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Review Article

Enlightenment on various aspects of neonatal septicemia: An expansive overview

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ABSTRACT

The neonatal intensive care units (NICUs) today face one common problem of tackling sepsis and neonatologists remain constantly baffled by the varying patterns of microbial flora and their sensitivity patterns. Neonatal septicemia remains one of the significant causes of mortality and morbidity despite considerable progress in hygiene, introduction of new and potent antimicrobial agents and advanced measures for diagnosis and treatment. Neonatal sepsis comprises two distinct illnesses based on onset. Early onset into which sepsis occurs in the first 7 days of life, is usually a fulminant and multisystemic infection; while late-onset sepsis is usually more insidious but may have an acute onset. Over the last two decades most of the organisms have developed higher drug resistance and management of the patients is becoming a major problem. Methicillin resistant Staphylococcus aureus (MRSA) was first described in 1961, reported after one year of introduction of methicillin and has risen as most common nosocomial pathogens. MRSA is of serious concern not because of its sole resistance to methicillin, but also due to resistance to many other antimicrobials that are indicated on a regular basis in hospitals. Current therapeutic options for MRSA are inadequate but few expensive drugs like vancomycin, linezolid, teicoplanin, daptomycin and streptogramins may be administered. In this article, we have reviewed numerous aspects of neonatal septicemia and its management.

Key Words: Neonatal Septicemia, MRSA, Staphylococcus Aureus.

INTRODUCTION

Sepsis neonatorum is the term refers to any systemic bacterial infection documented by a positive blood culture in the first month of life [1]. Neonatal septicemia remains one of the important causes of mortality and morbidity despite considerable progress in hygiene, introduction of new and potent antimicrobial agents and advanced measures for diagnosis and treatment [2]. Up to 10% of infants have infections in the first month of life [3] which are responsible for 30- 50% of total neonatal deaths in developing countries [4]. Classification of neonatal sepsis includes two relatively distinct illnesses based on the postnatal age at onset. (1) Early onset- sepsis occurs in the first 7 days of life, is usually a fulminant and multi-systemic infection; and has a higher case fatality rate. Whereas (2) Late-onset sepsis is usually more insidious but may have an acute onset [1]. Bacterial pathogens of neonatal septicemia may differ from one country to another and within a country from one hospital or region to another [5]. These organisms may even differ at various times within the same place [6, 7]. In developed countries Group B streptococcus (GBS), E. coli and Listeria monocytogenes are the most common origins of neonatal sepsis, although in developing countries, these bacteria are replaced by gram-negative bacilli, Coagulase negative staphylococcus (CONS) and others [8]. Over the last two decades most of the organisms have developed higher drug resistance and management of the patients is becoming a major problem [9]. Identification of the etiology is significant since it can induce a improvement in management policy [5]. For effective management of neonatal septicemia with suitable antibiotics that would lessen the risk of severe morbidity and mortality besides decreasing the emergence of multi-drug resistant organisms by rational antibiotic use, study of bacteriological profile and their antibiotic sensitivity pattern plays a vital role [1, 10]. Prior to the antibiotic era, the mortality from septicemia was 90%. But with presently available antimicrobial agents, it may be treated successfully and mortality from septicemia in neonates has declined to 24.58% [11, 12], However, with presently available antimicrobial

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agents, neonatal septicemia may be treated successfully.

Methicillin-Resistant Staphylococcus Aureus (MRSA): Staphylococcus aureus (S.aureus) is one of the most important pathogens involving humans, has acquired resistance to various antibiotics and is a main cause of hospital and community acquired infections, manifesting from minor skin diseases to life-threatening infections [13,14]. Methicillin resistant Staphylococcus aureus (MRSA) was first described in 1961, reported after one year of introduction of methicillin and has arisen as foremost nosocomial pathogens especially in the last two decades [15]. MRSA is of serious concern not due its sole resistance to methicillin, but also due to resistance to many other antimicrobials that are used on a regular basis in hospitals. Current therapeutic options for MRSA are limited few expensive drugs like vancomycin, linezolid, teicoplanin, daptomycin and streptogramins. Another alarming sign is that origin of resistance to Vancomycin, however, at a low level has been assessed [16]. Glycopeptides and linezolid continue to remain the mainstay of treatment for MRSA.

EPIDEMIOLOGY

The growing incidence of Sabacute Bacterial Endocarditis (SAB) is primarily driven by an increasing number of health care related infections [17, 18]. In the period 1980 to 1989 the incidence of nosocomial SAB increased by 283% in non-teaching hospitals and by 176% in large teaching hospitals in the United States (US) [19]. Similarly, in a study by Benfield et al. the incidence of SAB in Denmark increased 1.7-fold during a 20-year period from 1981 to 2000 [20]. Although specific risk factors for SAB vary with the development and structure of the health care system, its diagnosis is linked to such risk factors as intravascular devices, advanced age, diabetes, immunosuppressive treatment, invasive procedures and the emergence of human immunodeficiency virus (HIV) [21,17,22–24]. A growing number of patients are acquiring healthcare-associated SAB outside of the hospital [25]. For example, S. aureus is the second most commonly encountered microorganism among outpatients in the US [26].

Hemodialysis-recipients are at particularly high risk for non-nosocomial health care associated S. aureus infections [25,27, 28]. The problem of non-nosocomial health care associated S. aureus infection is still primarily US phenomenon, and reflects the growing emphasis on outpatient services in that environment [25]. However, as healthcare delivery in other parts of the world increasingly shifts towards the community, this problem is likely to spread. Another clinical problem of current interest is the continuing growing prevalence of MRSA in many parts of the world. In the US, more than 40% of S. aureus BSIs are caused by MRSA [26]. The prevalence of MRSA in Europe ranges widely. MRSA prevalence rates in the Mediterranean and United Kingdom (UK) exceed 30%, while rates in the Netherlands and Scandinavian countries are ~ 2% [29]. In these low incidence countries the emergence of livestock-associated MRSA have raised some concerns as it might have the potential to increase the incidence of MRSA infections also in humans. However, the importance of livestock-associated MRSA is so far limited due to a relative small number of human clinical cases. Furthermore, the far majority of livestock-associated cases has been in humans in close contact with animals and not in the general population [30–32]. Interestingly some countries, such as France, UK and Ireland, have been able to reverse the rising trend and lower the number of MRSA due to a dedicated effort to control the number of MRSA infections in inpatients [29]. In contrast to this positive development, it has become evident that S. aureus has emerged as an important cause of sepsis in the developing countries with increasing resistance as a major issue. In certain developing countries MRSA now accounts for more than 20% of the cases and is associated with mortality rates double that reported from developed countries. Resistance is also in these areas linked to healthcare contact and is fueled by uncontrolled access to over-the-counter antibiotics combined with a lack of microbiology facilities [33–36].

Traditionally, MRSA infections were confined to the health care environment. Over the past decade, however, the prevalence of community-associated MRSA (CA-MRSA) has increased exponentially. In many parts of North America, MRSA is now the most common identifiable cause of soft tissue infection among persons from the community without healthcare contact [37, 38]. Epidemic outbreaks have been reported in several well-defined populations, including prisoners, homosexual males, intravenous-drug users, athletes, indigenous populations of North America, Australia, and New Zealand, and military trainees [39–44]. In a recent population-based study, Gorwitz found that the prevalence of MRSA had doubled to 1.5% from just a few years previously. Interestingly, only 20% of these MRSA carriage isolates were community-associated clones (e.g., USA300 or USA400

Pulsed field gel electrophoresis genotypes), implying that the healthcare environment serves as a continuing reservoir for acquisition of MRSA in the community [45]. Although strains of CA-

MRSA primarily cause skin and soft tissue infection, they are emerging causes of bacteremia and necrotizing pneumonia [37,38,46]. Although CA-MRSA is generally more susceptible to antibiotics than strains originating from the healthcare system, its resistance profile in certain populations, such as North American homosexuals, has broadened considerably [44]. CA-MRSA most often harbour the staphylococcal chromosome cassette (SCC) mec type IV which contains the mecA gene as the sole resistance determinant. Using pulsed-field gel electrophoresis CA-MRSA have been designated to belong mainly to either the USA300 or USA400 lineage whereas most health-care related MRSA belong to USA100 [27,47]. Furthermore, CA-MRSA infections have been associated with the exotoxin Panton- Valentine leukocidin (PVL) that is believed to causes tissue necrosis and leukocyte destruction [46,48].

As the number of patients with community onset MRSA bacteremia grows the risk of inappropriate initial antimicrobial treatment and subsequently treatment failure and death is likely to increase [49,50]. This development calls for local treatment guidelines taking local resistance into account in order to ensure an effective initial treatment. Simultaneously, clinicians must balance the need for empiric antibiotic therapy that is sufficiently broad as to effectively cover drug-resistant pathogens with the need to limit unnecessary antibiotic administration, which drives the growing problem of antimicrobial resistance in the community.

DIAGNOSTIC CRITERIA

For proper diagnosis of neonatal septicemia diagnostic criteria can be divided in two groups; Clinical symptomatology and Investigational criteria [51]

Clinical features: The manifestations of neonatal septicemia are often vague and non-specific, and therefore, demand a high index of suspicion for its early diagnosis. Neonates with bacterial sepsis may have either non-specific signs and symptoms or focal signs of infection. The initial manifestations may have limited symptomatology and only one system involvement or it may be an acute catastrophic manifestation with multi-organ dysfunction. A variety of non-infectious conditions may occur together with neonatal infection and can make the diagnosis of infection more difficult. Because bacterial sepsis can be rapidly progressive, the physician must be alert for the development of signs and symptoms of possible infection and initiate diagnostic evaluation and empirical therapy**.** Neonates may have varied symptomatology like lethargy, refusal to feed, diarrhea, vomiting, hypothermia, jaundice, fever, cyanosis, tachypnea, chest retractions, apnea /gasping, seizures, excessive cry, shock, comatose, poor reflexes, abdominal distention, bleeding, renal failure, neck retraction, bulging fontanel etc [52]. In one study, it was observed that most common clinical presentation was lethargy or sluggish movement. Other frequent clinical presentation in septicemic neonates was respiratory distress, lethargy, jaundice, and poor feeding [53], whereas in another study the most common presenting feature was fever (61.2%).

INVESTIGATION CRITERIAS; (Neonatal sepsis screening) [51]:

It Comprises;

1. CBC (Complete blood count) and DLC (Differential leukocyte count Showing increase number of polymorphs. Neonatal septicaemia may be associated with leukopenia.
2. DLC: Band cells > 20%.
3. Increased Haptoglobin
4. CRP (C - reactive protein) value > 1 mg/dl indicates neonatal septicemia.
5. Micro ESR (Erythrocyte Sedimentation Rate) titer >55mm.
6. Gastric aspirate showing > 5 polymorphs per high power field.
7. Newborn CSF (Cerebrospinal Fluid) screen: Shows increased number of cells and proteins.
8. Culture and Sensitivity of microorganisms.

Band cells-In normal mature neutrophil has segmented nucleus and segments are connected by characteristic thin filamentous strand in contrast, the nucleus of band cells is indented by band like configuration or a lobulated appearance structure. It is calculated by ratio of immature and total neutrophil cells. Value> 0.20 indicates neonatal septicaemia [52].

Culturing for microorganisms from sample of cerebrospinal fluid (CSF), blood or urine, is the gold standard test for definitive diagnosis of neonatal sepsis. This can give false negatives due to the low sensitivity of culture methods and because of concomitant antibiotic therapy. Lumbar puncture should be done when possible as 10-15% presenting with sepsis also have meningitis, which warrants an antibiotic with a high CSF penetration [52].

Micro ESR- Micro ESR is obtained by collecting capillary blood in a standard pre-heparinized micro haematocrit glass tube (75 mm length internal diameter 1.1 mm, outer diameter1.5 mm) placing it vertically and reading the fall in the red cell column

after one hour . Peak value is 15mm at the end of first hour during neonatal period. High microESR is a specific test but it has only moderate sensitivity. [51].

TREATMENT

Supportive care and antibiotics are the two equally important components of treatment [52].

Supportive care- Good supportive care plays a significant role in the management of sick babies. Proper attention is needed to no. of aspects of it [51]. Such as,

- Provide warmth, ensure consistently normal temperature (36.5 c-37.5c). Kangaroo mother care is a beneficial modality in regulating temperature of small and sick babies.
- Start oxygen by hood or mask, if cyanosed or grunting. Provide bag and Mask ventilation with oxygen, if breathing is inadequate.
- To observe peripheral perfusion by palpating peripheral pulses. Assessing Capillary refill time (CRT) and skin color.
- Initiate intravenous line. Maintain fluid, electrolytes and glucose.
- Ensuring optimal nutrition is extremely helpful in sick babies. Enteral feeds should be introduced early if there is no abdominal distension and baby is hemodynamically stable and feeds mother's milk. Consider parenteral nutrition.
- Administer vitamin k1mg intramuscularly.
- Transfuse packed cells if baby has low hematocrit. Do not induce Blood /plasma.

Antibiotics – Frequently used in neonatal septicemia are [53,54]

Penicillin: The penicillin are classified as β-lactam drugs because of their unique four-membered lactam ring. Structural integrity of the 6-aminopenicillanic acid nucleus is essential for the biologic activity of these compounds. If the β-lactam ring is enzymatically cleaved by bacterial β-lactamases, the resulting product, penicilloic acid, lacks antibacterial activity. The penicillin is broadly divided into those that are stable against staphylococcal penicillinase enzyme and all others. Resistance to penicillin is due to one of the four general mechanisms: (1) inactivation of antibiotic by β-lactamases (2) modification of target protein binding proteins (PBPs) (3) impaired penetration of drug to target PBPs and (4) the presence of efflux pumps. Anti-staphylococcal Penicillin are resistant to staphylococcalβ-lactamases e.g. Naficillin. They are active against Staphylococci and Streptococci but inactive against enterococci, anaerobic bacteria and gram-negative rods. All remaining penicillinare susceptible to hydrolysis by staphylococcalβ-lactamases. Therefore, these are unreliable for treatment of staphylococcal infections [53,54].

Cephalosporin: These are semi synthetic antibiotics and are structurally related to Penicillin. These have been conventionally divided into four generations. This division has a chronological sequence of development, but more importantly, takes into consideration the overall antibacterial spectrum as well as potency. The first generation

Cephalosporin have excellent activity against Methicillin susceptible Staphylococci and Streptococci spp., but not against Enterococci. This group also has modest activity against the Enterobacteriaceae family such as E. coli, P. mirabilis and Klebsiella spp. The only important difference between members of the first generation is in their half-life. The second generation

Cephalosporin have extended spectrum against gram negative bacteria in comparison to first generation but lacks activity against many gram-negative rods. They can be used when susceptibility pattern are known or when community acquired infections with low probability of antimicrobial resistant bacteria are being treated. This class of antimicrobial agents is not reliable for empirical treatment of nosocomial gram-negative rod infections. The third generation

Cephalosporin have extended activity against gram-negative rods, including many resistant strains. In context of this gram-negative coverage, most of the members of this group have significantly less activity against Staphylococci and Streptococcal spp. than first and second generation Cephalosporin. The important distinction amongst the third generation Cephalosporin is between those significantly active against Pseudomonas spp. (Cefoperazone and ceftazidime) and those without (Cefotaxime, Ceftriaxone and Ceftizoxime). The fourth generation **Cephalosporin** (Cefepime and Cefpirome) have similar antibacterial spectrum to that of third generation Cephalosporin but are highly resistant to hydrolysis by chromosomal β-lactamases and some extended spectrum β-lactamases that inactivate many of the third generation Cephalosporin. These have good activity against Pseudomonas aeruginosa, Enterobacteriaceae family, Staphylococcus aureus and Streptococcus pneumoniae. Cefepime has good activity against most Penicillin resistant strains of Streptococci and it may be useful in treatment of Enterobacter infections**.** Fifth generation **Cephalosporin** (Ceftaroline, Ceftobiprole) are approved for treatment of community acquired pneumonia and MRSA infections [53, 54].

Monobactam: These are drugs with a monocyclic β-lactam ring. They are relatively resistant to β-lactamases and are active against gram-negative rods (including Pseudomonas and Serratia). They have no activity against gram-positive bacteria or anaerobes. Aztreonam is the only Monobactam available in the USA. It resembles Aminoglycosides in its spectrum of activity. Penicillin- allergic patients usually tolerate Aztreonam without reaction. The clinical usefulness of Aaztreonam has not been fully defined [53,54].

Sulfonamide: Sulfonamides had a wide range of antimicrobial activity against both gram-positive and gram-negative bacteria. Microorganisms that may be susceptible in vitro to sulfonamides include Streptococcus pyogenes, Streptococcus pneumoniae, H. influenzae, H. ducreyi, Nocardia, Actinomyces, C. granulomatis, C. trachomatis. Sulfonamide resistance may occur as a result of mutations that cause overproduction of PABA, cause production of a folic acid synthesizing enzyme that has low affinity for Sulfonamide, or cause a loss of permeability to the Sulfonamides. Trimethoprim given together with Sulfonamide, resulting in marked enhancement (synergism) of the activity of both drugs. The combination often is bactericidal, compared to the bacteriostatic activity of Sulfonamide [53,54].

Fluoroquinolones: Fluoroquinolones were originally developed because of their excellent activity against gram-negative aerobic bacteria; they had little activity against gram-positive organism. Several newer members have improved activity against gram-positive cocci, including some Methicillin-resistant Staphylococcus aureus (MRSA), although there is insufficient clinical information to recommend their routine use against Methicillin-resistant Staphylococci. The currently available members of first generation Fluoroquinolones are Norfloxacin, Ciprofloxacin, Ofloxacin and Pefloxacin. Ciprofloxacin (prototype of first generation) is most active agent of this group against gram-negative, Pseudomonas aeruginosa in particular. Gram-positive bacteria are inhibited at relatively higher concentrations. Second generation members are Lomefloxacin, Levofloxacin, Sparfloxacin, Gatifloxacin, Moxifloxacin and Trovafloxacin. Levofloxacin, Moxifloxacin and Trovafloxacin have longer half-life with improved activity against gram-positive organisms, particularly Streptococcus pneumonia [53,54].

Aminoglycosides: For many years the aminoglycoside class of antimicrobial agents was the only reliable class of drugs for the empiric treatment of serious gram-negative infections. The availability of a third generation Cephalosporin, extended spectrum Penicillin, Monobactam, Carbapenem and Fluoroquinolone has greatly reduced the instances when Aminoglycosides must be used. Aminoglycosides have a very wide range of activity against both aerobic and facultative anaerobic gram-negative rods. They have a very broad activity against gram-positive cocci but are an important component of synergistic therapy against Enterococci when combined with Penicillin or Vancomycin. Many clinicians now reserve Aminoglycosides for specific therapy for resistant organism or as a part of synergistic combination to treat serious Enterococcal infections [53,54].

Macrolides: Erythromycin, a macrolide antibiotic, is effective against gram-positive organism especially Pneumococci, Streptococci, Staphylococci and Corynebacterium as well as gram-negative organism like Neisseria species, B. pertussis etc. Hemophilusinflenzae is somewhat less susceptible. It has found widespread use, however as an oral agent (Erythromycin base) used in combination with Aminoglycoside to reduce numbers of bacterial flora. It is sometimes used as an alternative agent for those patients who are allergic to Penicillin [53,54].

Tetracycline: Tetracycline is broad spectrum bacteriostatic antibiotic. They are active against gram-positive and gram-negative bacteria, including anaerobes, Rickettsia, Chlamydia and Mycoplasma [53,54].

Glycopeptide: Vancomycin is primarily active against gram-positive cocci, especially the Methicillin resistant Staphylococci, for which it is the only reliable agent. It also has modest activity against Enterococci. Vancomycin resistant strains of Enterococci, primarily Enterococcus faecium, have emerged as a major nosocomial pathogen in hospitals of United States. Teicoplanin is similar to Vancomycin in chemical structure, mechanism of action, spectrum of activity and route of elimination. It is only active against gram-positive bacteria. It is bactericidal against susceptible strains, except for Enterococci. Some strains of Staphylococci, both coagulase positive and negative, as well as Enterococci and other organism that is intrinsically resistant to Vancomycin (i.e. Lactobacillus species and Leuconostocspecies) are resistant to Teicoplanin [53,54].

Clindamycin: It is a Lincosamide antibiotic similar in mechanism of action (inhibits protein synthesis by binding with 50S ribosome) and spectrum of Erythromycin with which it exhibits partial cross-resistance. It inhibits most gram-

positive cocci (including penicillinase producing Staphylococcus aureus, but not Methicillin resistant Staphylococcus aureus),
Corynebacteriumdiptheriae, Nocardia, actinomyces, Toxoplasmosis, but the distinctive feature is its high activity against a variety of anaerobes specially Bacteroides fragilis. Aerobic gram-negative bacilli are not affected [53,54].

Linezolid: Linezolid is active against gram-positive organism including Staphylococci, Streptococci, Enterococci, gram-positive anaerobic cocci, and gram-positive rods such as Corynebacterium spp. and Listeria monocytogens. It has poor activity against most gram-negative aerobic and anaerobic bacteria. It is bacteriostatic against Enterococci and Staphylococci and bactericidal against Streptococci. Because of its unique mechanism of action, Linezolid is active against strains that are resistant to multiple agents, including penicillin-resistant strains of S. pneumoniae, Methicillin-resistant and Vancomycin-resistant strains of Enterococci [53,54].

Pristinamycin: Quinupristin and Dalfopristin is a combination of Streptogramin B, Quinupristin, with Streptogramin A, Dalfopristin, in 30:70 ratio. These compounds are semi-synthetic derivatives of naturally occurring Pristinamycins, produced by Streptomyces pristinaspiralis. Quinupristin and Dalfopristin are more soluble derivatives of Pristinamycin IA and Pristinamycin IIA respectively. These bind with different targets in the peptidyl transferase domain of 23 ribosomal subunit and inhibit protein elongation by means of different steps. Streptogramin A and B act synergistically in- vivo; the mixture of the two compounds is more powerful (bactericidal) than the individual compounds (bacteriostatic) and their combined action is irreversible. These are bacteriostatic when used separately but acts synergistically when combined, such that in some case they are bactericidal, mainly against gram-positive bacteria. Quinupristin/ Dalfopristin is active against S. pneumoniae, beta-hemolytic and alpha hemolytic strains of Streptococci, E. faecium (but not E.faecalis) and Staphylococci, both coagulase-positive and coagulase negative strains. The combination is largely inactive against gram-negative organisms, although M. catarrhalis and Neisseria spp. are susceptible. It is active against organism responsible for atypical pneumonia, M. pneumoniae, Legionella spp. and C. pneumoniae. The combination is bactericidal against Streptococci and many strains of Staphylococci, but bacteriostatic against E. faecium [53,54].

Pristinamycin has been available as an oral agent in France since 1960[10].The first Staphylococcal clinical isolate resistant to the Pristinamycin was reported in France in 1975.Staphylococcal resistance to the above antibiotic mixture is always associated with resistance to compounds A e.g., Dalfopristin, but is notnecessarily for compounds B e.g. Quinupristin.

Antibiotics can cause serious toxicity and injudicious use of antimicrobial agents promotes development of resistant microorganisms. Of course, following definitive identification, antibiotics often may be used if disease is severe and if it seems likely that withholding therapy will result in failure to manage a potentially life threatening infections. Initiation of optimal empirical antibiotic therapy requires knowledge of the most likely infecting microorganism and their susceptibilities to antimicrobial drugs**.** Nosocomial infections resulted in considerable morbidity and mortality among neonates in high risk nurseries.
In one study it was found that bacteriology of neonatal septicemia in Nigeria and found the incidence to be 55% in high risk neonates. In their study, the most frequent isolate was Staphylococcus aureus (16.8%), followed by coagulase negative Staphylococcus aureus(11%), Listeria monocytogens (8.4%),
Pseudomonasaeruginosa (3%),
Klebsiellapneumoniae (14%), Escherichia coli (7%), Enterobacteraerogens (5%), Citrobacterfreundi, Salmonella Spp. and Proteus spp. (2% each).Group-B Streptococci was not isolated. Many workers throughout the world have reported outbreaks of Klebsiellapneumoniae and Enterobacter in nurseries. DNA fingerprinting confirmed an Enterobacter Cloacae epidemic in a neonatal intensive care unitin Germany [55], while in another study has shown that neonatal septicemia in high risk babies in South-Eastern Nigeria and observed that the most common bacterial isolates in septicemic neonates were Staphylococcus aureus. Klebsiella species is the most common offender in the first week of life followed by Enterobacter species, Escherichia coli, takes the third place in contradiction to the western report [56].

CONCLUSION

The cost of treatment in NICU enhances manifold with neonatal sepsis and its complications like requirements for prolonged ventilatory support, requirement of newer (costly) antibiotics, intravenous immunoglobulins, colony stimulating factors and blood products. Despite the indications of the most modern armamentarium, the combat with neonatal sepsis, more often than not displays a

dismal picture; not to mention the mental, physical and economical burden it lays down on the parents and the government. Therefore it should be managed effectively. The knowledge of the prevailing strains and the antibiotic sensitivity patterns in the region is essential to encounter the challenge of neonatal sepsis with equal competence and opposing force. Large-scale multi-centric prospective studies are essential to recognize the varying patterns of the prevailing flora and susceptibility to numerous antibiotics.

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