86%
Birth asphyxia	13	18.57%
NICU stay		
Apnoea	36	51.43%
Bacterial sepsis with shock	25	35.71%

Neonatal seizures	16	22.86%
NEC	18	25.79%
Neonatal seizures	16	22.86%
MIS-N	13	18.57%
Meningitis	8	11.43%
MAS	6	8.57%
Neonatal hepatitis	1	1.43%

Figure 18. Neonatal Risk Factors in newborns with fungal sepsis



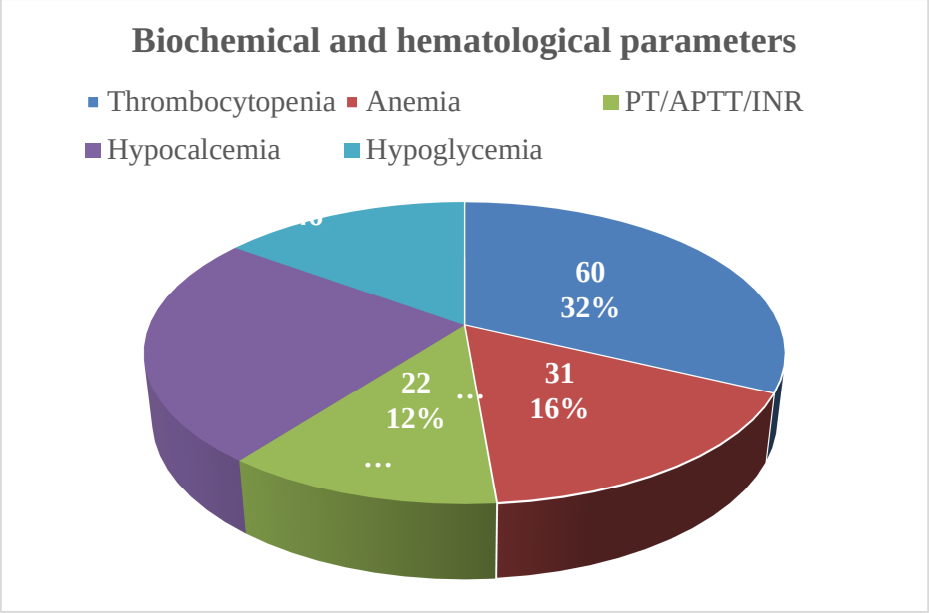
VII. Biochemical and hematological parameters in newborns with fungal sepsis

Among 70 newborns, 60 newborns(85.7%) had thrombocytopenia and all of thses required random donor platelets (RDP) transfusions , 31 newborns (44.3%)had anemia requiring packed red cell (PCV) transfusion, 22 newborns(31.4%) had deranged coagulation profile, all received fresh frozen plasma (FFP). 46 newborns(65.7%) had hypo calcemia followed by 28 newborns(40.0%) with hypoglycemia.

Table 8. Biochemical and hematological parameters in newborns with fungal sepsis

Blood parameters	Frequency	Percent
Thrombocytopenia	**60**	**85.7**
Anemia	**31**	**44.3**
Deranged PT/APTT/INR	**22**	**31.4**
Hypocalcemia	**46**	**65.7**
Hypoglycemia	**28**	**40.0**

Figure 19. Biochemical and hematological parameters in newborns with fungal sepsis



.

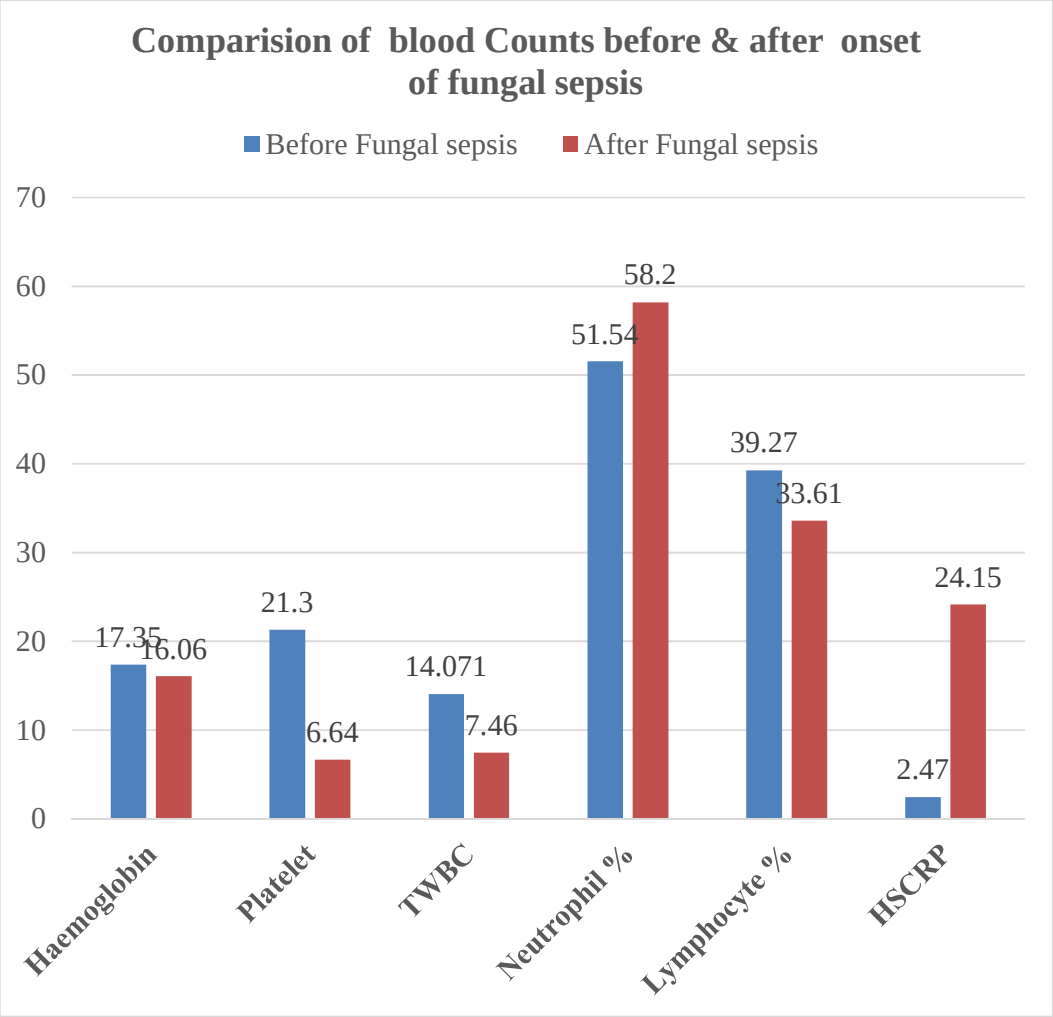
VIII.Comparision of Blood Counts before & after onset of fungal sepsis

Hematological parameters were assessed before and after onset of fungal sepsis. Fall in Haemoglobin, Platelet count ,Total white blood count (TWBC), and rise in High- sensitivity C- reactive protein (Hscrp) showed a statistically significant difference between mean scores across the newborns with before and after the onset of fungal sepsis. We did not observe any significant change in the differential leucocyte count.

Table 9.. Comparision of blood Counts before & after onset of fungal sepsis

Pair	Group		Mean diff.	Paired 't' test p value
	Before Fungalsepsis	After Fungal sepsis		
Haemoglobin	17.35 (± 2.18)	16.06 (± 2.9)	1.29286	0.001
Platelet	213542.86 (± 72642.4)	66400 (± 62201.03)	147143	0.001
TWBC	14071.43 (± 7880.63)	7468.57 (± 3855.15)	6602.86	0.001
Neutrophil %	51.54 (± 16.51)	58.2 (± 18.4)	-6.6571	0.024
Lymphocyte %	39.27 (± 16.01)	33.61 (± 17.48)	5.65714	0.043
HSCRP	2.47 (± 9.81)	24.15 (± 35.55)	-21.689	0.001

Figure 20. Comparision of blood Counts before & after onset of fungal sepsis



IX. Interventions and their duration in newborns with fungal sepsis.

Among 70 newborns with fungal sepsis, all newborns received broad spectrum antibiotics of mean 13.14, ranging from 3 to 30 days, 53(75.71%) newborns had received antibiotics more than 10 days, 17(24.28%) newborns had received antibiotics less than 10 days . 68(97.14%) newborns had received Intravenous fluids including TPN of mean 11.3 ranging from 2 to 28 days. 65(92.85%) newborns required non invasive oxygen support of mean 9.29 ranging from 2 to 30 days,17 (24.28%) newborns were on mechanical ventilation of mean 7.29 ranging from 2 to 25 days , 49(70%) babies had long line insertion of mean 10.45 ranging from 3 to 20 days. 17 (24.29%) newborns received steroids as pulse therapy of mean 3.32 for 3 to 5 days as a treatment protocol for MIS-N, 27 (38.6%) newborns were administered Ionotropes of mean 5.7 ranging from 2 to 10 days.

Table 10. Interventions and their duration in newborns with fungal sepsis

Intervention	Mean	S.D.	Minimum	Maximum	Frequency	Percent
Duration of Long line insertion	10.45	4.01	3.0	20.0	49	70.0
TPN duration	11.35	6.79	2.0	28.0	68	97.1
Non invasive Oxygen support	9.29	7.09	2.0	30.0	55	78.6
Days on mechanical ventilation	7.29	6.28	2.0	25.0	17	24.3
Days on Broad spectrum antibiotics	13.14	6.27	3.0	30.0	70	100
Days on steroids	3.32	0.75	3.0	5.0	19	27.1
Days on ionotropes	5.7	2.81	2.0	10.0	27	38.6

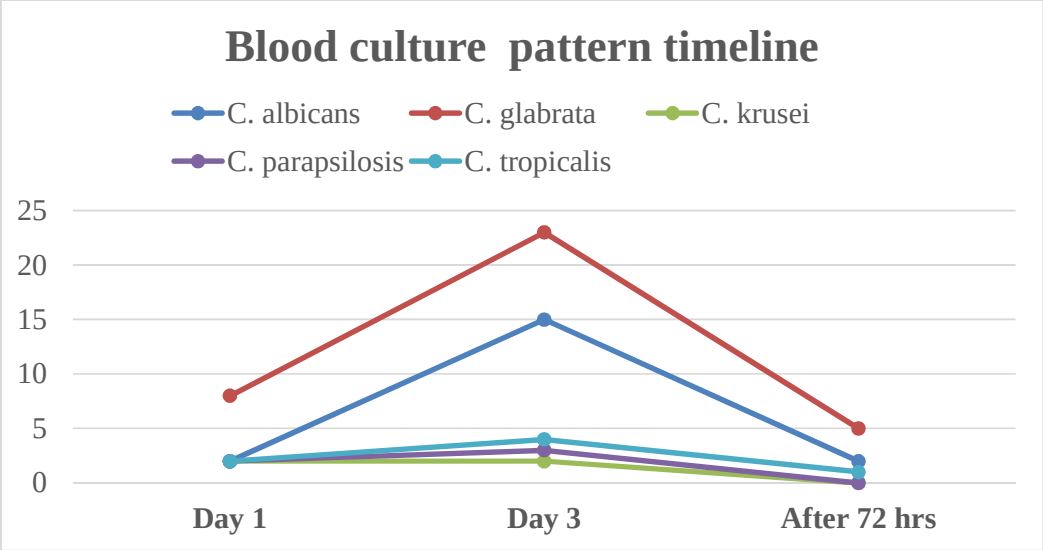
X.Blood culture pattern timeline

Out of 70 newborns, 16 newborns blood cultures were positive for fungal growth on day 1 , 47 newborn blood cultures were positive for fungal growth on day3(<72hrs), and 7 newborns blood cultures were positive after 72 hrs suggesting that most of the newborns were found to have early onset fungal sepsis

Table 11. Blood culture pattern timeline

	Day 1 Blood C&S	**Day 3 Blood C&S**	**Blood C&S after 72 hrs**
C. albicans	2	15	2
C. glabrata	8	23	5
C. krusei	2	2	0
C. parapsilosis	2	3	0
C. tropicalis	2	4	0
Total	16	47	7
%	22.8	67.1	10

Figure 21. Blood culture pattern timeline



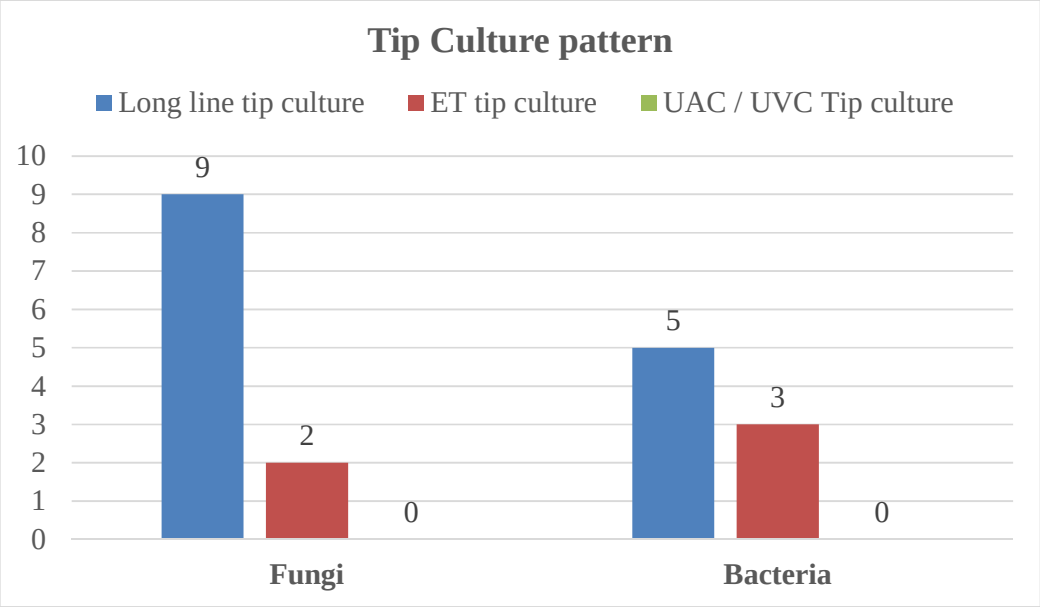
XI. Tip Culture pattern

In this study, tip cultures for long line, Endotracheal tube (ET), umbilical lines were sent, of which 9 long line tip cultures and 2 ET tip cultures were positive for fungal growth . None of umbilical line tip cultures showed fungal growth. 5 long line tip cultures , 3 ET tip cultures and 1 umbilical line culture showed bacterial growth.

Table 12.Tip Culture pattern

	Long line tip culture	**ET tip culture**	**UAC / UVC Tip culture**
Fungal	9	2	0
Bacterial	5	3	1
NOGC	35	12	1

Figure 22.Tip Culture pattern



XII.CSF Culture & sensitivity

Among the newborns with fungal sepsis, none of CSF cultures showed fungal growth . 1 newborn Csf culture showed positive for bacterial growth (Enterobacter)

Table 13.CSF Culture & sensitivity

CSF Culture & sensitivity	Frequency	Percent
Bacteria	1	1.43
Fungal	0	0.00
NOGC	69	98.57
Total	70	100.00

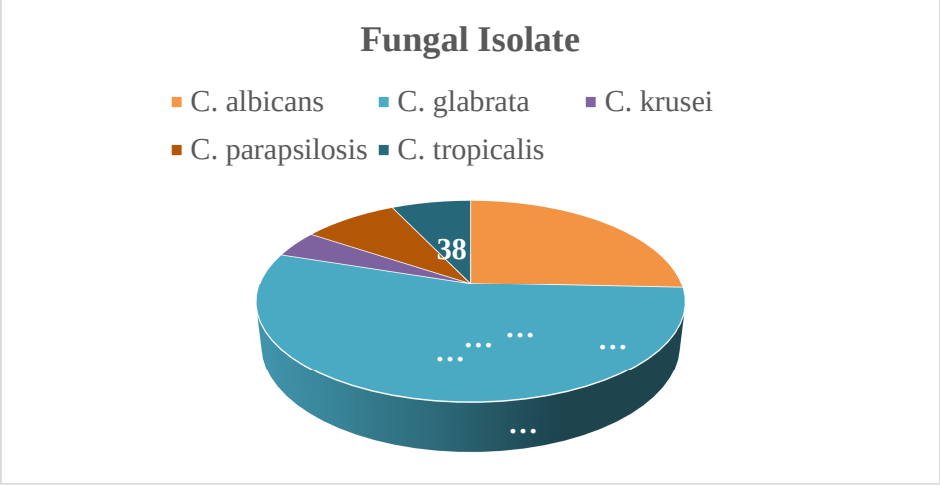
XIII.Fungal Isolate

Among 70 newborns, 38 (54.29%) newborns blood culture isolated C. glabrata . 18 (25.71%) newborns blood culture isolated C. albicans followed by 6 (8.57%) newborns for C. parapsilosis, 5 (7.14%) newborns for C. tropicalis and 3 (4.29%) newborns for C. krusei.

Table 14.Fungal Isolate

Fungal Isolate	Frequency	Percent
C. albicans	18	25.71
C. glabrata	38	54.29
C. krusei	3	4.29
C. parapsilosis	6	8.57
C. tropicalis	5	7.14
Total	70	100.00

Figure 23.Fungal Isolate



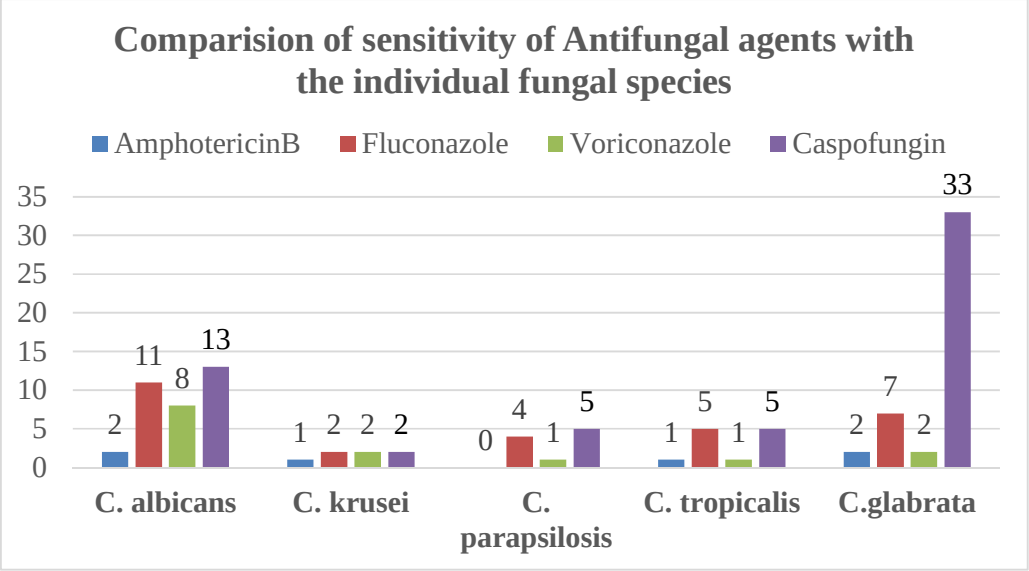
XIV. Comparision of sensitivity of antifungal agents with the individual Fungal species:

Out of 38 isolates of C. glabrata, 33 were sensitive to Caspofungin and 7 were sensitive to Fluconazole. Out of 18 isolates of C.albicans, 13 were sensitive to Caspofungin and 11 were sensitive to Fluconazole. Out of 6 isolates of C. parapsilosis, 5 were sensitive to Caspofungin. For C. tropicalis, all 5 isolates were sensitive to Caspofungin. Out of 3 C. krusei isolates, 2 were sensitive to caspofunginResistance of fungal isolate was high to Amphotericin- B and Voriconazole

Table 15.Comparision of sensitivity of antifungal agents with the individual Fungal species:

Fungalisolate	AmphotericinB		Fluconazole		Voriconazole		Caspofungin		Total
	R	S	R	S	R	S	R	S	
C. albicans	16	2	7	11	10	8	5	13	18
C. krusei	2	1	1	2	1	2	1	2	3
C. parapsilosis	6	0	2	4	5	1	1	5	6
C. tropicalis	4	1	0	5	4	1	0	5	5
C.glabrata	36	2	31	7	36	2	5	33	38

Figure 24. Comparision of sensitivity of antifungal agents with the individual Fungal species:



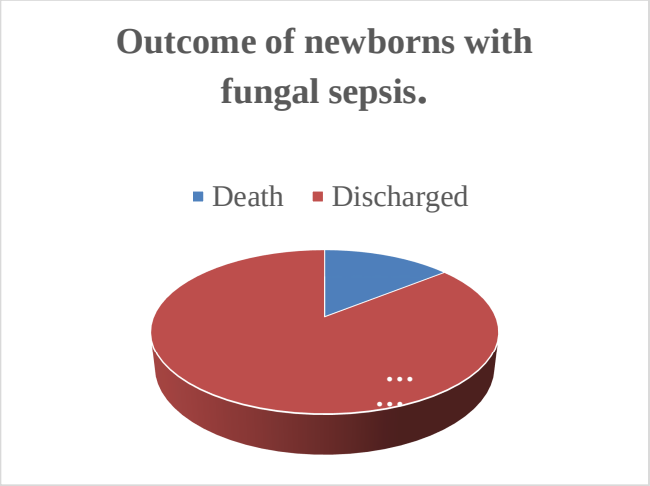
XV.Outcome of newborns with fungal sepsis.

Among the newborns, 60 (85.71%) newborns were recoverd and 10 (14.29%) died.

Table 16.Outcome of newborns with fungal sepsis.

Outcome	Frequency	Percent
Death	10	14.29
Discharged	60	85.71
Total	70	100.00

Figure 25.Outcome of newborns with fungal sepsis.



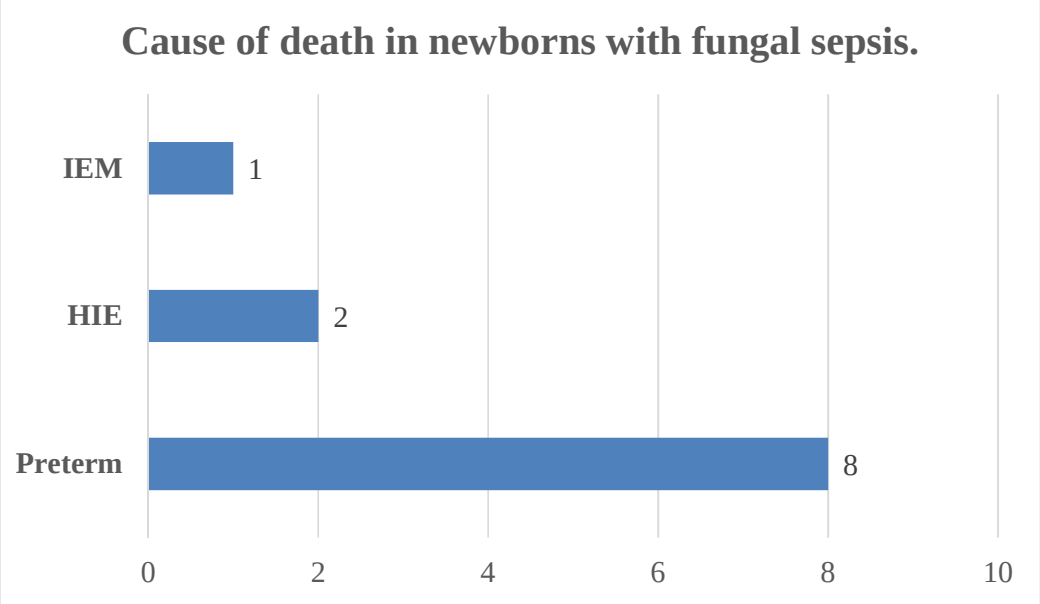
XVI.Cause of death in newborns with fungal sepsis.

In this study, most common cause of death is due to prematurity , followed by Hypoxic ischemic encephalopathy (HIE) followed by inborn errors of metabolism (IEM).

Table 17.Cause of death in newborns with fungal sepsis.

Cause of death	Frequency	Percent
Preterm	8	80.00
HIE	2	20.00
IEM	1	10.00
Total	10	100.00

Figure 26.Cause of death in newborns with fungal sepsis.



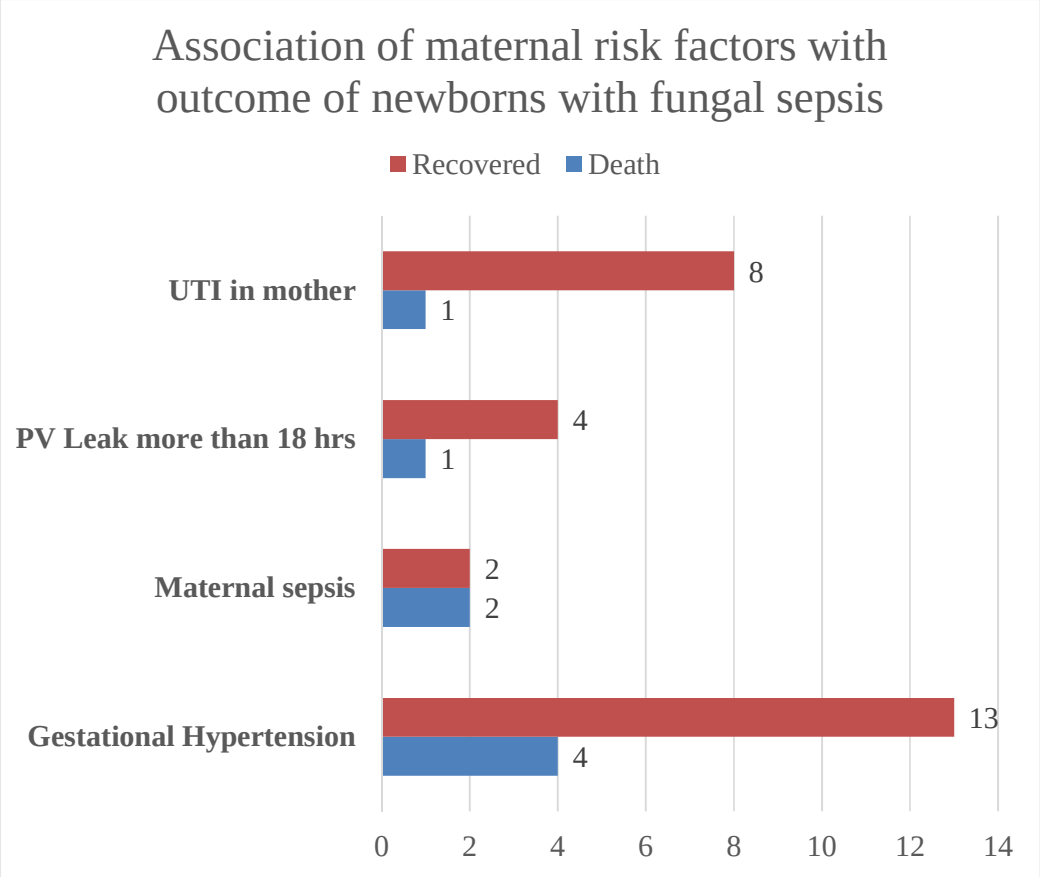
XVII.Association of maternal risk factors with outcome of newborns with fungal sepsis

When we compared the maternal risk factors to the outcome of the newborns, Gestational hypertension, Maternal sepsis, PV leak after 18 hrs and UTI in mother found to be associated with higher mortality in the newborns. The respective percentages being 40% of Gestational hypertension, 20% of maternal sepsis, 10% each for Prolonged PV leak and UTI in mothers, though the differences were not statistically significant

Table 18. Association of maternal risk factors with outcome of newborns with fungal sepsis

Maternal Risk factors	Outcome		Chi sq. p value
	Death	Recovered	
Gestational Hypertension	4 (40%)	13 (21.7%)	0.138
Maternal sepsis	2(20%)	2 (3.3%)	0.087
PV Leak more than 18 hrs	1 (10%)	4 (6.7%)	0.403
UTI in mother	1 (10%)	1 (10%)	0.393
Maternal hypothyroidism	0(0%)	6 (10%)	0.382
GDM	0 (0%)	6 (10%)	0.382

Figure 27. Association of maternal risk factors with outcome of newborns with fungal sepsis



XVIII.Association of neonatal risk factors with outcome of newborns with fungal sepsis

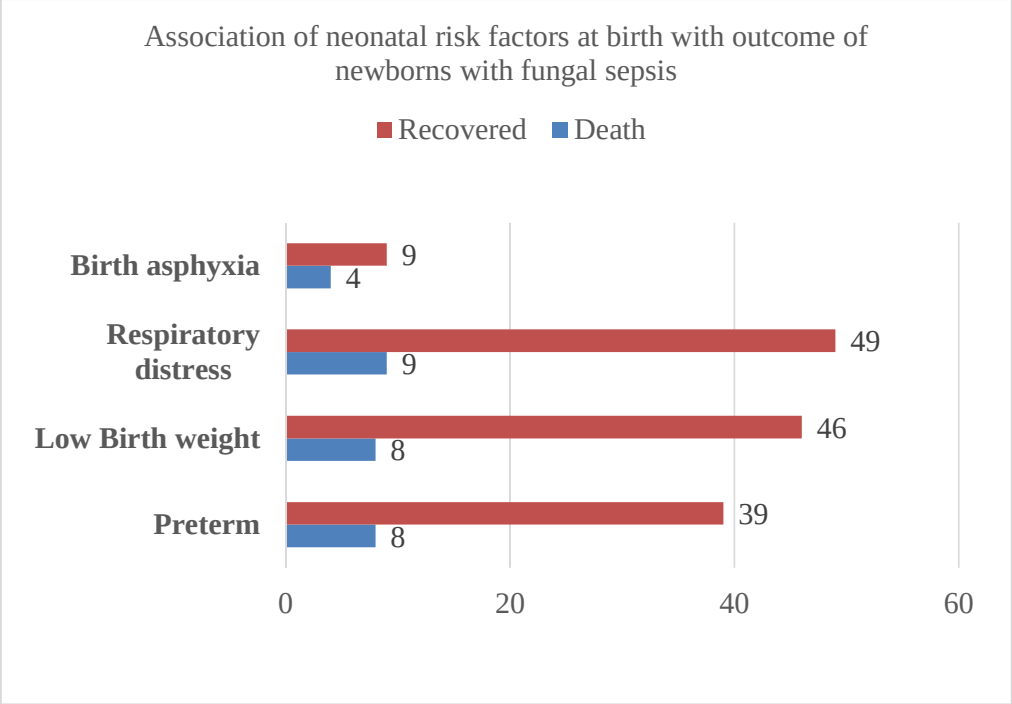
1. Association of neonatal risk factors at birth with outcome of newborns with fungal sepsis

Preterm, LBW, Respiratory distress, Birth asphyxia were the neonatal risk factors at birth, associated with high mortality when compared to newborns who recovered. But none of these were statistically significant.

Table 19. Association of neonatal risk factors at birth with outcome of newborns with fungal sepsis

	Outcome		
Neonatal Risk factors at birth.	**Death**	**Recovered**	**Chi sq. p value**
Preterm	**8(80%)**	**39(65%)**	**0.201**
Low Birth weight	**8 (80%)**	**46 (76.7%)**	**0.315**
Respiratory distress	**9 (90%)**	**49 (81.7%)**	**0.322**
Birth asphyxia	**4(40%)**	**9(15%)**	**0.065**

Figure 28.Association of neonatal risk factors at birth with outcome of newborns with fungal sepsis



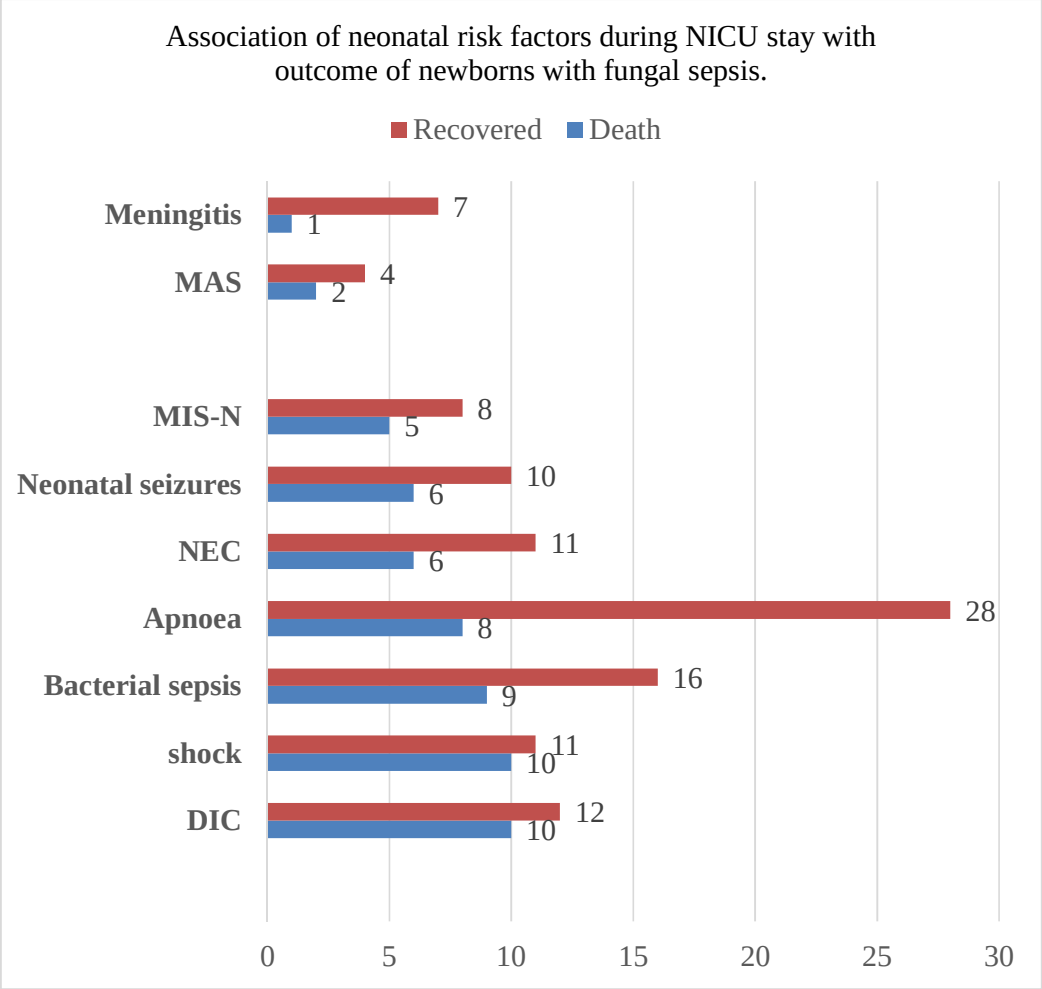
2. Association of neonatal risk factors during NICU stay with outcome of newborns with fungal sepsis.

The following table gives the list of the risk factors developed during NICU stay and their association with mortality. The risk factors associated with mortality which were statistically significant were newborns with apnoea, NEC, neonatal seizures, bacterial sepsis, shock, DIC, MIS-N. MAS and meningitis though they were seen in newborns who died, the differences were not statistically significant.

Table 20. Association of neonatal risk factors during NICU stay with outcome of newborns with fungal sepsis.

Neonatal Risk factors During NICU Stay.	Outcome		Chi sq. p value
	Death	Recovered	
Apnoea	8(80%)	28(46.7%)	0.043
NEC	6(60%)	11(18.3%)	0.009
Bacterial sepsis	9(90%)	16(26.7%)	0.001
Shock	10(100%)	11(18.3%)	0.001
DIC	10(100%)	12(20%)	0.001
MIS-N	5(50%)	8(13.3%)	0.014
MAS	2(20%)	4(6.7%)	0.167
Meningitis	1(10%)	7(11.7%)	0.409

Figure 29. Association of neonatal risk factors during NICU stay with outcome of newborns with fungal sepsis.



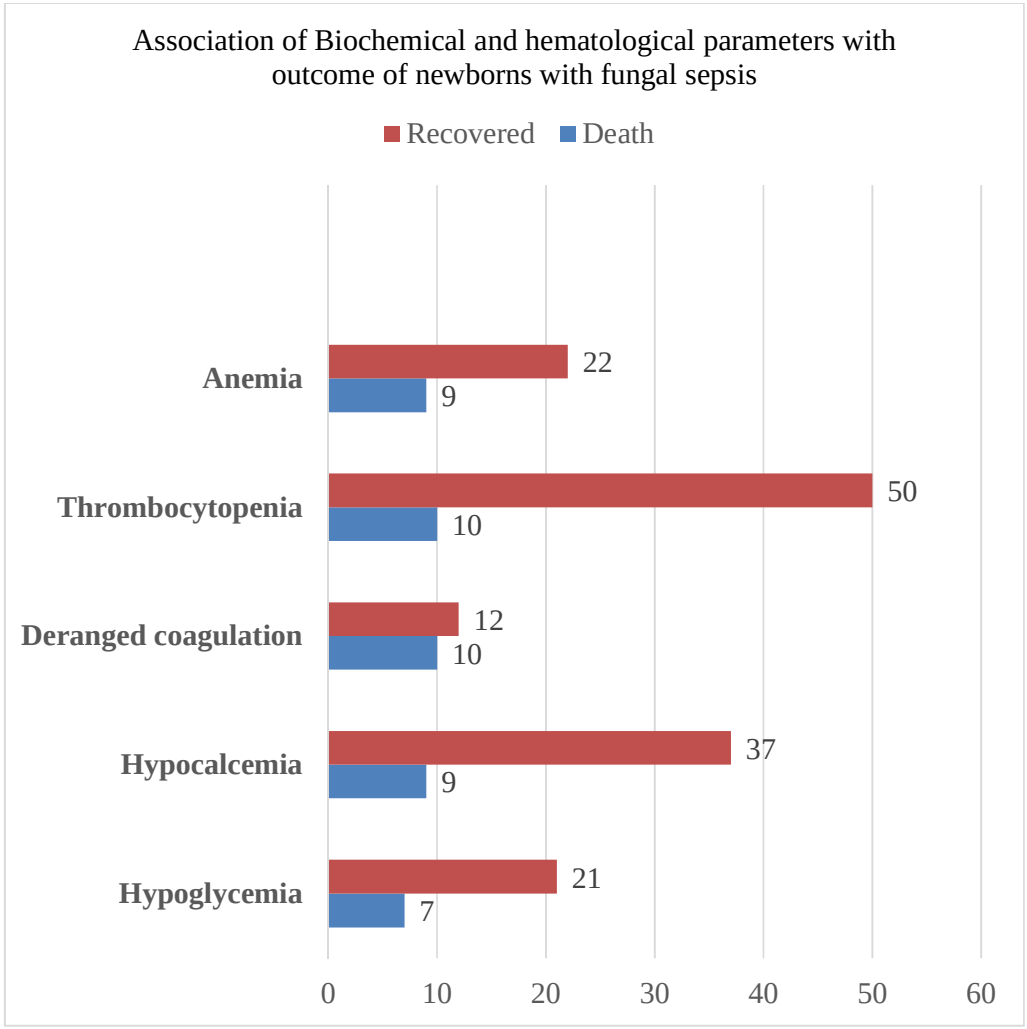
XIX.Association of Biochemical and hematological parameters with outcome of newborns with fungal sepsis.

When we compared the biochemical and hematological parameters with outcome, we found that Deranged coagulation , hypoglycemia and anemia were associated with higher mortality and these findings were statistically significant. Though hypocalcemia and thrombocytopenia were associated with mortality, the differences were not statistically significant.

Table 21. Association of Biochemical and hematological parameters with outcome of newborns with fungal sepsis

Biochemical and haematological parameters.	Outcome		Chi sq. p value
	Death	Recovered	
Hypoglycaemia	7 (70%)	21 (35%)	0.034
Hypocalcaemia	9 (90%)	37 (61.7%)	0.067
Thrombocytopenia	10 (100%)	50 (83.3%)	0.19
Anaemia	9 (90%)	22 (36.7%)	0.002

Figure 30. Association of Biochemical and hematological parameters with outcome of newborns with fungal sepsis



.

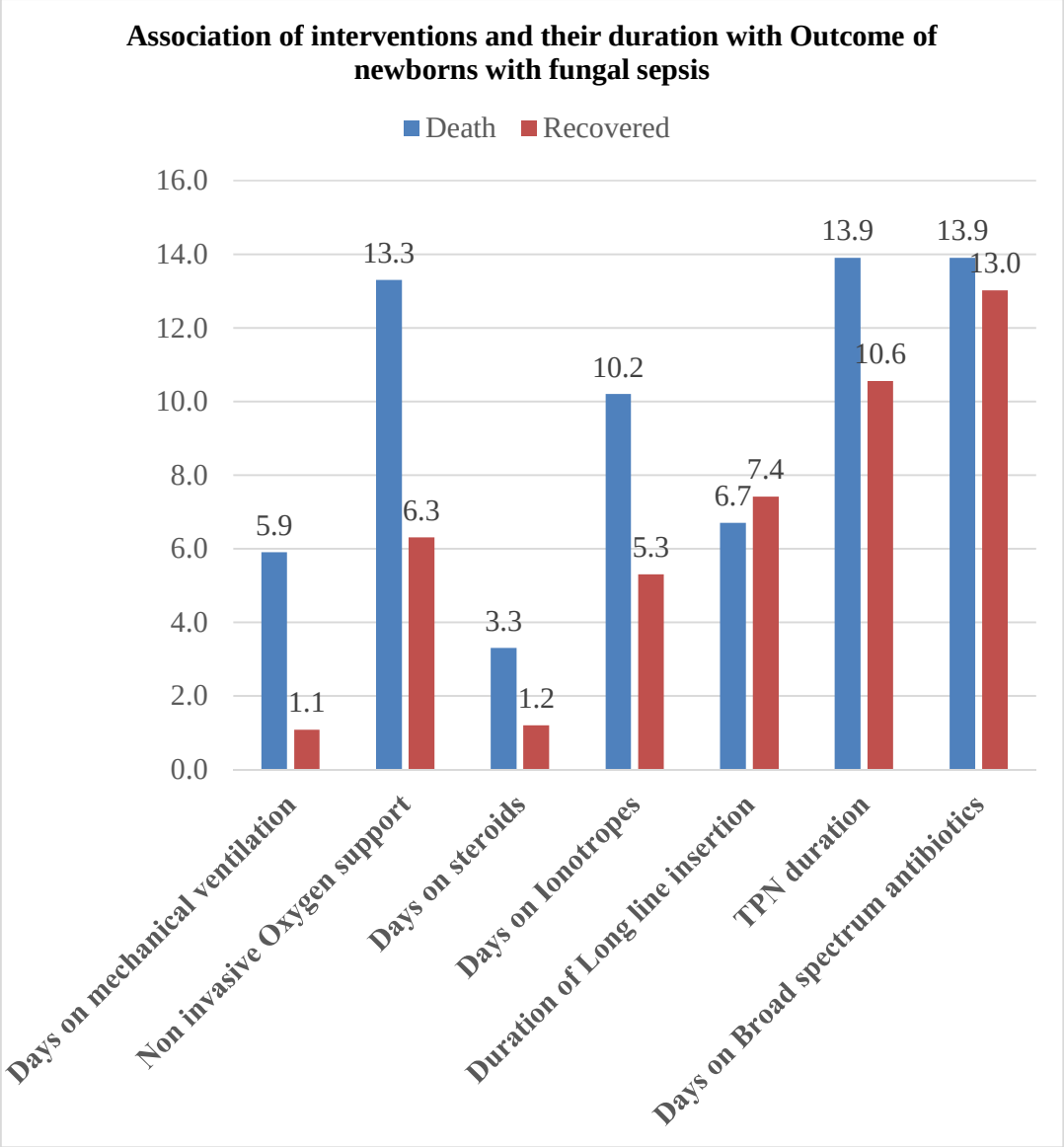
XX.Association of interventions and their duration with Outcome of newborns with fungal sepsis

When we compared the interventions and their duartion with outcome, we found that duration of mechanical ventilation more than 6 days and non invasive oxygen support more than 13 days , use of steroids more than 3 days and inotropes more than 6 days were associated with higher mortality and these were statistically significant. The longer the duration of these interventions were associated with higher mortality. Duration of long line insertion, TPN and use of broad spectrum antibiotics, though there were higher in mortality, the differences were not statistically significant.

Table 22. Association of interventions and their duration with Outcome of newborns with fungal sepsis

Days of Intervention	Outcome		p value by 't' test
	Death	Recovered	
Days on mechanical ventilation	5.9 (± 4.31)	1.08 (± 4.01)	0.001
Non invasive Oxygen support	13.3 (± 9.71)	6.3 (± 6.46)	0.045
Days on steroids	3.3(± 2.12)	1.2(±0.22)	0.009
Days on ionotropes	10.2(±5.34)	5.3(±4.03)	0.001
Duration of Long line insertion	6.7 (± 3.33)	7.42 (± 6.2)	0.594
TPN duration	13.9 (± 9.24)	10.55 (± 6.48)	0.160
Days on Broad spectrum antibiotics	13.9 (± 9.24)	13.02 (± 5.73)	0.775

Figure 31. Association of interventions and their duration with Outcome of newborns with fungal sepsis



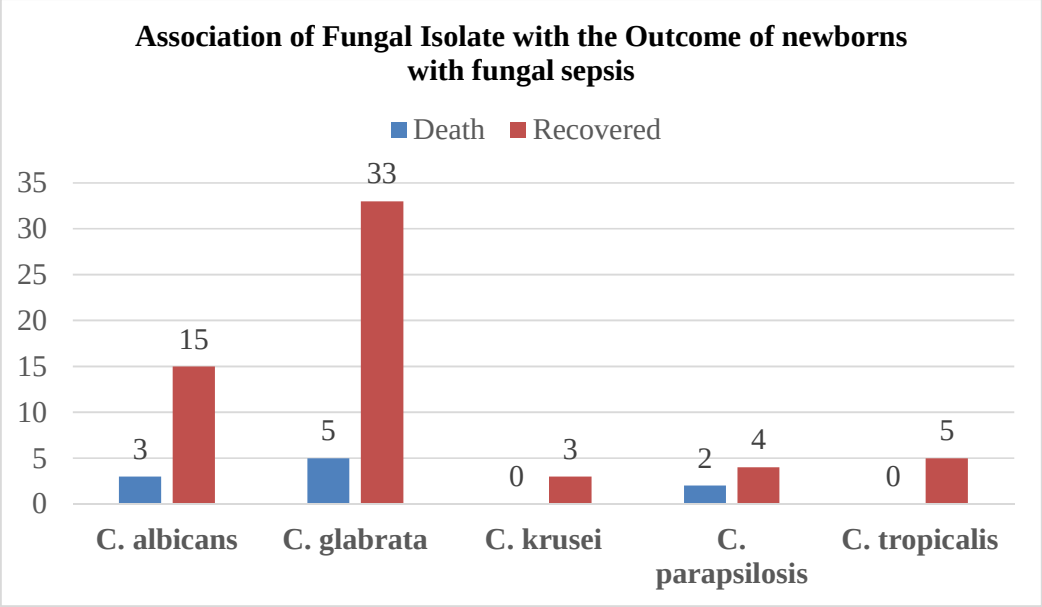
XX1.Association of Fungal Isolate with the Outcome of newborns with fungal sepsis

Comparing the Fungal Isolate with Outcome, non candida albicans (46.48%) were associated with higher mortality when compared to Candida albicans (16.66%). Of the non candida albicans , C. parapsilosis had higher proportion of mortality with 33.33% followed by C. glabrata with 13.15% .

Table 23. Association of Fungal Isolate with the Outcome of newborns with fungal sepsis

Fungal Isolate	Outcome		Total
	Death	Recovered	
C. albicans	3 (16.66%)	15 (83.33%)	18 (100%)
C. glabrata	5 (13.15%)	33 (86.84%)	38 (100%)
C. krusei	0 (0%)	3 (100%)	3 (100%)
C. parapsilosis	2 (33.33%)	4 (66.66%)	6 (100%)
C. tropicalis	0 (0%)	5 (100%)	5 (100%)
Total	10 (14.28%)	60 (85.71%)	70 (100%)

Figure 32. Association of Fungal Isolate with the Outcome of newborns with fungal sepsis



DISCUSSION

Systemic fungal infections, occurs in 5% of low birth weight babies admitted to NICU.(10,11) Candida species commonly causes Neonatal nosocomial bloodstream infections, especially in premature infants. The mortality is as high as 50% and the disability due to neurodevelopmental impairment poses a significant burden. (12,13) Hence the early identification and appropriate empirical therapy specific to the regional prevalence, among the high-risk neonates is essential.

This is a Prospective Observational study, of new-borns (<28 days old), admitted to neonatal intensive care unit, under the KLEH DR Prabhakar Kore Charitable Hospital, Department of Paediatrics, Jawaharlal Nehru Medical College, Belagavi.

70 newborns with proven fungal sepsis were included in the study. We collected data regarding gender, gestational age, birth weight, mode of delivery, maternal risk factors, neonatal risk factors at birth and during their stay in NICU, duration of interventions and assessed biochemical and hematological parameters. Also, data regarding blood counts were collected and were compared with onset of fungal sepsis. Data regarding Fungal isolates, trend in blood culture and sensitivity pattern were compared. All these risk factors, blood parameters, interventions were compared with outcome The data obtained was tabulated into Microsoft Excel sheets and processed using software version 2.3.0.

Gender: We studied 70 newborns with fungal sepsis admitted in NICU, our study showed a higher number of male newborns (55.71%) having fungal sepsis than female newborns(44.29%).

Meng Qi Zhang et al, in their review, studied the Sex- and Gender-Dependent Differences in clinical and preclinical sepsis. They observed that in neonates, males were more commonly affected, and the attributes they postulated were related to oxidative stress and the cytokine response difference.(65)

Shruti Murthy et al, did a systematic review and meta-analysis, and observed that male gender was a risk factor for the occurrence of the neonatal fungal sepsis in India. (66)

Mode of delivery: In this study, 42 newborns were delivered by LSCS and 28 were delivered by vaginal delivery. When we compared the mode of delivery with outcome of newborns withh fungal sepsis, the differences were not statistically significant suggesting maternal transmission of fungal sepsis through delivery is unlikely.

A study conducted by **Huang et al,** found that there was no statistically significant association between fungal sepsis with mode of delivery though 55 % of neonates with fungal sepsis delivered by LSCS.

Birth weight and gestational age: Various studies have reported that the birth weight is related to both morbidity and mortality in fungal sepsis.In this study, Out of 70 newborns, 54 newborns were LBW indicating that LBW is the risk factor for developing fungal sepsis. High mortality (80%) was observed with LBW, but the differences were not statistically significant suggesting us no role of birth weight in regard of mortality due to fungal sepsis. **Evangelia Farmakiet al**, observed that the very low birth weight was identified as the single independent factor associated with the fungal infection. (18)

In this study, majority of newborns were preterm (67.1%) indicating that preterm is the risk factor for developing fungal sepsis. Preterms were also associated with higher mortality, though the differences were not statistically significant suggesting prematurity as a poor predictor of mortality in newborns with fungal sepsis.**L Saiman et al**, in their cohort study, observed that the Preterm births were associated with increased incidence of fungal sepsis . (68)

Therefore from this study, LBW and prematurity considered as one of the risk factors for predicting fungal sepsis.

Maternal risk factors in newborns with fungal sepsis:

In this study,maternal risk factors observed in newborn with fungal sepsis were gestational hypertension (24.3%), UTI in mothers(12.9%), GDM (8.6%), Hypothyroid (8.6%),prolonged rupture of membranes(7.1%)and maternal sepsis (5.7%).

In a study conducted by **Shruti Murthy et al**, it was found that premature rupture of membranes and maternal sepsis emerged as risk factor for neonatal fungal sepsis.

Neonatal risk factors, biochemical and haematological parameters Interventions performed in NICU in newborns with fungal sepsis.

The neonatal risk factors play a crucial role in occurrence of the disease and predicting the outcomes. In this study, we studied various risk factors at birth and risk factors during hospital stay in association with fungal sepsis .Risk factors observed in newborns with fungal sepsis at birth were Preterm(67.1%), LBW(77.1%), respiratory distress (82.86%) and birth asphyxia (18.57%).During hospital stay, many newborns

developed apnoea(51.4%), Bacterial sepsis (35.7%) with shock, DIC(31.43%), NEC(24.29%) Neonatal seizures (22.86%), MIS-N(18.57%), meningitis (11.43%), MAS(8.57%) and neonatal hepatitis (1.43%).

Similarly, when we studied biochemical and haematological parameters of newborns with fungal sepsis 60 newborns(85.7%) had thrombocytopenia,31 newborns(44.3%) had anemia,22 newborns(31.4%) had deranged coagulation profile (p= 0.02), 46 newborns(65.7%) had hypocalcemia and 28 newborns(40.0%) had hypoglycaemia. When we studied the interventions performed in NICU and their duration in newborns with fungal sepsis, all newborns received broad spectrum antibiotics like Cephalosporins, Aminoglycosides prior to the culture, 53(75.71%) newborns had received antibiotics more than 10 days, 17(24.28%) newborns had received antibiotics less than 10 days. 68(97.14%) newborns had received Intravenous fluids including TPN, 65(92.85%) newborns required non invasive oxygen support by Continuos positive airway pressure (CPAP) or by nasal prongs,17 (24.28%) newborns were on mechanical ventilation, 49(70%) babies had long line insertion, 17 (24.29%) newborns received steroids as pulse therapy as a treatment protocol for MIS-N, and 27 (38.6%) newborns were administered Ionotropes.

In a study by **Neerul Panditaet al**, they observed that the Risk factors for the neonatal fungal sepsis include factors such as the low birth weight, prematurity, broad spectrum antibiotic usage, Mechanical ventilation, total parenteral nutrition.(59)

Yingfang Yu et al, observed that the Mechanical ventilation for more than 6 days, usage of peripherally inserted central venous catheter, use of third-generation cephalosporin, previous history of abdominal surgeries, and neutropenia during first

week of life < 1500 million cells/L were identified as a significantly associated risk factors with the presence of invasive fungal infection.(55)

Bashir Ahmad Charoo et al, where they observed that the major complications associated with fungal illness in neonates were found to be respiratory distress, shock, Necrotizing enterocolitis and disseminated intravascular coagulation, and thrombocytopenia.(58)

Comparision of blood Counts before & after onset of fungal sepsis: When we compared the blood counts before and after onset of fungal sepsis as a parameter to suspect the fungal sepsis, we found that drop in haemolobin,platelet count, TWBC and sudden rise in Hscrp was significantly associated with occurrence of fungal sepsis and these predictors were statistically significant. Hence, parameters like haemoglobin,platelets, TWBC and Hscrp could be used as predictors for onset of fungal sepsis in newborns.

A study conducted in India by **Charoo, et al** regarding systemic candida infection majority of preterm neonates with fungal sepsis developed thrombocytopenia.

Blood culture pattern timeline: We studied blood culture pattern of fungal growth on day 1 , day 3 and after 72 hrs of newborns with fungal sepsis, of which, 16 fungal isolates were on day 1, 47 on day 3 and 7 after 72 hrs suggesting, 77% of the newborns were found to have late onset fungal sepsis.

A study done by **Kelly Ross et al,** observed majority of cultures were positive for fungal growth after 72 hrs of life.

A study conducted by **S. Rao et al**, observed 64% of babies had late onset fungal sepsis.

Fungal Isolates and their sensitivity pattern: The fungal species reported in different regions were different, candida albicans being the most common cause in developed countries, non-albicans were common in developing countries. In this study , majority of our newborns with fungal sepsis isolated C. non albicans (74.29%) of which C. glabrata(73%) was common , followed by C. albicans (25.71%).

Yingfang Yu et al, observed that the Candida parapsilosis was isolated in majority (33.3%) of the neonates.(55)**Evangelia Farmakiet al**, observed that the Candida non albicans was isolated in majority (42%) of the neonates. (18). These observations suggest that C. non albicans is an emerging fungal infection in the NICU's.

In this study, we compared the sensitivity of antifungal agents with the individual fungal species. The antifungal agents such as Amphotericin-B, Fluconazole, Voriconazole and Caspofungin were studied. Our study showed higher sensitivity to Caspofungin and Fluconazole as 58 isolates and 29 isolates were sensitive to Caspofungin and Fluconazole respectively. High resistance was observed with Amphotericin –B and voriconazole. Resistance to routine antfungals like Amphotericin- B and azole groups is an emerging problem in NICU, this could be due to over use of these drugs in the NICU's.

Daynia E.Ballot et al observed fluconazole resistance in 50% of C. non albicans isolates (16 out of 32). However, a study conducted in tertiary care center in North India showed flucanazole resistance of 33 % in C.non albicans and 43% in C. albicans.

Hence, from these observations, we recommend that fluconazole should be the first line of antifungal to be used empirically in newborns having risk factors for fungal sepsis and subsequently use of other anti fungal drugs should be based on culture & sensitivity reports.

Outcome of newborns with fungal sepsis: The main outcome studied was mortality. In our study, we found that mortality rate was 14.29% as 10 out of 70 newborns with fungal sepsis died.

The mortality rate in different studies ranges between 10% to 60%. **Jyotsna Agarwal et al**, observed that the Crude mortality among the neonates having fungal sepsis was 52.6%.(45)**Daynia E. Ballot et al**, in their study showed a mortality rate neonatal fungal blood stream infections was 45.8%.(53)**Rita Silva et al**, observed that the Mortality rate among the 15 cases of neonatal fungal sepsis was 46.7% (n = 7).(60)

Cause of death in newborns with fungal sepsis: In our study, Preterm(80%) was the most common cause of death in newborns with fungal sepsis followed by HIE(10%) and IEM(10%). This is similar to the study findings of the **Bashir Ahmad Charooet al**, where they observed that the Mortality rate in their study was found to be due to Prematurity, LBW and associated bacterial sepsis.(58)

Association of Maternal and neonatal risk factors, biochemical and haematological parameters, Interventions performed in NICU with mortality/outcome of newborns with fungal sepsis: In this study, we analysed the risk factors associated with mortality.

When we analysed maternal risk factors with mortality, we found that higher mortality was associated with Gestational Hypertension (p= 0.138), Maternal sepsis (p=0.087), prolonged rupture of membranes(p= 0.403) and Urinary tract infection(p= 0.393). however the differences were not statistically significant. Hence, maternal risk factors observed in our study were poor predictors of mortality in newborns with fungal sepsis.

Similarly, neonatal risk factors associated with higher mortality at birth were Preterm births (p= 0.201),Low Birth weight(p= 0.315), respiratory distress(p=0.322) and birth asphyxia (p= 0.065) .Though they were associated with higher mortality , differences were not stastistically significant.

When we compared biochemical and haematological parameters with mortality, statistically significant parameters associated with high mortality were deranged coagulation profile(p= 0.001) , hypoglycemia (p= 0.034) and anemia (p= 0.002) were statistically significant parameters , associated with high mortality. Though hypocalcemia(p= 0.067) and thrombocytopenia (p= 0.19) were associated with higher mortality, the differences were not statistically significant. Hence, presence of hypoglycemia, anemia, deranged coagulation profile can predict higher mortality in newborns with fungal sepsis. Similarly when we compared the interventions and their duration, we observed invasive ventilation for more than 7 days (p= 0.001), use of steroids(p=0.009) and ionotropes (p= 0.001) for more than 3 days and 6 days respectively ,were associated with increased mortality in newborns with fungal sepsis which were statistically significant.

Hence in our study complications like apnoea, NEC, neonatal seizures, associated bacterial sepsis with shock , DIC , MIS-N and presence of hypoglycemia, anemia, deranged coagulation profile and interventions like invasive ventilation, use of steroids and ionotropes were important predictors of mortality in newborns with fungal sepsis.

One such study conducted in India which is a prospective observational study regarding epidemiology, clinical spectrum and outcomes of fungal sepsis in neonates in neonatal intensive care unit, done by **Yunus et al** observed that VLBW and mechanical ventilation were significant risk factors and important predictors of mortality with fungal sepsis in

NICU.(71)

Kheya Ghosh Uttam et al, observed that the preterm, low birth weight, need for mechanical ventilation, parenteral nutrition, and use of broad-spectrum antibiotics play a significant role as risk factors in morbidity and mortality associated with fungal sepsis. (56)

Daynia E. Ballot et al, showed Mortality due to neonatal fungal blood stream infections was significantly associated with low birth weight (P= 0.046) and necrotizing enterocolitis (P= 0.034).(53)

Association of Fungal Isolate with the Outcome of newborns with fungal sepsis: In this study, C. non albicans was associated with high mortality, of which Candida parapsilosis had higher proportion of deaths with 33.33%(6 out of 70) followed by Candida glabarta (13.15%). We did not observe deaths in c. tropicalis and C. krusei infections.

The findings of our study are similar to the study done by **Deepak joyal et al** who showed a mortality of 34.85% (46 out of 132) due to C. non albicans. **Yingfang Yu et al**, observed that the Candida parapsilosis (15 out of 45 ; 33.3%) was associated with significantly higher mortality which was similar to our study.(55) However,, in a study conducted by **Kheya Ghosh Uttam et al**, they observed that the Candida tropicalis (34 out of 79; 42.3%)infections were associated with significantly higher mortality. These observations suggest that C. non albicans fungal sepsis in newborns is associated with higher mortality. However the numbers being small further studies were required to emphasize these observations

LIMITATION

The limitation of the study was our small sample size which was due to COVID Pandemic and hence we had limited cases admitted in NICU. Hence studies with larger sample size or multicentric studies are required for development of a clinical prediction model. This will also facilitate representing a larger population of newborns from all NICUs with appropriate geographic representation.

Secondly, as this study was carried out in a teritiary care hospital, the results might not corresponds to those from primary and secondary care settings.

CONCLUSION

- This is a Prospective Observational study, of new-borns (<28 days old), admitted to neonatal intensive care unit, under the KLEH DR Prabhakar Kore Charitable Hospital, Department of Paediatrics, Jawaharlal Nehru Medical College, Belagavi.
- 70 newborns with proven fungal sepsis were included in the study to correlate the risk factors associated with fungal sepsis.
- . We collected data regarding gender, gestational age, birth weight, mode of delivery, maternal risk factors, neonatal risk factors at birth and during their stay in NICU, duration of interventions and assessed biochemical and hematological parameters. Also, data regarding blood counts were collected and were compared with onset of fungal sepsis. Data regarding Fungal isolates, trend in blood culture and sensitivity pattern were compared..
- Maternal risk factors in newborns with fungal sepsis observed were gestational hypertension, GDM, hypothyroidism, UTI, prolonged rupture of membranes, maternal sepsis.
- Neonatal risk factors in newborns with fungal sepsis at birth observed were preterm, LBW, respiratory distress and birth asphyxia .Similarly, neonatal problems developed during NICU stay were apnoea, NEC, MIS-N, Meningitis, Neonatal seizures, MAS, Neonatal hepatitis, bacterial sepsis with shock and DIC.
- NICU interventions observed in newborns with fungal sepsis were use of broad spectrum antibiotics like third generation Cephalosporins,, prolonged use of Iv fluids including TPN, non invasive oxygen support, long line insertion, invasive ventilation , use of steroids and ionotropes .

- Blood parameters observed in newborns with fungal sepsis were thrombocytopenia, anemia, deranged coagulaton profile, hypocalcemia and hypoglycaemia.
- A drop in haemoglobin, platelet count, TWBC and sudden rise in Hscrp were significantly associated with onset of fungal sepsis and they could be used as predictors for onset of fungal sepsis in newborns having risk factors.
- In 70 newborns we had a mortality rate of 14.29% and we found that the risk factors associated with mortality were prematurity being most common followed by NICU complications such as apnoea, NEC, neonatal seizures, bacterial sepsis with shock, DIC, MIS-N. Presence of hypoglycemia, anemia, deranged coagulation profile and use of steroids, ionotropes and prolonged invasive ventilation were high predictors for mortality as they were statistically significant.
- In our study, majority of fungal isolates were C. non albicans of which glabrata species was most common. Majority of fungal isolates showed sensitivity to Caspofungin (58 of 70) followed by Fluconazole (29 out 70) with high resistance to Amphotericin- B (64 of 70) and Voriconazole (56 of 70). Hence, we suggest fluconazole should be the first line of antifungal to be used empirically in newborns having risk factors for fungal sepsis and subsequently use of other anti fungal drugs should be based on culture & sensitivity reports.
- To conclude, observations made in this study suggest the risk factors for predicting the mortality associated with fungal sepsis in newborns admitted to NICU.

SUMMARY

- **Gender:** Among the newborns, 39 (55.71%) newborns were Males and 31 newborns (44.29%) were Females.
- **Mode of delivery:** Among the newborns, 42 (60%) newborns delivered by LSCS delivery and 28 (40%) newborns by vaginal delivery.
- **Gestational Birth weight:** Among the newborns, 26 (37.14%) newborns were VLBW followed by 25 (35.71%) newborns were LBW and 3 (4.29%) newborns were Extremely LBW.
- **Gestational age:** Among the newborns, 23 (32.86%) newborns were Term followed by 21 (30%) newborns were Preterm and 5 (7.14%) newborns were Extremely preterm.
- **Maternal Risk Factors:** In this study, maternal risk factors observed in newborns with fungal sepsis were gestational hypertension (24.3%), UTI in mothers (12.9%), GDM (8.6%), Hypothyroid (8.6%), prolonged rupture of membranes (7.1%)and maternal sepsis (5.7%).
- **Neonatal Risk Factors at birth:** Risk factors observed in newborns with fungal sepsis at birth were Preterm (67.1%), LBW(77.1%), respiratory distress (82.86%) and birth asphyxia (18.57%).
- **Neonatal Risk Factors during NICU stay:** 36 newborns developed apnoea(51.4%) 25 had Bacterial sepsis (35.7%) with shock , 22 had DIC(31.43%), 18 had NEC(24.29%) 16 had Neonatal seizures(22.86%) 13 had MIS-N(18.57%), 8 had meningitis(11.43%),6 had MAS(8.57%) and 1newborn had neonatal hepatatis(1.43%).

- **Comparision of blood Counts before & after onset of fungal sepsis:** Drop in Haemoglobin(p=0.001), platelet count(p=0.001), TWBC(p=0.001) and sudden rise in Hscrp (p=0.001) was significantly associated with occurrence of fungal sepsis.
- **Intervention and their duration :** the interventions performed in NICU and their duration in newborns with fungal sepsis were all newborns received broad spectrum . 68(97.14%) newborns had received Intravenous fluids including TPN , 65(92.85%) newborns required non invasive oxygen support,17 (24.28%) newborns were on mechanical ventilation, 49(70%) babies had long line insertion, 17 (24.29%) newborns received steroids for MIS-N, and 27 (38.6%) newborns were administered Ionotropes.
- **Blood culture pattern:** In the study, late onset sepsis was observed in majority (54 out of 70; 77.1%)
- **Fungal Isolate:** Majority of our newborns isolated C. non albicans (74.29%) followed by C. albicans (25.71%). C. glabrata (54.29%) was the most common among the C. non albicans.
- **Sensitivity of antifungal agents with the individual Fungal species:** High sensitivity to Caspofungin (82.8%) and Fluconazole (41.4%) with high resistance was observed with Amphotericin –B (91.4%) and voriconazole (80%) was observed in our study.
- **Outcome:** Among the 70 newborns, 60 (85.71%) newborns were Discharged and 10 (14.29%) newborns died.
- **Cause of death:** Among the 70 newborns, 8(80%) newborns were premature, followed by HIE (10%) followed by IEM (10%).

- **Association of factors with mortality/outcome of newborns with fungal sepsis :**
  - The maternal risk factors associated with mortality were Gestational Hypertension, Maternal sepsis, prolonged rupture of membranes and Urinary tract infection, though not statistically significant.
  - The Neonatal risk factors at birth associated with higher mortality were preterm, Low Birth weight, respiratory distress and birth asphyxia , though not statistically significant.
  - Neonatal complications that developed during hospital stay which were significantly associated with higher mortality were apnoea, NEC, neonatal seizures, bacterial sepsis with shock,, MIS-N, DIC and were statistically significant.
- **Association of Biochemical and haematological parameters with outcome of newborns with fungal sepsis:** Parameters such as hypoglycaemia, deranged coagulation, anaemia were significantly associated with higher rates of mortality.
- **Association of interventions and their duration with Outcome of newborns with fungal sepsis:** The longer the mean duration of long line insertion, iv fluids, non-invasive Oxygen support and use of broad spectrum antibiotics were associated with higher mortality, though the differences were not statistically significant. The mean duration of mechanical ventilation more than 6 days, use of steroids and ionotropes for more than 3 days and 6 days respectively, were significantly associated with higher mortality and the differences were statistically significant.

- **Association of Fungal Isolate with the Outcome of newborns with fungal sepsis :** In this study, C. non albicans was associated with high mortality. Of which, Candida parapsilosis had higher proportion of deaths with 33.33% followed by Candida glabarta (13.15%).

.

BIBLIOGRAPHY

1. Liu L, Johnson HL, Cousens S, Perin J, Scott S, Lawn JE, et al. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. Lancet [Internet]. 2012 [cited 2022 Sep 30];379 (9832):2151–61. Available from: https://pubmed.ncbi.nlm.nih.gov/22579125/

2. Lawn JE, Cousens S, Zupan J. 4 million neonatal deaths: when? Where? Why? Lancet [Internet]. 2005 Mar 5 [cited 2022 Sep 30];365(9462):891–900. Available from: https://pubmed.ncbi.nlm.nih.gov/15752534/

3. Stoll BJ, Hansen N, Fanaroff AA, Wright LL, Carlo WA, Ehrenkranz RA, et al. Changes in pathogens causing early-onset sepsis in very-low-birth-weight infants. N Engl J Med [Internet]. 2002 Jul 25 [cited 2022 Sep 30];347(4):240–7. Available from: https://pubmed.ncbi.nlm.nih.gov/12140299/

4. Boghossian NS, Page GP, Bell EF, Stoll BJ, Murray JC, Cotten CM, et al. Late-onset sepsis in very low birth weight infants from singleton and multiple-gestation births. J Pediatr [Internet]. 2013 [cited 2022 Sep 30];162(6). Available from: https://pubmed.ncbi.nlm.nih.gov/23324523/

5. Wynn JL, Wong HR. Pathophysiology of Neonatal Sepsis. undefined. 2017 Jan 1;1536-1552.e10.

6. Barton L, Hodgman JE, Pavlova Z. Causes of death in the extremely low birth weight infant. Pediatrics [Internet]. 1999 [cited 2022 Sep 30];103(2):446–51. Available from: https://pubmed.ncbi.nlm.nih.gov/9925839/

7. Cohen-Wolkowiez M, Moran C, Benjamin DK, Cotten CM, Clark RH, Benjamin DK, et al. Early and late onset sepsis in late preterm infants. Pediatr Infect Dis J [Internet]. 2009 Dec 1 [cited 2022 Sep 30];28(12):1052–6. Available from: https://pubmed.ncbi.nlm.nih.gov/19953725/

8. Vergnano S, Buttery J, Cailes B, Chandrasekaran R, Chiappini E, Clark E, et al. Neonatal infections: Case definition and guidelines for data collection, analysis, and presentation of immunisation safety data. Vaccine [Internet]. 2016 Dec 12 [cited 2022 Oct 1];34(49):6038. Available from: /pmc/articles/PMC5139809/

9. Camacho-Gonzalez A, Spearman PW, Stoll BJ. Neonatal Infectious Diseases: Evaluation of Neonatal Sepsis. Pediatr Clin North Am [Internet]. 2013 Apr [cited 2022 Oct 1];60(2):367. Available from: /pmc/articles/PMC4405627/

10. Kaufman DA. Fungal infections in neonates: Update on prevention and treatment. Minerva Ginecol. 2007 Jun;59(3):311–29.

11. Systemic fungal infections in neonates - PubMed [Internet]. [cited 2022 Sep 30]. Available from: https://pubmed.ncbi.nlm.nih.gov/16519252/

12. Hsieh E, Smith PB, Jacqz-Aigrain E, Kaguelidou F, Cohen-Wolkowiez M, Manzoni P, et al. Neonatal fungal infections: when to treat? Early Hum Dev [Internet]. 2012 May [cited 2022 Sep 30];88(Suppl 2):S6. Available from: /pmc/articles/PMC3512570/

13. Benjamin DK, DeLong E, Cotten CM, Garges HP, Steinbach WJ, Clark RH. Mortality following blood culture in premature infants: increased with Gram-negative bacteremia and candidemia, but not Gram-positive bacteremia. J

Perinatol [Internet]. 2004 Mar [cited 2022 Sep 30];24(3):175–80. Available from: https://pubmed.ncbi.nlm.nih.gov/14985775/

14. Stoll BJ, Gordon T, Korones SB, Shankaran S, Tyson JE, Bauer CR, et al. Late-onset sepsis in very low birth weight neonates: a report from the National Institute of Child Health and Human Development Neonatal Research Network. J Pediatr [Internet]. 1996 [cited 2022 Sep 30];129(1):63–71. Available from: https://pubmed.ncbi.nlm.nih.gov/8757564/

15. Makhoul IR, Sujov P, Smolkin T, Lusky A, Reichman B. Epidemiological, clinical, and microbiological characteristics of late-onset sepsis among very low birth weight infants in Israel: a national survey. Pediatrics [Internet]. 2002 [cited 2022 Sep 30];109(1):34–9. Available from: https://pubmed.ncbi.nlm.nih.gov/11773539/

16. Manzoni P, Farina D, Leonessa M, D'Oulx EA, Galletto P, Mostert M, et al. Risk Factors for Progression to Invasive Fungal Infection in Preterm Neonates With Fungal Colonization. Pediatrics [Internet]. 2006 Dec 1 [cited 2022 Sep 30];118(6):2359–64. Available from: https://publications.aap.org/pediatrics/article/118/6/2359/69749/Risk-Factors-for-Progression-to-Invasive-Fungal

17. Yu Y, Du L, Yuan T, Zheng J, Chen A, Chen L, et al. Risk factors and clinical analysis for invasive fungal infection in neonatal intensive care unit patients. Am J Perinatol [Internet]. 2013 [cited 2022 Sep 30];30(7):589–94. Available from: http://www.thieme-connect.com/products/ejournals/html/10.1055/s-0032-1329688

18. Farmaki E, Evdoridou J, Pouliou T, Bibashi E, Panagopoulou P, Filioti J, et al. Fungal colonization in the neonatal intensive care unit: Risk factors, drug susceptibility, and association with invasive fungal infections. Am J Perinatol [Internet]. 2007 Feb [cited 2022 Sep 30];24(2):127–35. Available from: http://www.thieme-connect.com/products/ejournals/html/10.1055/s-2007-970078

19. Bettauer V, Massahi S, Khurdia S, Costa A, Omran RP, Khosravi N, et al. Candida albicans exhibits distinct cytoprotective responses to anti-fungal drugs that facilitate the evolution of drug resistance. bioRxiv [Internet]. 2020 Apr 18 [cited 2022 Sep 30];2020.01.21.914549. Available from: https://www.biorxiv.org/content/10.1101/2020.01.21.914549v3

20. Richardson M, Lass-Flörl C. Changing epidemiology of systemic fungal infections. Clinical Microbiology and Infection [Internet]. 2008 [cited 2022 Sep 30];14(SUPPL. 4):5–24. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/j.1469-0691.2008.01978.x

21. Srivastava V, Singla RK, Dubey AK. Emerging Virulence, Drug Resistance and Future Anti-fungal Drugs for Candida Pathogens. Curr Top Med Chem. 2018 May 29;18(9):759–78.

22. Arcens M, Stirnemann J, Mayor G, John G. [Epidemiology and strategy to prevent urinary catheters related complications]. Rev Med Suisse. 2018 Aug;14(616):1518–21.

23. Dagasso G, Conley J, Parfitt E, Pasquill K, Steele L, Laupland K. Risk factors associated with bloodstream infections in end-stage renal disease patients: a population-based study. Infect Dis (Lond). 2018;50(11–12):831–6.

24. Butler-Laporte G, De L'Étoile-Morel S, Cheng MP, McDonald EG, Lee TC. MRSA colonization status as a predictor of clinical infection: A systematic review and meta-analysis. J Infect. 2018 Dec;77(6):489–95.

25. Hotchkiss RS, Moldawer LL, Opal SM, Reinhart K, Turnbull IR, Vincent JL. Sepsis and septic shock. Nat Rev Dis Primers. 2016;2(1):16045.

26. Weinstein MP, Towns ML, Quartey SM, Mirrett S, Reimer LG, Parmigiani G, et al. The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of bacteremia and fungemia in adults. Clinical Infectious Diseases. 1997;24(4): 584–602.

27. Riedel S, Carroll KC. Blood cultures: key elements for best practices and future directions. Journal of infection and chemotherapy. 2010;16(5):301–16.

28. Lin WH, Wang MC, Tseng CC, Ko WC, Wu AB, Zheng PX, et al. Clinical and microbiological characteristics of Klebsiella pneumoniae isolates causing community-acquired urinary tract infections. Infection. 2010;38(6):459–64.

29. Wu SW, Liu KS, Lin CK, Hung TW, Tsai HC, Chang HR, et al. Community-acquired urinary tract infection in kidney transplantation: risk factors for bacteremia and recurrent infection. Journal of the Formosan Medical Association. 2013;112(3):138–43.

30. Finkelstein R, Kassis E, Reinhertz G, Gorenstein S, Herman P. Community-acquired urinary tract infection in adults: a hospital viewpoint. Journal of Hospital Infection. 1998;38(3):193–202.

31. Woll C, Neuman MI, Pruitt CM, Wang ME, Shapiro ED, Shah SS, et al. Epidemiology and Etiology of Invasive Bacterial Infection in Infants ≤60 Days Old Treated in Emergency Departments. J Pediatr. 2018 Sep;200:210-217.e1.

32. Antonio M, Gudiol C, Royo-Cebrecos C, Grillo S, Ardanuy C, Carratalà J. Current etiology, clinical features and outcomes of bacteremia in older patients with solid tumors. J Geriatr Oncol. 2019 Mar;10(2):246–51.

33. Munro APS, Blyth CC, Campbell AJ, Bowen AC. Infection characteristics and treatment of Staphylococcus aureus bacteraemia at a tertiary children's hospital. BMC Infect Dis. 2018 Aug;18(1):387.

34. Bouza E, Cobo-Soriano R, Rodríguez-Créixems M, Muñoz P, Suárez-Leoz M, Cortes C. A Prospective Search for Ocular Lesions in Hospitalized Patients with Significant Bacteremia. Clin Infect Dis. 2000 Feb 1;30:306–12.

35. Simonsen KA, Anderson-Berry AL, Delair SF, Dele Davies H. Early-onset neonatal sepsis. Clin Microbiol Rev [Internet]. 2014 [cited 2022 Sep 30];27(1):21–47. Available from: https://pubmed.ncbi.nlm.nih.gov/24396135/

36. Singh M, Alsaleem M, Gray CP. Neonatal Sepsis. StatPearls [Internet]. 2022 May 17 [cited 2022 Sep 30]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK531478/

37. Chakraborty RK, Burns B. Systemic inflammatory response syndrome. 2019;

38. Kaukonen KM, Bailey M, Pilcher D, Cooper DJ, Bellomo R. Systemic inflammatory response syndrome criteria in defining severe sepsis. New England Journal of Medicine. 2015;372(17):1629–38.

39. Kaukonen KM, Bailey M, Bellomo R. Systemic Inflammatory Response Syndrome Criteria for Severe Sepsis. N Engl J Med. 2015;373(9):881.

40. Lamy B, Dargère S, Arendrup MC, Parienti JJ, Tattevin P. How to optimize the use of blood cultures for the diagnosis of bloodstream infections? A state-of-the art. Front Microbiol. 2016;7:697.

41. Opota O, Croxatto A, Prod'hom G, Greub G. Blood culture-based diagnosis of bacteraemia: state of the art. Clinical Microbiology and Infection. 2015 Apr 1;21(4):313–22.

42. Neonatal Sepsis: Pathogenesis, and Overview of Clinical Findings | Calgary Guide [Internet]. [cited 2022 Sep 30]. Available from: https://calgaryguide.ucalgary.ca/neonatal-sepsis-pathogenesis-and-overview-of-clinical-findings/

43. Smith DA, Nehring SM. Bacteremia. Pediatric Emergency Medicine. 2022 May 2;530–4.

44. Saha R. The Confrontation of Fungal Sepsis in Neonates. Indian Pediatr. 2017;542.

45. Agarwal J, Bansal S, Malik GK, Jain A. Trends in neonatal septicemia: emergence of non-albicans Candida. Indian Pediatr. 2004;41(7):712–5.

46. Kaufman D, Fairchild KD. Clinical Microbiology of Bacterial and Fungal Sepsis in Very-Low-Birth-Weight Infants. Clin Microbiol Rev [Internet]. 2004 Jul [cited 2022 Sep 30];17(3):638. Available from: /pmc/articles/PMC452555/

47. Al-Sweih N, Khan Z, Khan S, Devarajan L v. Neonatal candidaemia in Kuwait: a 12-year study of risk factors, species spectrum and antifungal susceptibility. Mycoses [Internet]. 2009 Nov [cited 2022 Oct 1];52(6):518–23. Available from: https://pubmed.ncbi.nlm.nih.gov/18983425/

48. Spiliopoulou A, Dimitriou G, Jelastopulu E, Giannakopoulos I, Anastassiou ED, Christofidou M. Neonatal intensive care unit candidemia: epidemiology, risk factors, outcome, and critical review of published case series. Mycopathologia [Internet]. 2012 Apr [cited 2022 Oct 1];173(4):219–28. Available from: https://pubmed.ncbi.nlm.nih.gov/22076411/

49. Rodriguez D, Almirante B, Park BJ, Cuenca-Estrella M, Planes AM, Sanchez F, et al. Candidemia in neonatal intensive care units: Barcelona, Spain. Pediatr Infect Dis J [Internet]. 2006 Mar [cited 2022 Oct 1];25(3):224–9. Available from: https://pubmed.ncbi.nlm.nih.gov/16511384/

50. Kaufman DA. Aiming for zero: Preventing invasive Candida infections preterm infants. Neoreviews. 2011 Jul;12(7).

51. Seth R, Xess I, Jana M. Diagnosis of invasive fungal infections in children. Indian Pediatr. 2019;56(3):229–36.

52. Baley JE. Neonatal Candidiasis: The Current Challenge. Clin Perinatol. 1991 Jun 1;18(2):263–80.

53. Ballot DE, Bosman N, Nana T, Ramdin T, Cooper PA. Background changing patterns of neonatal fungal sepsis in a developing country. J Trop Pediatr

[Internet]. 2013 Dec 1 [cited 2022 Oct 1];59(6):460–4. Available from: https://academic.oup.com/tropej/article/59/6/460/1659691

54. CHOC - Children's Health Orange County [Internet]. [cited 2022 Oct 1]. Available from: https://www.choc.org/

55. Yu Y, Du L, Yuan T, Zheng J, Chen A, Chen L, et al. Risk factors and clinical analysis for invasive fungal infection in neonatal intensive care unit patients. Am J Perinatol [Internet]. 2013 [cited 2022 Oct 1];30(7):589–94. Available from: http://www.thieme-connect.com/products/ejournals/html/10.1055/s-0032-1329688

56. Uttam KG, Gupta P, Poddar S. Fungal Sepsis in a Tertiary Neonatal Intensive Care Unit: A Cross-sectional Study. Pediatr Infect Dis. 2022 Jun 1;4(2):33–7.

57. Chaurasia D, Goel M, Dhruw S, Dubey D, Dwivedi R. Changing pattern of neonatal fungal sepsis: a matched case–control study. Natl J Med Allied Sci. 2015;4(1):3–7.

58. Charoo BA, Ashraf Y, Bhat JI, Qazi IA. Systemic Candida infection in preterm babies: Experience from a tertiary care hospital of North India. J Clin Neonatol [Internet]. 2019 [cited 2022 Oct 1];8(3):151. Available from: https://www.jcnonweb.com/article.asp?issn=2249-4847;year=2019;volume=8;issue=3;spage=151;epage=154;aulast=Charoo

59. Pandita N, Kumar Bhat N, Peshin C, Wasim S, Gupta A. Profile of fungal septicaemia in new born at a tertiary care hospital in North India. International Journal of Contemporary Pediatrics Pandita N et al Int J ContempPediatr

[Internet]. [cited 2022 Oct 1];4(2):455–9. Available from: http://www.ijpediatrics.com

60. Silva R, Grilo M, Pissarra S, Guimarães H. Fungal sepsis in a Level III Neonatal Intensive Care Unit: a 10-year retrospective analysis. Journal of Pediatric and Neonatal Individualized Medicine (JPNIM) [Internet]. 2014 Oct 23 [cited 2022 Oct 1];3(2):e030212–e030212. Available from: https://www.es.jpnim.com/index.php/jpnim/article/view/030212

61. Ojogba OM, Grace AM, Bose TO, Esther EA, Inyang O, Abel I, et al. Neonatal fungal sepsis in Jos North-Central Nigeria. J Med Trop [Internet]. 2020 [cited 2022 Oct 1];22(2):80. Available from: https://www.jmedtropics.org/article.asp?issn=2276-7096;year=2020;volume=22;issue=2;spage=80;epage=85;aulast=Ojogba

62. Zhang X, Ru XF, Wang Y, Li X, Sang T, Feng Q. [Clinical characteristics of neonatal fungal sepsis in neonatal intensive care unit]. Beijing da xuexue bao Yi xue ban = Journal of Peking University Health Sciences [Internet]. 2017 Oct 1 [cited 2022 Oct 1];49(5):789–93. Available from: https://europepmc.org/article/med/29045957

63. Ahmed SH, Mokhtar EM, El-Kholy IM, Essawy AK el, El-Din AA, Shetaia YM. Fungal neonatal and infantile sepsis in Egypt: Risk factors and identification of fungal isolates. African Journal of Clinical and Experimental Microbiology [Internet]. 2019 Oct 30 [cited 2022 Oct 1];21(1):14–20. Available from: https://www.ajol.info/index.php/ajcem/article/view/190670

64. Jajoo M, Manchanda V, Chaurasia S, Jeeva Sankar M, Gautam H, Agarwal R, et al. Alarming rates of antimicrobial resistance and fungal sepsis in outborn neonates in North India. PLoS One [Internet]. 2018 Jun 1 [cited 2022 Aug 26];13(6):e0180705. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0180705

65. Zhang MQ, Macala KF, Fox-Robichaud A, Mendelson AA, Lalu MM. Sex- and Gender-Dependent Differences in Clinical and Preclinical Sepsis. Shock [Internet]. 2021 Aug 1 [cited 2022 Oct 3];56(2):178–87. Available from: https://journals.lww.com/shockjournal/Fulltext/2021/08000/Sex__and_Gender_Dependent_Differences_in_Clinical.4.aspx

66. Murthy S, Godinho MA, Guddattu V, Lewis LES, Sreekumaran Nair N. Risk factors of neonatal sepsis in India: A systematic review and meta-analysis. PLoS One [Internet]. 2019 Apr 1 [cited 2022 Oct 3];14(4). Available from: https://pubmed.ncbi.nlm.nih.gov/31022223/

67. Oeser C, Vergnano S, Naidoo R, Anthony M, Chang J, Chow P, et al. Neonatal invasive fungal infection in England 2004–2010. Clinical Microbiology and Infection. 2014 Sep 1;20(9):936–41.

68. 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. Pediatric Infectious Disease Journal. 2001;20(12):1119–24.

69. Baltimore RS. Neonatal Sepsis. Pediatric Drugs 2003 5:11 [Internet]. 2012 Aug 21 [cited 2022 Oct 3];5(11):723–40. Available from: https://link.springer.com/article/10.2165/00148581-200305110-00002

70. Khaertynov KS, Boichuk S v., Khaiboullina SF, Anokhin VA, Andreeva AA, Lombardi VC, et al. Comparative Assessment of Cytokine Pattern in Early and Late Onset of Neonatal Sepsis. J Immunol Res. 2017;2017.

71. Mohd Yunus, Vikas Agarwal, Priya Tomer, Priyanka Gupta, Amit Upadhyay: Epdemiology, Clinical Spectrum and Outcomes of Fungal Sepsis in Neonates inNeonatal Intensive Care Unit : A Prospective Observational Study. InternationalJournal of Contemporary Medical Research Volume 5;Issue1;January2018;ICV:77.83

72. Daniel K. Benjamin, Barbara J. Stoll and Ronald N. Goldberg: Ne- onatal Candidiasis: Epidemiology, Risk Factors, and Clinical Judege- ment. Pediatrics 2010 October : 126(4): e865 e873.doi :10.1542/peds. 2009-3412

ANNEXURE - I –

CONSENT FOR PARTICIPATION IN RESEARCH

"**Correlation of Risk Factors associated with Fungal sepsis in Neonates admitted to Neonatal Intensive Care Unit – One year hospital based observational study**"

Principal Investigator: - Dr.

Co-investiator : - Dr.

You have been asked to involve your child in the said study to be conducted at neonatal care unit of Department of paediatrics KAHER's Dr. Prabhakar Kore Charitable Hospital, Belagavi by Dr._____PG student in department of paediatrics at Jawaharlal Nehru medical college, Belagavi.

Purpose of the study: Participation of your baby will help us to assess the risk factors associated with fungal sepsis and the need for the use of appropriate anti fungal medication. You are free to discontinue the participation in the study at any time for any reasons and you will not be paid any reimbursement for participation in the research. Hence involving your child in the study is your Voluntary decision, whether or not to participate will not affect your current or future relationship with KLEs Dr. Prabhakar Kore Hospital & Medical research centre, Belagavi.

Risk and benefits: There are no risks involved.

Use of photography/Identifying details: Any photography or identification details will be disclosed only with your permission.

Storage of sample: The samples collected will be sent to the laboratory for further processing.

Privacy and Confidentiality: The only people who will know that you are a research participant are member of the research team. No information about you or provided by you, during research will be disclosed to others without your written consent. When the results of the research are published or discussed in the conferences, no information will be disclosed that would reveal your identity. Any information obtained in connections with this study and that can be identified with you remain confidential and will be disclosed only with your permission.

Financial incentive for participation: You or your child will not be paid any reimbursement for participation in this study

Queries
If you have any queries you may contact
DR. Post Graduate Student
Department of Paediatrics
JNMC, Belagavi-590010
Phone No.
If you have any queries regarding or rights or research participation you may contact

DR.
PRINCIPAL,
PROFESSOR
DEPARTMENT OF PAEDIATRICS,
JNMC, Belagavi-590010
Phone No.

If you have any questions about your rights or research participation you may contact
DR. HARSHA HEGDE
Chairperson, JNMC
IEC & Scientist D
ICMR, National Institute of Traditional Medicine
Belagavi.
Phone no. 9480422506.

You will be given a copy of this form for your information and to keep for your records.

STATEMENT OF CONSENT

I hereby voluntarily agree for participation of my child name _____ age _____ in this study. I understand that I have the liberty to withdraw at any time. My signature below indicates that I have read or have been told in the language I understand, about this entire consent form including the risks and benefits and have had all my questions answered. I will be given a copy of this consent form.

Signature of the authorized representative/ parent: _____

Date: _____

Name: _____

Relation to the Subject: _____

Signature of the witness: _____

Date: _____

Name: _____

Signature of investigator: _____

Date: _____

Name: _____

ANNEXURE –II – PROFORMA

S.No.

PATIENT PARTICULAR'S: -

Name: - Sex:- M/F DoB: - / /

I.P no. Mother's Blood group :-

Baby's blood group :-

Address: -

Mb. /Phone No: -

Socio economic status :

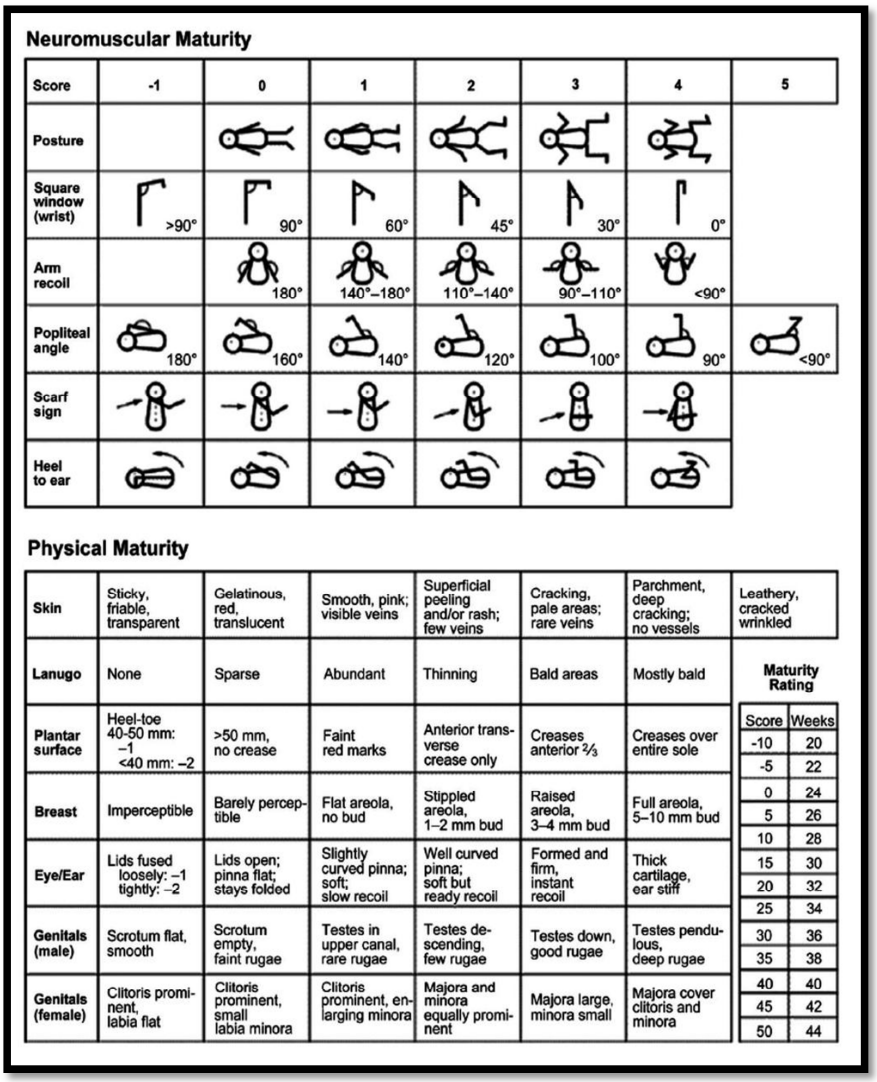
LMP: - EDD: - GA: - (a/c LMP)

Birth Wt:

HISTORY: -

ANTE-NATAL	NATAL	POST-NATAL
1st trimester **2nd trimester** **3rd trimester** **H/o** GDM / G-HTN / HYPOTHYROID /UTI / PV-leak **Anomaly scan: -** **Others**:-	**Mode of delivery: -** (indication-) **Resuscitation required?** Y/N **Cried at** **Apgar at** 1m 5m **Cong. Anomalies: -**	**Respiratory support and duration: -** **Sepsis: -** **Received any** Blood components: - Antibiotics: - **Others: -**

EXAMINATION: -



Neuromuscular Maturity

Score	-1	0	1	2	3	4	5
Posture							
Square window (wrist)	>90°	90°	60°	45°	30°	0°	
Arm recoil		180°	140°–180°	110°–140°	90°–110°	<90°	
Popliteal angle	180°	160°	140°	120°	100°	90°	<90°
Scarf sign							
Heel to ear							

Physical Maturity

Skin	Sticky, friable, transparent	Gelatinous, red, translucent	Smooth, pink; visible veins	Superficial peeling and/or rash; few veins	Cracking, pale areas; rare veins	Parchment, deep cracking; no vessels	Leathery, cracked wrinkled
Lanugo	None	Sparse	Abundant	Thinning	Bald areas	Mostly bald	
Plantar surface	Heel-toe 40-50 mm: –1 <40 mm: –2	>50 mm, no crease	Faint red marks	Anterior transverse crease only	Creases anterior ⅔	Creases over entire sole	
Breast	Imperceptible	Barely perceptible	Flat areola, no bud	Stippled areola, 1–2 mm bud	Raised areola, 3–4 mm bud	Full areola, 5–10 mm bud	
Eye/Ear	Lids fused loosely: –1 tightly: –2	Lids open; pinna flat; stays folded	Slightly curved pinna; soft; slow recoil	Well curved pinna; soft but ready recoil	Formed and firm, instant recoil	Thick cartilage, ear stiff	
Genitals (male)	Scrotum flat, smooth	Scrotum empty, faint rugae	Testes in upper canal, rare rugae	Testes descending, few rugae	Testes down, good rugae	Testes pendulous, deep rugae	
Genitals (female)	Clitoris prominent, labia flat	Clitoris prominent, small labia minora	Clitoris prominent, enlarging minora	Majora and minora equally prominent	Majora large, minora small	Majora cover clitoris and minora	

Maturity Rating

Score	Weeks
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

General physical	Systemic examination
AF PF Back and spine	R/S: -
Genitals: - Anal opening	CVS: -
Other significant: -	PA: -
Temp RR HR	CNS: -
Pulse CRT	

day of inclusion in study)-

S.No	PROBLEMS	1	2	3	4	5	6	7	8	9	10
1.	PRETERM/LBW										
2.	RESPIRATORY DISTRESS SYNDROME										
3.	APNOEA OF PREMATURITY										
4.	NEC										
5.	MECONIUM ASPIRATION SYNDROME										
6.	BIRT ASPHYXIA										
7.	NEONATAL SEIZURES										
8.	HYPOGLYCEMIA										
9.	HYPOCALCEMIA										
10.	HYPERBILIRUBINEMIA										
11.	BACTERIAL SEPSIS										
12.	SEPTIC SHOCK										
13.	THROMBOCYTOPENIA										
14.	ANEMIA										
15.	MODS										
16.	MENINGITIS										
17.	DIC										
18.	NEONATAL HEPATITIS										
19.	MIS-N										
20.	OTHERS										

S.No	PROBLEMS	11	12	13	14	15	16	17	18	19	20
1.	PRETERM/LBW										
2.	RESPIRATORY DISTRESS SYNDROME										
3.	APNOEA OF PREMATURITY										
4.	NEC										
5.	MECONIUM ASPIRATION SYNDROME										
6.	BIRT ASPHYXIA										
7.	NEONATAL SEIZURES										
8.	HYPOGLYCEMIA										
9.	HYPOCALCEMIA										
10.	HYPERBILIRUBINEMIA										
11.	BACTERIAL SEPSIS										
12.	SEPTIC SHOCK										
13.	THROMBOCYTOPENIA										
14.	ANEMIA										
15.	MODS										
16.	MENINGITIS										
17.	DIC										
18.	NEONATAL HEPATITIS										
19.	MIS-N										
20.	OTHERS										

S.No	PROBLEMS	21	22	23	24	25	26	27	28	29	30
1.	PRETERM/LBW										
2.	RESPIRATORY DISTRESS SYNDROME										
3.	APNOEA OF PREMATURITY										
4.	NEC										
5.	MECONIUM ASPIRATION SYNDROME										
6.	BIRT ASPHYXIA										
7.	NEONATAL SEIZURES										
8.	HYPOGLYCEMIA										
9.	HYPOCALCEMIA										
10.	HYPERBILIRUBINEMIA										
11.	BACTERIAL SEPSIS										
12.	SEPTIC SHOCK										
13.	THROMBOCYTOPENIA										
14.	ANEMIA										
15.	MODS										
16.	MENINGITIS										
17.	DIC										
18.	NEONATAL HEPATITIS										
19.	MIS-N										
20.	OTHERS										

DAY	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Hb															
PCV															
TWBC															
PLT															
HsCRP															
Blood C&S															
Urine R&M															
Urine C&S															
CSF Cytology															
CSF Glucose															
CSF Proteins															
CSF C&S															

DAY	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Hb															
PCV															
TWBC															
PLT															
HsCRP															
Blood C&S															
Urine R&M															
Urine C&S															
CSF Cytology															
CSF Glucose															
CSF Proteins															
CSF C&S															

TREATMENT	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
IV TAXIM															
IV AMPICILLIN															
IV CIPLOX															
IV AMIKACIN															
IV GENTAMICIN															
IV MEROPEREM															
IV METRONIDAZOLE															
OTHERS															
TRANSFUSIONS															
PACKED CELLS															
RDP															
FFP															
IV FLUIDS															
NON INVASIVE OXYGGEN SUPPORT															
INVASIVE VENTILATION															
LONGG LINE INSERTION															
IONOTROPES															
STEROIDS															

TREATMENT	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
IV TAXIM															
IV AMPICILLIN															
IV CIPLOX															
IV AMIKACIN															
IV GENTAMICIN															
IV MEROPEREM															
IV METRONIDAZOLE															
OTHERS															
TRANSFUSIONS															
PACKED CELLS															
RDP															
FFP															
IV FLUIDS															
NON INVASIVE OXYGGEN SUPPORT															
INVASIVE VENTILATION															
LONGG LINE INSERTION															
IONOTROPES															
STEROIDS															

DATA COLLECTION: -

MATERNAL RISK FACTORS

Fever	
UTI	
GDM	
HYPOTHYROID	
PV LEAK	

NEONATAL RISK FACTORS

Gestational age	
Birth weight	
Ventilation	
Intubation	
Long line insertion	
Total parenteral nutrition	
Duration of stay	
Broad spectrum antibiotics	

Broad spectrum antibiotics- antibiotics effective against gram positive and gram negative bacteria TPN- in this study, considering only dextrose/aminoacid solution

Fungal agent isolated	**Blood culture**	**Anti fungal sensitivity**

ANNEXURE-III- PHOTOGRAPHS

Figure 33.Candida species

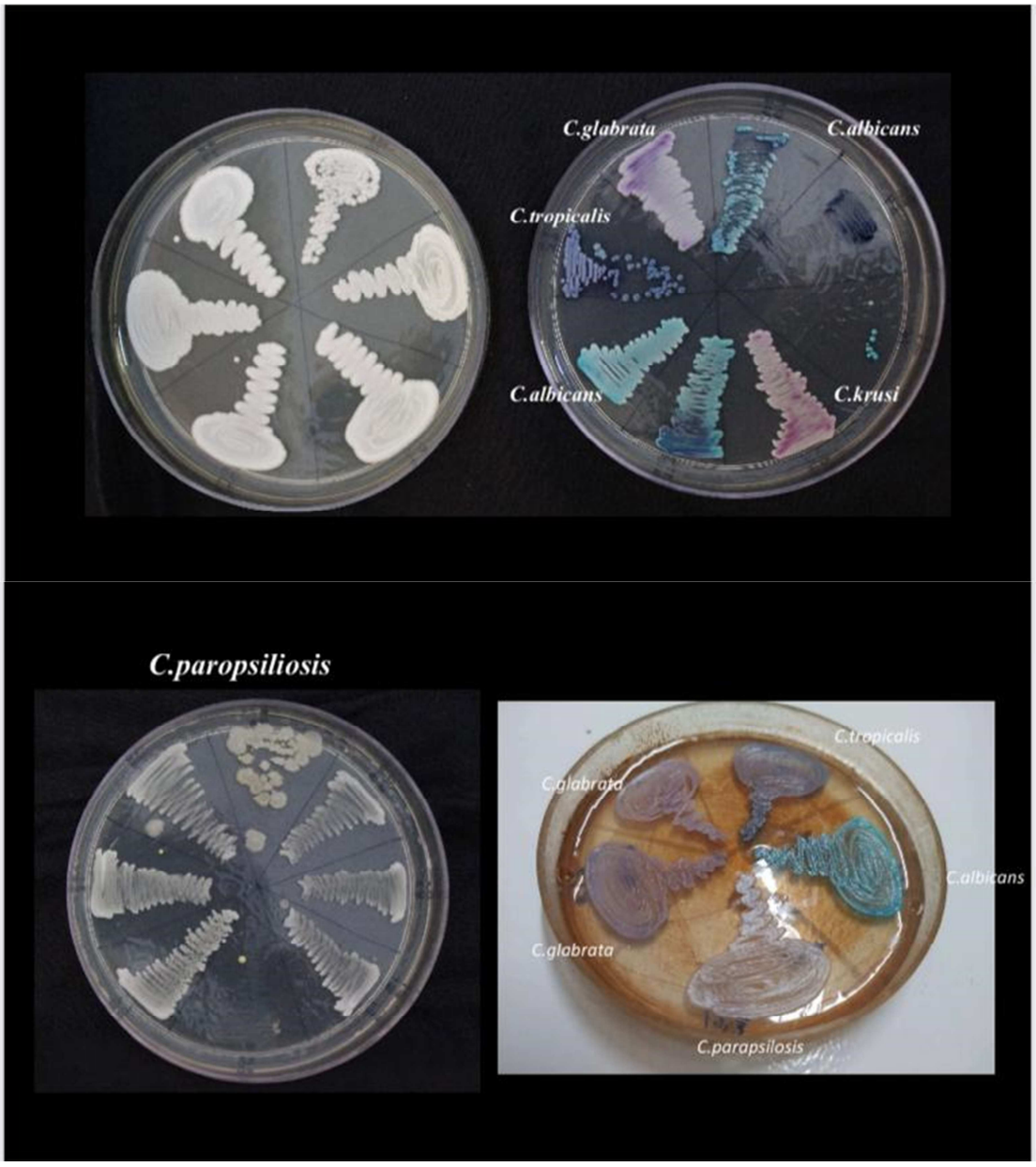


Figure 34.Antifungal susceptibility(DD- method)

Figure 35.Neonate with fungal sepsis

Figure 36.Long line

ANNEXURE-IV- KEY TO MASTER CHART

1.Gender	-	Male-1, Female-0
2.Mode of delivery	-	Lscs-1, Vaginal delivery-0
3.Maternal sepsis	-	YES-1, No-0
4.GDM	-	YES-1, No-0
5.Hypothyroid	-	YES-1, No-0
6.Gestational hypertension	-	YES-1, No-0
7. PV >18hrs	-	YES-1, No-0
8.UTI in mother	-	YES-1, No-0
9.Gestational age	-	Preterm-1, Term-0
10. Birth weight	-	LBW-1, Normal weight-0
11.**Respiratory distress**	-	YES-1, No-0
12.**Birth asphyxia**	-	YES-1, No-0
13.**Apnoea**	-	YES-1, No-0
14-NEC	-	YES-1, No-0
15.MAS	-	YES-1, No-0
16.Neonatal seizures	-	YES-1, No-0
17.Bacterial sepsis	-	YES-1, No-0
18.Shock	-	YES-1, No-0
19. Meningitis	-	YES-1, No-0
20.MIS-N	-	YES-1, No-0
21. DIC	-	YES-1, No-0
22.Neonatal hepatitis	-	YES-1, No-0
23.Hypoglycemia	-	YES-1, No-0

24. Hypocalcemia	-	YES-1, No-0
25.Thrombocytopenia	-	YES-1, No-0
26.Anemia	-	YES-1, No-0
27.Deranged PT/APTT	-	YES-1, No-0
28.Long line insertion	-	YES-1, No-0
29. TPN	-	YES-1, No-0
30. Non invasive oxygen support	-	YES-1, No-0
31. Mechanical ventilation	-	YES-1, No-0
32.Use of steroids	-	YES-1, No-0
33.Broad spectrum antibiotics	-	YES-1, No-0
34.Ionotropes	-	YES-1, No-0
35.Anti fungal sensitivity	-	Resistant-R, Sensitive-S

IP.no	Name	Gender	Mode of delivery	Maternal sepsis	GDM	Hypothyroid	Gest.HTN	PV Leak more than 18 hrs	UTI in mother	Gestational age	Birth weight	Respiratory distress	Birth asphyxia	Apnoea	NEC	MAS	Neonatal seizures	Bacterial sepsis	shock	Meningitis	MIS-N	DIC	Neonatal hepatitis	Hypoglycemia	Hypocalcemia	Thrombocytopenia	Anemia	DerangedPT/INR	Long line insertion	TPN	Non invasive Oxygen support	mechanical ventilation	Use of steroids	Broad spectrum antibiotics	Ionotropes
1034219	b/o Ashwini sanjeev	0	1	0	0	0	1	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
1034467	b/o Uma manjunath	1	1	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	1	0	1	1	1	0	1	1	1	0	1	1	1
1035093	b/o Devakka bharatesh	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0
1037083	b/o Meenaz twin -1	1	1	0	1		1	0	0	1	1	1	0	1	0	0	0	1		0		0	0	1	1	1	1	0	1	1	0	0	0	1	0
1040330	b/o Pratiksha	1	1	0	0	0	0	1	1	1	1	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	1	0	0	1	1	0
1041263	b/o Deepali	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	1	1	1	1	1	1	1	1	1	0	0	0	1	1
1041642	b/o Ruksar	1	1	0	0	0	0	1	0	1	1	1	0	1	1	0	0	1	1	1	0	1	0	1	1	1	1	1	1	1	0	1	0	1	1
1046736	b/o Shanta patil	1	1	0	0	1	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	1	1	1	0	0	1	0
1049651	b/o Smita	0	1	0	0	0	1	0	0	1	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	1	0
1051240	b/o Sukanya	0	0	0	0	0	0	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	1	0	1	1	0
1051283	b/o vidyashree	1	1	0	0	1	0	0	0	1	1	0	0	1	0	0	0	1	0	0	0	0	0	0	0	1	1	0	1	1	0	0	1	1	0
1051368	b/o Renuka milind twin-1	0	1	0	0	1	0	1	0	1	1	1	0	1	0	0	1	1	1	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1
1051621	b/o Tasbiya	1	0	0	0	0	1	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	1	0	0	1	0
1051622	b/o Zulekha	1	1	0	0	0	1	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	0	0	1	0
1052129	b/o savita	1	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	0
1052567	b/o Akshata twin-1	0	1	0	0		0	0	0	1	1	1	0	0	1	0	0	0		0		0	0	0	0	1	0	0	1	1	1	0	0	1	0
1052567	b/o Akshata twin-2	0	1	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	1	1	1	0	0	1	0
1052675	b/o Lakshmi mallesh twin-1	1	0	0	0	0	1	0	1	1	1	1	0	1	0	0	0	0	1	0	0	0	0	1	1	1	1	0	1	1	1	0	0	1	1
1053401	b/o Pooja nivruti	1	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1	0	0	0	0	1	0	0	1	1	1	1	1	1	1	0	1	1	1
1054175	b/o Deepa. T	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	1	1	0	0	0	1	1	0	0	1	0
1054177	b/o Gufran	1	0	0	1	0	0	0	0	1	1	1	0	1	0	0	0	1	0	1	0	0	0	1	1	1	1	0	0	1	1	0	0	1	1
1054181	b/o Deepa basavalingayya	0	0	0	0	0	0	0	0	0	1	1	0	0	0	1	0	1	0	0	0	0	0	0	1	1	0	0	1	1	1	0	1	1	0
1054925	b/o Roshini. P	1	1	0	1	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	1	1	1	0	0	1	0
1055136	b/o Lakshmi narayan	1	1	0	1	0	0	0	1	1	1	1	0	1	0	0	1	0	0	0	0	0	0	1	1	1	0	0	1	1	1	1	0	1	1
1055496	b/o Veena .k	1	1	0	0	0	0	0	0	0	0	1	0	0	0	1	1	1	1	0	0	1	0	1	1	1	1	1	1	1	1	1	0	1	1
1055837	b/o Radha	1	0	1	0	0	1	0	0	1	1	1	1	1	1	0	1	1	1	1	0	1	0	1	1	1	1	1	1	1	1	1	0	1	1
1056312	b/o Mahadevi twin-1	0	1	0	0	0	0	0	1	1	1	1	0	1	0	0	1	0	0	1	1	0	0	1	1	1	0	0	1	1	1	0	0	1	1
1056458	b/0 Ganga twin-2	1	1	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	1	0	0	1	0
1056599	b/0 Manisha	1	1	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	1	0	1	0
1056620	b/o Shilpa. W	0	1	0	0	0	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	0	0	0	1	0
1057060	b/o Sushma	1	1	0	0	0	1	0	0	1	1	1	0	1	1	0	1	1	1	0	0	1	0	1	1	1	1	1	1	1	1	1	0	1	1
1057706	b/o Veena..M	1	0	0	0	0	0	1	0	0	0	1	0	0	0	1	1	1	1	0	1	1	0	1	1	1	1	1	0	1	1	1	1	1	1
1057874	b/o Rajashree	0	1	1	0	0	0	0	0	1	1	1	1	1	0	0	1	1	1	0	1	1	0	1	1	1	1	1	1	1	1	1	0	1	1
1058441	b/o sangeeta	1	0	0	1	0	0	0	0	1	1	1	0	1	1	0	1	0	0	1	0	0	0	0	1	1	1	0	1	1	1	0	0	1	0
1058995	b/o Kaveri twin-2	0	1	0	0	0	0	0	0	1	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	1	0	0	1	0
1059034	b/o shobha	1	1	0	0	0	0	0	1	0	1	1	0	0	0	0	1	1	0	1	0	0	0	1	1	1	0	0	1	0	0	0	0	1	0
1060565	b/o shilpa twin-1	0	0	0	0	0	0	0	0	1	1	1	0	1	1	0	0	1	1	0	1	1	0	1	1	1	0	1	1	1	1	1	0	1	0
1060566	b/o shilpa twin-2	0	0	0	0	0	0	0	0	1	1	1	0	1	1	0	0	0	0	1	0	1	0	1	1	1	0	1	1	1	1	0	1	1	1

IP.no	Name	Gender	Mode of delivery	Maternal sepsis	GDM	Hypothyroid	Gest.HTN	PV Leak more than 18 hrs	UTI in mother	Gestational age	Birth weight	Respiratory distress	Birth asphyxia	Apnoea	NEC	MAS	Neonatal seizures	Bacterial sepsis	shock	Meningitis	MIS-N	DIC	Neonatal hepatitis	Hypoglycemia	Hypocalcemia	Thrombocytopenia	Anemia	DerangedPT/INR	Long line insertion	TPN	Non invasive Oxygen support	mechanical ventilation	Use of steroids	Broad spectrum antibiotics	Ionotropes
1062071	b/o Saraswati. G	0	0	0	0	0	0	0	1	0	1	1	0	0	0	1	0	1	0	0	1	0	0	0	0	0	0	0	0	1	1	1	0	0	1	1
1062340	b/o Shilpa. W twin-1	0	1	0	0	0	0	0	0	1	1	1	0	1	0	0	1	1	1	0	0	1	0	0	0	1	1	1	1	1	1	1	0	1	1
1063308	b/o Nirmala . M	1	0	0	0	0	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	0	0	1	1	1	1	0	1	1	0	0	0	1	0
1063695	b/o Rashi	1	1	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	0	0	1	0
1063868	b/o Sheetal. G	1	1	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	1	1	1	1	0	1	0
1063988	b/o manjula	1	0	0	1	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	0	1	1	0
1064795	b/o preetika	0	1	0	0	0	1	0	0	1	1	0	0	1	1	0	0	1	0	0	1	0	0	0	0	1	1	0	1	1	1	0	0	1	0
1064997	b/o Goura. B triplet-3	0	1	0	0	0	0	0	0	1	1	1	0	1	0	0	0	0	0	0	1	1	0	1	1	1	1	1	1	1	1	0	0	1	0
1065030	b/o Rukmini. H	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	0	1	1	0	0	1	0
1065523	b/o shaila triplet -3	1	1	0	0	0	0	0	1	1	1	1	0	1	1	0	0	0	1	0	1	0	0	1	1	1	0	0	1	1	1	0	0	1	0
1065726	b/o laxmi umesh	1	0	0	0	0	0	0	0	0	1	1	1	0	1	0	1	1	1	0	0	1	0	1	1	1	0	1	1	1	1	0	0	1	1
1074310	b/o Ratna. Y twin-1	1	0	0	0	0	0	0	0	1	1	1	0	1	1	0	1	0	1	0	0	1	0	1	1	1	1	1	1	1	1	1	0	1	1
1074324	b/o Shobha. K	1	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	1	0	0	0	0	0	0	1	1	1	0	0	1	1	0	0	1	0
1074340	b/o Sarika. K	0	1	0	0	0	1	0	0	1	1	1	0	1	M	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1	1	0	1	1	1
1074653	b/o Sujata	1	1	0	0	0	0	0	0	1	1	1	0	1	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	1	1	0	0	1	0
1076213	b/o Pushpa twin-2	1	1	0	0	0	1	0	0	1	1	0	0	1	1	0	0	0	1	0	1	1	0	0	1	1	0	1	1	1	1	0	1	1	1
1089067	b/o Deepa. G	0	1	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1	1	0	0	1	0
1091229	b/o Renuka. P	1	0	0	0	0	0	0	0	1	1	1	0	1	0	0	0	0	1	0	1	0	0	0	1	1	0	0	1	1	1	0	1	1	1
1091236	b/o Rjeswari. K	1	1	0	0	0	1	0	0	1	1	0	1	1	1	0	0	0	1	0	1	1	0	0	1	1	1	1	1	1	1	1	0	1	1
1091246	b/o Dinar. S	0	0	1	0	0	0	0	0	1	1	1	0	1	0	0	1	0	0	0	0	0	0	1	1	1	1	0	1	1	1	0	0	1	0
1092346	b/o Pooja. M twin-2	0	1	0	0	0	0	0	1	1	1	1	0	1	1	0	0	1	1	0	1	1	0	0	1	1	1	1	1	1	1	1	0	1	1
1092963	b/o Zeba. M	1	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	1	1	0
1098427	b/o Mayuri. T	0	1	0	0	0	0	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	0	1	1	1	0	1	1	0
1111691	b/o Radhika .H twin-1	0	1	0	0	0	1	0	0	1	1	1	1	1	1	0	0	1	1	0	0	1	0	1	1	1	1	1	1	1	1	1	0	1	1
1111696	b/o Renuka. A	0	1	0	0	1	0	0	0	1	1	1	0	1	0	0	0	0	0	0	0	1	0	0	1	1	0	1	0	1	1	0	0	1	0
1112921	b/o Vijayalakshmi. M	0	1	0	0	0	0	0	0	1	1	1	0	1	1	0	0	0	1	0	0	0	0	0	1	1	1	0	1	1	1	0	1	1	1
1114686	b/o Rukaiyya.T	1	1	0	0	0	1	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	1	0	0	0	1	0
1117513	b/o Suprita. H	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	0	1	1	0
1119416	b/o Tasmiya. H	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0
1119959	b/o Mahemuda. A	0	0	0	0	1	1	0	0	1	1	1	0	1	0	0	0	1	1	0	0	1	0	1	1	1	1	1	1	1	1	0	1	1	1
1125195	b/o Sneha rani	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	0	0	1	0
	b/o Mahadevi twin-2	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	1	0	0	0	1	0	0	1	1	0

S.no	IP.no	Name	Day 1 Blood C&S	Day 3 Blood C&S	Blood c & s after 72 hrs	Day 21 Blood c&s	Long line tip culture	ET tip culture	UAC/UVC tip culture	Hb before Fungalsepsis	Hb after Fungal sepsis	Plt before Fungal sepsis	Plt after Fungal sepsis	TWBC before Fungal sepsis	TWBC after Fungal sepsis	N% before fungal sepsis	N% after Fungal sepsis	L% after Fungal sepsis	L% after Fungal sepsis	Hscrp before Fungal sepsis	Hscrp after Fungal sepsis	CSF c&s	CSF Routine	Urine c&s	Fungal Isolate	Outcome
3	1034219	b/o Ashwini sanjeev	NOGC	C.glabrata	NOGC	0	0	0	0	15.6	15.6	2,06,000	52,000	12,700	4000	26	86	60	11	0.4	47.3	NOGC	Normal	NOGC	C.glabrata	Discharged
1	1034467	b/o Uma manjunath	NOGC	C. albicans	CONS	0	NOGC	0	0	20.6	20.9	82,000	8,000	25,200	5,800	44	64	48	25	16.5	25	NOGC	Deranged	NOGC	C. albicans	Discharged
2	1035093	b/o Devakka bharatesh	NOGC	C.glabrata	NOGC	0	0	0	0	15.9	18.9	2,22,000	1,50,000	31,000	10,300	30	71	58	15	0.2	4.6	NOGC	Normal	NOGC	C.glabrata	Discharged
4	1037083	b/o Meenaz twin -1	C.glabrata	C. albicans	NOGC	0	0	0	0	14.6	14.1	3,76,000	1,55,000	17,500	6,200	65	71	28	20	0.1	1.3	NOGC	Normal	NOGC	C. albicans	Discharged
5	1040330	b/o Pratiksha	CONS	C.glabrata	NOGC	0	0	0	0	16.4	15.8	3,00,00	1,32,000	16,000	3,200	68	54	26	32	0.4	34	NOGC	Normal	NOGC	C.glabrata	Discharged
6	1041263	b/o Deepali	NOGC	C.glabrata	0	0	0	0	0	20	21.6	1,13,000	1,38,000	10,000	9,400	74	60	21	35	0.2	8.4	NOGC	Normal	NOGC	C.glabrata	Discharged
7	1041642	b/o Ruksar	NOGC	C.glabrata	0	0	0	0	0	14.6	13.5	2,00,000	2,40,000	24,600	16,900	67	55	23	33	0.1	5	NOGC	Normal	NOGC	C.glabrata	Discharged
8	1046736	b/o Shanta patil	C. krusei	C.tropicalis	NOGC	0	NOGC	0	0	17.2	19.4	2,36,000	75,000	7,300	6,600	37	70	52	22	0.4	10.2	NOGC	Normal	NOGC	C. tropicalis	Discharged
9	1049651	b/o Smita	NOGC	NOGC	C.glabrata	NOGC	0	0	0	19.7	16	2,60,000	22,000	21,500	15,200	74	32	22	58	0.4	7.6	NOGC	Normal	NOGC	C.glabrata	Disharged
10	1051240	b/o Sukanya	NOGC	C.glabrata	Klebsiella	NOGC	NOGC	0	0	20.1	15.7	82,000	48,000	5,500	3,900	69	22	28	65	0.2	1.4	NOGC	Normal	NOGC	C.glabrata	Discharged
13	1051283	b/o vidyashree	NOGC	C.glabrata	NOGC	0	C.glabrata	0	0	15.1	18.7	1,73,000	95,000	12,700	3,900	67	44	19	46	0.2	16.4	NOGC	Normal	NOGC	C.glabrata	Discharged
17	1051368	b/o Renuka milind twin-1	NOGC	C.glabrata	0	NOGC	Candida	0	0	18.4	16.5	2,00,000	48,000	16,000	8,600	64	72	26	28	0.4	5	NOGC	Normal	NOGC	C.glabrata	Discharged
12	1051621	b/o Tasbiya	NOGC	C. albicans	CONS	NOGC	Candida	NOGC	0	15	14.7	2,00,000	14,000	7,400	5,000	56	52	37	34	0.5	0.9	NOGC	Normal	NOGC	C. albicans	Discharged
11	1051622	b/o Zulekha	NOGC	C. albicans	NOGC	0	0	0	0	17.2	16	2,82,000	1,12,000	8,200	4,200	49	53	46	32	0.3	9	NOGC	Normal	NOGC	C. albicans	Discharged
14	1052129	b/o savita	NOGC	NOGC	NOGC	0	NOGC	0	0	19.8	14.7	2,02,000	1,11,000	8,400	8,900	67	45	24	43	0.6	11.3	NOGC	Normal	NOGC	C. parapsilosis	Discharged
15	1052567	b/o Akshata twin-1	NOGC	C.glabrata	0	NOGC	NOGC	0	0	16.6	15.4	1,18,000	22,000	12,800	4,600	46	38	34	62	0.6	0.9	NOGC	Normal	NOGC	C.glabrata	Discharged
66	1052567	b/o Akshata twin-2	C.glabrata	C. albicans	0	0	0	0	0	12.8	12.5	3,11,000	3,18,000	22,000	13,900	55	71	38	23	0.6	1.4	NOGC	Normal	NOGC	C. albicans	Discharged
16	1052675	b/o Lakshmi mallesh twin-1	NOGC	C. krusei	NOGC	0	0	0	0	19.2	18.7	2,80,000	1,55,000	12,000	7,000	78	60	14	32	1.3	6.6	NOGC	Normal	NOGC	C. krusei	Discharged
21	1053401	b/o Pooja nivruti	NOGC	C.glabrata	NOGC	0	NOGC	0	0	17.8	17.7	2,37,000	26,000	11,500	13,700	64	33	26	57	0.4	14	NOGC	Normal	NOGC	C.glabrata	Discharged
70	1054175	b/o Deepa. T	C.glabrata	C. albicans	NOGC	0	0	0	0	15.1	13.9	4,16,000	89,000	6,000	3,800	49	57	44	42	0.6	4	NOGC	Normal	NOGC	C. albicans	Discharged
20	1054177	b/o Gufran	NOGC	C.glabrata	0	0	NOGC	0	0	12.1	12.7	4,65,000	2,41,000	9,700	5,000	60	69	36	24	0.6	6	NOGC	Normal	NOGC	C.glabrata	Discharged
19	1054181	b/o Deepa basavalingayya	Klebsiella	C.glabrata	0	0	C.glabrata	0	0	17.2	15.7	1,26,000	4,000	11,800	9,700	37	22	57	74	0.1	25	NOGC	Normal	NOGC	C.glabrata	Discharged
65	1054925	b/o Roshini. P	C.glabrata	C. albicans	NOGC	0	0	0	0	18.4	16	1,95,000	1,10,000	16,300	13,000	68	65	21	23	0.3	12	NOGC	Normal	NOGC	C. albicans	Discharged
23	1055136	b/o Lakshmi narayan	NOGC	C.glabrata	CONS	0	0	0	0	20.8	18.5	2,62,000	1,09,000	17,700	12,300	66	68	23	28	0.4	12.2	NOGC	Normal	NOGC	C.glabrata	Discharged
18	1055496	b/o Veena .k	NOGC	C.albicans	NOGC	0	0	0	0	17.5	19.7	1,18,000	75,000	10,800	7,400	51	60	38	36	0.2	1.1	NOGC	Normal	NOGC	C. albicans	Discharged
22	1055837	b/o Radha	C. albicans	C.glabrata	NOGC	0	NOGC	0	0	16.9	19.6	2,29,000	1,23,000	13,100	2,200	41	47	50	47	0.6	5	NOGC	Normal	NOGC	C.glabrata	Discharged
24	1056312	b/o Mahadevi twin-1	NOGC	C. tropicalis	NOGC	0	NOGC	0	0	16.9	18.1	1,77,000	15,000	10,900	9,500	38	90	54	6	1.9	46	NOGC	Normal	NOGC	C. tropicalis	Discharged

S.no	IP.no	Name	Day 1 Blood C&S	Day 3 Blood C&S	Blood c & s after 72 hrs	Day 21 Blood c&s	Long line tip culture	ET tip culture	UAC/UVC tip culture	Hb before Fungalsepsis	Hb after Fungal sepsis	Plt before Fungal sepsis	Plt after Fungal sepsis	TWBC before Fungal sepsis	TWBC after Fungal sepsis	N% before fungal sepsis	N% after Fungal sepsis	L% after Fungal sepsis	L% after Fungal sepsis	Hscrp before Fungal sepsis	Hscrp after Fungal sepsis	CSF c&s	CSF Routine	Urine c&s	Fungal Isolate	Outcome
27	1056458	b/0 Ganga twin-2	NOGC	C. parapsilosis	NOGC	0	NOGC	0	0	13.6	14.1	1,99,000	8,000	31,000	15,400	46	48	40	33	0.6	14	NOGC	Normal	NOGC	C. parapsilosis	Discharged
26	1056599	b/0 Manisha	NOGC	C. albicans	Staphylococcus	NOGC	0	0	0	20.6	20.9	82,000	8,000	25,200	5,800	44	64	48	25	0.2	18.6	NOGC	Normal	NOGC	C. albicans	Discharged
61	1056620	b/o Shilpa. W	C. tropicalis	C.glabrata	0	NOGC	NOGC	NOGC	0	19.1	16.9	1,58,000	22,000	26,400	4,000	30	76	40	30	0.8	6	NOGC	Normal	NOGC	C.glabrata	Discharged
28	1057060	b/o Sushma	NOGC	C.glabrata	0	NOGC	NOGC	0	0	16.3	11.5	1,73,000	80,000	5,600	5,500	42	87	48	8	12	100	NOGC	Normal	NOGC	C.glabrata	Discharged
30	1057706	b/o Veena..M	NOGC	C.glabrata	NOGC	NOGC	NOGC	0	0	16.8	17	2,73,000	22,000	12,300	2,600	33	51	56	42	0.6	17.5	NOGC	Normal	NOGC	C.glabrata	Discharged
29	1057874	b/o Rajashree	NOGC	C. albicans	0	NOGC	0	0	0	16.6	16.9	1,82,000	14,000	15,400	8,300	46	46	48	45	0.2	5	NOGC	Normal	NOGC	C. albicans	Discharged
33	1058441	b/o sangeeta	NOGC	C.glabrata	0	NOGC																NOGC	Deranged	NOGC	C.glabrata	Discharged
35	1058995	b/o Kaveri twin-2	NOGC	NOGC	C.glabrata	NOGC	NOGC	0	0	20.5	20.1	1,89,000	41,000	8,200	8,300	58	79	32	11	0.9	52.2	NOGC	Normal	NOGC	C.glabrata	Discharged
34	1059034	b/o shobha	NOGC	NOGC	C. parapsilosis	NOGC	NOGC	0	0	16.9	15.7	2,19,000	11,000	8,600	3,900	37	50	56	45	0.2	7.9	NOGC	Normal	NOGC	C. parapsilosis	Discharged
31	1060565	b/o shilpa twin-1	NOGC	NOGC	C.glabrata	NOGC	NOGC	0	0	13.9	12.6	2,43,000	82,000	14,100	8,700	29	51	58	37	0.6	8	NOGC	Normal	NOGC	C.glabrata	Discharged
32	1060566	b/o shilpa twin-2	NOGC	NOGC	C.glabrata	NOGC	NOGC	0	0	19.7	20.4	2,06,000	73,000	7,300	2,200	42	62	51	27	0.4	17.7	NOGC	Normal	NOGC	C.glabrata	Discharged
63	1062071	b/o Saraswati. G	C. tropicalis	C.glabrata	0	0	Candida	0	0	18	17.2	2,52,000	1,33,000	12,700	9,300	60	75	29	14	0.7	50.9	NOGC	Normal	NOGC	C.glabrata	Discharged
56	1062340	b/o Shilpa. W twin-1	NOGC	C.glabrata	0	NOGC	0	0	0	18.1	14.4	2,37,000	9000	5,500	2,600	46	40	44	47	0.4	7	NOGC	Normal	NOGC	C.glabrata	Discharged
64	1063308	b/o Nirmala . M	C.glabrata	C. tropicalis	NOGC	0	NOGC	0	0	21.8	21	2,07,000	32,000	4,500	6,400	7	82	78	15	0.2	8	NOGC	Normal	NOGC	C. tropicalis	Discharged
39	1063695	b/o Rashi	NOGC	Klebsiella	C.glabrata	NOGC	NOGC	0	0	16.4	14	3,00,000	10,000	21,800	11,500	71	68	25	24	0.1	47.4	enterobacter	Deranged	NOGC	C.glabrata	Discharged
67	1063868	b/o Sheetal. G	C. parapsilosis	C.glabrata	0	NOGC	0	0	0	18.3	14.4	2,40,000	1,63,000	23,200	6,800	76	90	18	4	0.1	15.7	NOGC	Normal	NOGC	C.glabrata	Discharged
36	1063988	b/o manjula	NOGC	C. albicans	NOGC	0	0	0	Klebsiella	14,8	10.4	1,75,000	69,000	6,700	5,200	64	69	31	26	0.4	19.8	NOGC	Normal	NOGC	C. albicans	Discharged
40	1064795	b/o preetika	NOGC	C.albicans	NOGC	0	NOGC	0	0	16.2	13.7	1,76,000	43,000	9,200	8,800	59	63	32	23	0.4	8.3	NOGC	Normal	NOGC	C.glabrata	Discharged
68	1064997	b/o Goura. B triplet-3	C.glabrata	C.glabrata	0	NOGC	NOGC	0	0	17.6	14	2,10,000	10,000	36,800	6,800	65	14	28	75	78	14	NOGC	Normal	NOGC	C.glabrata	Discharged
62	1065030	b/o Rukmini. H	C. albicans	C. albicans	0	0	NOGC	0	0	18.4	12.9	1,22,000	26,000	23,200	15,500	46	35	12	53	0.8	4	NOGC	Normal	NOGC	C. albicans	Discharged
38	1065523	b/o shaila triplet -3	NOGC	C. tropicalis	Klebsiella	0	NOGC	0	0	15.6	15	2,15,000	98,000	25,300	1,900	72	59	20	37	0.4	7	NOGC	Normal	NOGC	C. tropicalis	Discharged
37	1065726	b/o laxmi umesh	NOGC	NOGC	C. tropicalis	NOGC	Acinetobacter	0	0	17.2	18.9	2,01,000	44,000	17,700	13,000	73	89	23	9	0.4	48	NOGC	Normal	NOGC	C. tropicalis	Discharged
54	1074310	b/o Ratna. Y twin-1	NOGC	NOGC	0	NOGC	Enterococcus	0	0	15.9	15.5	3,00,000	55,000	12,700	9,100	26	48	64	37	0.4	10.8	NOGC	Normal	NOGC	C. krusei	Discharged
57	1074324	b/o Shobha. K	NOGC	NOGC	C. albicans	NOGC	MRSA	0	0	18.6	13.2	1,45,000	16,000	10,200	12,000	28	34	64	58	0.5	8	NOGC	Normal	NOGC	C. albicans	Discharged
53	1074340	b/o Sarika. K	NOGC	C.glabrata	C.glabrata	NOGC	NOGC	0	0	18.2	14.7	1,95,000	38,000	20,200	9,100	81	69	11	22	0.2	14	NOGC	Normal	NOGC	C.glabrata	Discharged
41	1074653	b/o Sujata	NOGC	C. krusei	CONS	C krusei	C. krusei	0	0	20.6	19.9	2,26,000	28,000	6,000	3,400	36	46	57	32	0.1	45.2	NOGC	Normal	NOGC	C. krusei	Discharged
42	1076213	b/o Pushpa twin-2	NOGC	C.glabrata	0	0	NOGC	0	0	18.7	17	2,14,000	72,000	11,900	10,700	70	82	22	11	0.6	27.3	NOGC	Normal	NOGC	C.glabrata	Death

S.no	IP.no	Name	Day 1 Blood C&S	Day 3 Blood C&S	Blood c & s after 72 hrs	Day 21 Blood c&s	Long line tip culture	ET tip culture	UAC/UVC tip culture	Hb before Fungalsepsis	Hb after Fungal sepsis	Plt before Fungal sepsis	Plt after Fungal sepsis	TWBC before Fungal sepsis	TWBC after Fungal sepsis	N% before fungal sepsis	N% after Fungal sepsis	L% after Fungal sepsis	L% after Fungal sepsis	Hscrp before Fungal sepsis	Hscrp after Fungal sepsis	CSF c&s	CSF Routine	Urine c&s	Fungal Isolate	Outcome
47	1089067	b/o Deepa. G	NOGC	C. albicans	Klebsiella	NOGC	NOGC	0	0	19.9	19.6	2,39,000	27,000	12,700	11,500	39	27	52	62	0.6	6	NOGC	Normal	NOGC	C. albicans	Discharged
58	1091229	b/o Renuka. P	C. parapsilosis	C. parapsilosis	0	0	NOGC	NOGC	0	18.4	17.6	1,70,000	20,000	16,000	8,100	64	55	22	37	0.2	7	NOGC	Normal	NOGC	C. parapsilosis	Death
60	1091236	b/o Rjeswari. K	C.glabrata	C. albicans	Klebsiella	0	0	Stapyloccocus.aureus	0	14.6	13.2	71,000	26,000	6,200	4200	74	62	20	26	10	14	NOGC	Normal	NOGC	C. albicans	Death
55	1091246	b/o Dinar. S	NOGC	Peudomonas	C. parapsilosis	0	Candida	Acinetobacter	0	14.3	14.9	2,01,000	37,000	4,300	15,300	23	71	72	20	0.2	84.3	NOGC	Normal	NOGC	C. parapsilosis	Discharged
59	1092346	b/o Pooja. M twin-2	C.glabrata	C.glabrata	C.glabrata, CONS	0	NOGC	0	0	20.5	13.8	1,62,000	23,000	9,700	4,000	28	42	69	54	0.4	72	NOGC	Normal	NOGC	C.glabrata	Discharged
48	1092963	b/o Zeba. M	NOGC	C.glabrata	C.glabrata	0	NOGC	C.glabrata	0	16.5	10.9	3,03,000	1,40,000	11,800	9,000	50	55	44	33	0.5	46.1	NOGC	Normal	NOGC	C.glabrata	Death
46	1098427	b/o Mayuri. T	NOGC	C. parapsilosis	NOGC		Staphylococcus	0	0	14.2	11.4	2,70,000	35,000	8,900	5,600	43	33	49	55	0.4	9	NOGC	Normal	NOGC	C. parapsilosis	Death
44	1111691	b/o Radhika .H twin-1	NOGC	Klebsiella	C. albicans	0	Staphylococcus	NOGC	0	18.7	15.5	1,94,000	13,000	19,700	7,800	82	65	15	24	0.2	1	NOGC	Deranged	NOGC	C. albicans	Death
45	1111696	b/o Renuka. A	NOGC	C.glabrata	C.glabrata	0	NOGC	NOGC	0	19.4	16.3	2,08,000	63,000	10,200	3,400	50	73	43	20	15	146.7	NOGC	Normal	NOGC	C.glabrata	Death
52	1112921	b/o Vijayalakshmi. M	NOGC	C. albicans	0	0	NOGC	NOGC	0	21.6	18.5	2,32,000	11,000	6,900	3,500	36	55	58	33	0.2	15	NOGC	Normal	NOGC	C. albicans	Death
43	1114686	b/o Rukaiyya.T	NOGC	C.glabrata	NOGC	0	0	0	0	16.2	15	2,86,000	78,000	10,200	4,200	53	62	42	46	0.2	24	NOGC	Normal	NOGC	C.glabrata	Discharged
50	1117513	b/o Suprita. H	NOGC	C.glabrata	0	0	NOGC	0	0	16.3	18.2	2,40,000	97,000	36,000	8,500	50	74	40	21	0.4	7	NOGC	Normal	NOGC	C.glabrata	Discharged
51	1119416	b/o Tasmiya. H	NOGC	C.glabrata	Streptococcus	NOGC	NOGC	0	0	19	17.1	2,51,000	69,000	6,500	4,800	44	93	45	4	15	82.4	NOGC	Normal	NOGC	C.glabrata	Death
49	1119959	b/o Mahemuda. A	NOGC	C. albicans	0	NOGC	Candida	Citrobacter	0	15.9	9.4	2,36,000	22,000	26,300	6,300	38	70	55	26	0.2	15.4	NOGC	Normal	NOGC	C. albicans	Discharged
69	1125195	b/o Sneha rani	C krusei	C.glabrata	Klebsiella	Klebsiella	NOGC	Klebsiella	0	17.5	22.2	2,40,000	46,000	3,500	2,700	47	73	40	17	0.1	222.6	NOGC	Normal	NOGC	C.glabrata	Death
25		b/o Mahadevi twin-2	NOGC	NOGC	C.glabrata,Enterococci	NOGC	Candida	C.glabrata	0	15.8	12.1	1,12,000	43,000	4,000	3,200	53	34	38	58	0.2	9.4	NOGC	Normal	NOGC	C.glabrata	Discarged

S.no	Amphotericin-B	Fluconazole	Voriconazole	Caspofungin	Fungal isolate
1	R	R	R	R	C.glabrata
2	R	R	R	S	C.glabrata
3	R	R	R	S	C.glabrata
4	R	R	R	S	C.glabrata
5	R	S	R	S	C.glabrata
6	R	R	R	S	C.glabrata
7	S	S	R	S	C. tropicalis
8	S	S	S	S	C. krusei
9	R	R	R	S	C.glabrata
10	R	S	R	S	C. albicans
11	R	R	S	S	C. albicans
12	R	S	S	S	C. albicans
13	R	R	R	R	C. albicans
14	R	R	R	S	C.glabrata
15	R	R	R	R	C. albicans
16	R	R	R	R	C. albicans
17	R	R	R	R	C. albicans
18	S	S	S	S	C.glabrata

S.no	Amphotericin-B	Fluconazole	Voriconazole	Caspofungin	Fungal isolate
19	R	R	R	S	C.glabrata
20	R	R	R	S	C.glabrata
21	S	S	S	S	C. albicans
22	S	S	S	S	C.glabrata
23	R	R	R	S	C.glabrata
24	R	R	R	S	C.glabrata
25	R	S	R	S	C. parapsilosis
26	R	S	R	S	C. parapsilosis
27	R	S	R	S	C.glabrata
28	R	S	R	S	C.glabrata
29	R	S	S	S	C. albicans
30	R	R	R	R	C.glabrata
31	R	R	R	S	C.glabrata
32	R	S	S	S	C. tropicalis
33	R	S	R	R	C. albicans
34	R	R	R	S	C.glabrata
35	R	S	R	S	C. tropicalis
36	R	R	R	S	C.glabrata

S.no	Amphotericin-B	Fluconazole	Voriconazole	Caspofungin	Fungal isolate
37	R	R	R	R	C.glabrata
38	R	R	R	S	C.glabrata
39	R	R	R	S	C.glabrata
40	R	R	R	R	C.glabrata
41	S	S	S	S	C. albicans
42	R	S	R	S	C.glabrata
43	R	R	R	R	C.glabrata
44	R	R	R	R	C. krusei
45	R	R	R	S	C. parapsilosis
46	R	S	R	S	C. tropicalis
47	R	R	R	S	C.glabrata
48	R	R	R	S	C.glabrata
49	R	R	R	R	C. parapsilosis
50	R	S	S	S	C. albicans
51	R	S	R	S	C. parapsilosis
52	R	R	R	S	C.glabrata
53	R	R	R	S	C.glabrata
54	R	S	R	S	C. tropicalis

S.no	Amphotericin-B	Fluconazole	Voriconazole	Caspofungin	Fungal isolate
55	R	S	S	S	C. albicans
56	R	S	S	S	C. albicans
57	R	R	R	S	C.glabrata
58	R	R	R	S	C. albicans
59	R	S	R	S	C.glabrata
60	R	S	S	S	C. parapsilosis
61	R	R	R	S	C.glabrata
62	R	S	S	S	C. krusei
63	R	S	R	S	C. albicans
64	R	R	R	S	C. albicans
65	R	R	R	S	C.glabrata
66	R	R	R	S	C.glabrata
67	R	R	R	S	C.glabrata
68	R	R	R	S	C.glabrata
69	R	R	R	S	C.glabrata
70	R	S	R	S	C. albicans