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Research Article

Blood contamination in neonates: clinicians' dilemma

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ABSTRACT

Background: Neonatal sepsis is an important cause of mortality and morbidity among neonates. Many laboratory tests aid to diagnose sepsis but isolation of bacteria in the blood is the gold standard for diagnosis of sepsis. Growth of contaminants in the blood nullifies the utility of blood culture. Coagulase Negative Staphylococcus aureus (CoNS) is a common blood contaminant, but it can be a pathogen among neonates admitted to intensive care unit. Difficulty in differentiating true infection of CoNS from blood contamination can results in inappropriate treatment of contaminants with antibiotics like vancomycin. There are advanced microbiological tests to distinguish true growth of CoNS from contaminants but they are not easily available and not cost effective in developing countries. There were numerous blood culture reports of CoNS and other contaminants from our neonatal intensive care unit of a rural based medical college hospital. Aim and objectives of the study were to differentiate true infection with positive blood cultures by correlation of clinical features, risk factors and clinical setting for CoNS sepsis.
Methods: Retrospective case record analysis of 50 positive blood cultures for clinical significance of blood contaminants including CoNS.
Results: Clinical correlation showed that 39 culture reports were false positives. Five positive blood cultures had pathogenic bacteria and six positive culture reports with blood contaminates and CoNS were true infection needed treatment with escalation of antibiotics.
Conclusions: The source of blood contamination was from hospital environment probably due to lack of proper hand hygiene and blood sampling method. Implementation of quality control strategies on hand wash and blood collection method can reduce blood contamination.

Keywords: Blood contamination, Coagulase negative Staphylococcus, CoNS, Neonatal sepsis

INTRODUCTION

Septicemia continues to be a major problem for neonates admitted to neonatal intensive care units (NICU) around the world. Neonatal sepsis is one of the four leading cause of neonatal mortality in India.[1] Early onset neonatal sepsis (EONS) occurs within 3 days of birth resulting from vertical transmission of bacteria from mother to the neonate during the intrapartum period and late onset neonatal sepsis (LONS) after 3days due to the horizontal transmission of pathogens from the environment or the hands of the caregiver.[2] As signs and symptoms of sepsis are nonspecific, antimicrobial therapy is empirically initiated after appropriate blood culture. Coagulase negative *Staphylococcus aureus* (CoNS) is one of the important organisms encountered during evaluation of clinical sepsis in a neonate.[3] On one hand, there is increased survival of low birth weight (LBW) and preterm babies needing invasive procedures which predisposes to CoNS infections; on the other hand vague clinical symptoms of this low virulent organisms with

difficulties to differentiate contaminants from true bacteremia in blood culture, coupled with no clear laboratory confirmative evidence of sepsis makes the clinician less confident to withhold reserve antibiotics like vancomycin from sick babies at NICU.

Earlier, CoNS were the most common blood culture contaminants but now they could be pathogens due to medical advancement and judging the clinical significance of them in blood has proven to be problematic.[4] More over treating CoNS contamination rather than infection would lead to unnecessary use of resources for additional laboratory tests, longer hospital stays, and unwarranted antibiotic exposures. Most appropriate and economic way to handle this predicament in a developing country is to make a proper clinical judgment of likely CoNS sepsis and enhancing the validity of single blood culture by strict aseptic blood sampling. There was an alarming growth of CoNS and other contaminants from the blood culture of newborns with suspected sepsis admitted to our NICU. We hypothesized that CoNS growth in blood culture as contaminants. We clinically identified the true CoNS infection in a neonate by the presence of risk factors and intensive care settings for CoNS sepsis as well as by monitoring the neonate for clinical deterioration and in its presence treating the neonate by escalating the antibiotics.

Aims

The aims of the study were to know the clinical profile of newborns with blood contaminants including CoNS and to differentiate between blood contamination and true infection due to CoNS in a neonate by clinical evaluation.

METHODS

Single blood culture reports of all the newborns screened for suspected sepsis at admission to a NICU of a rural based hospital, were collected from microbiology department database for a period of six months from April to September 2014. The data was analysed for culture positivity, bacteriological profile and antibiotic sensitivity. At least 1 ml of blood was collected from the peripheral vein of a neonate with suspected sepsis before starting antibiotics, either by a needle or a new cannula, using aseptic methods. This was injected into a culture bottle with 10 ml of brain heart infusion broth and 0.025% sodium polyaenthol sulphonate anticoagulant. Bottles were incubated at 37°C for 7 days. Subcultures were made on 2nd, 4th and 7th day on MacConkey and chocolate agar. Growth was identified by colonial characteristics and standard biochemical tests. Antibiotic sensitivity testing was done by modified Kirby-Bauer disc diffusion method as per CLSI (clinical and laboratory standards institute) recommendations.

Neonates with suspected sepsis either by clinical features or by high risk antenatal or postnatal factors for sepsis were treated with cefotaxime and amikacin as first line antibiotics. If there was no bacterial growth and the newborn showed clinical improvement, the antibiotics were stopped at the earliest. But once if clinical deterioration identified antibiotics were upgraded with or even without positive blood culture.

All the available case records of neonates with positive blood isolates were retrospectively analysed for clinical characteristics including the risk factors for development of CoNS sepsis. The data was tabulated and analysed by using standard Statistical methods.

RESULTS

457 neonates were admitted to NICU during the study period, of which 205 (44.8%) neonates were screened for sepsis by septic screen including blood culture. Of this, 58 blood samples had bacterial growth which included 18 contaminants. The reported contaminants (31%) in blood culture were (*Corynebacterium* spp., *Bacillus* spp., *Propionibacterium acnes*, *Micrococcus* spp.). Culture positive rate was 19.5% (40/205) after excluding contaminants. Blood contamination rate was 8.7 percent (18/205).

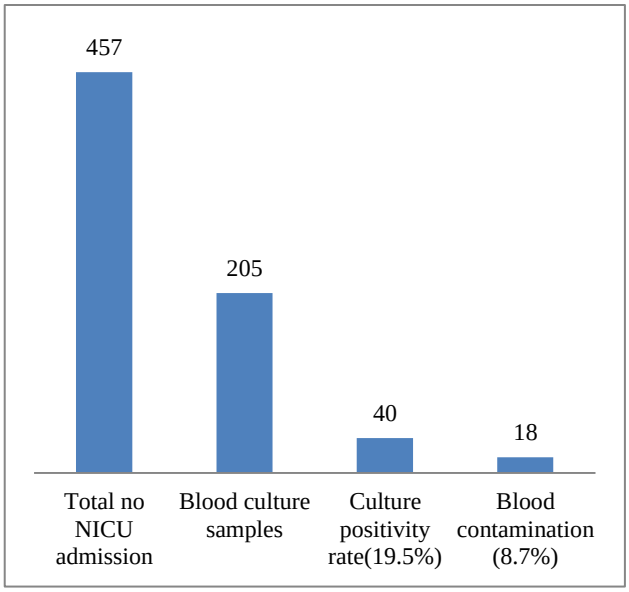

Figure 1: Showing the blood culture positive rate and blood contamination.

The bacteriological spectrum of 40 (40/58) blood culture showed, gram-positive organisms (37) constituting 92.5 percent. Of these, 26 CoNS (65%), 5 (12.5%) Methicillin resistant CoNS (MRCoNS), 3 Enterococci (7.5%), 2 Staphylococci (5%) including MRSA and one Streptococci. Of the 3 Gram negative organisms, 2 were Gram negative non fermenters and one was E. coli.

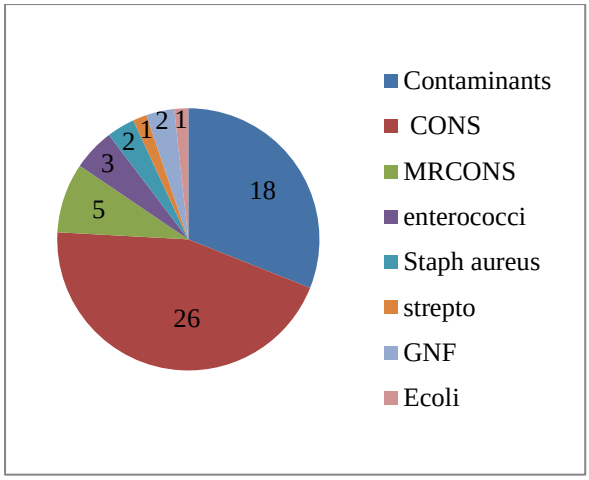

Figure 2: Showing the blood culture isolates.

Of the 58 positive blood isolates 49 were either reported as contaminants or grew CoNS contributing to 84.4% of the total growth. CoNS being a universal skin commensal, their growth from a single blood culture could most likely be false positive but still they can be a potential pathogen in a particular NICU setting**.** To ascertain possible pathogens from all the contaminants, we analysed 50 available case records of all positive blood isolates for risks factors, clinical profile and outcome of sepsis.

Table 1: Clinical profile of contaminants and pathogenic bacteria.

Clinical characteristics	Total No. (50)	CoNS & other contaminants (n=45)	Pathogenic bacteria (n=5)
Male	31	29 (64%)	3
EONS	42 (84%)	40 (88.8%)	2
Inborn	41	39 (86.6%)	3
preterm	10	9 (20%)	1
LBW	13	12 (26%)	1
Low APGAR	6	5 (11.1%)	1
LSCS	20	19 (42.2%)	1
central line	1	0	1
CRP >6 mg/dl	25	20 (44.4%)	5
2nd line antibiotic	11	6 (13.3%)	5
Vancomycin	6 (13.6%)	4 (8.8%)	2
Mortality	Nil	Nil	nil

Among 50 blood isolates, 45 included (CoNS, MRCoNS and other contaminants) in contaminant group. Pathogenic bacteria group had only 5 neonates positive for one E. coli, 2 Enterococci and 2 Gram negative nonfermenter. Clinical profile of contaminant group showed EONS was suspected in 88.8%, only 20% were preterm (32-36 weeks) and 26% had LBW (1500-2500 grams), 42% of neonates were delivered by caesarean section. All the 5 neonates with pathogenic bacteria had positive C-reactive protein (CRP), their clinical condition deteriorated and needed change of antibiotics depending on the culture and sensitivity (vancomycin in 2 Enterococci, meropenem in 2 and piperacillin in 1). In the contaminant group, few had risk factors for sepsis (low birth weight, prematurity, low APGAR) and CRP was positive in 44.4 percent. No one had invasive procedures, ventilation or central lines which predisposes to CoNS sepsis and their clinical condition was stable while on first line antibiotics except for 6 neonates (13.3%) of which (2 were preterm, 2 had lethargy and 2 had low APGARs) and positive CRP needed change of antibiotics as per blood culture sensitivity in 4 CoNS treated with vancomycin and in 2 contaminants treated with empirical meropenem. There was no mortality in both the groups.

DISCUSSION

Isolation of microorganisms from blood is the standard method to diagnose sepsis in the newborn infant.[5] Blood culture positivity rate is highly variable, different studies report as 25-60% and rarely as high as 82 percent.[1,6] This may be due to various reasons like changing epidemiology of neonatal sepsis, prior use of antibiotics, intermittent bacteremia, blood broth ratio and culture methods. In the present study it is 19.5% similar to studies.[1,7,8] The low culture positivity here could be due to insufficient volume, high contamination rate or blood sampling high risk neonates before the onset of sepsis.

Blood culture is a gold standard for diagnosis of neonatal sepsis in spite of low sensitivity and reporting delay.[5] The blood culture contamination represents an ongoing source of frustration for the microbiologists and the clinicians.[9] The quality assurance benchmark standard for blood contamination rate is set at 2-3, even though the actual rates for the contamination vary widely from institution to institution, ranging from 0.6% to over 6%.[10] Rate of blood contamination in different studies are 16% and 3.9% and more so for neonates.[9,11,12] In this study, in our NICU it is 8.7 percent.

The bacteriological profile of neonatal sepsis is variable between developed and developing countries as well as within regions of developing country.[13] EONS as reported by various studies are 57.5%, 79% and 78 percent.[6,7,13] LONS was reported in two different studies as 66.9 %and 25.2 percent.[1,8] Our study had 84% EONS which is high compared to other studies and it could be due to more intra mural admissions. The report of the National Neonatal Perinatal Database showed Klebsiella pneumoniae as the predominant pathogen.[14] Similarly some studies reported it in 66% and in 38 percent.[6,13] There are studies showing predominant growth of Gram positive organisms, Staphylococcus aureus in 38.8% and CoNS in 21.3 percent.[6] CoNS growth was 65% in our study, while other studies showed 59.5% and 57.3 percent.[15,16] In these studies the possibility of CoNS being false positives could not be ruled out.

CoNS is the most common blood culture contaminants, typically representing 70% to 80% of all contaminated blood culture, but various studies show true bacteremia of 10-24.5% due to CONS.[10]

There are not many studies where clinical correlation of blood contaminants including CoNS has been done to identify the true infections. In the present study clinical correlation of 45 neonates in the contaminant group showed that in many there were no risk factors or NICU interventions predisposing to CoNS sepsis. Further, their clinical condition improved while on empirical antibiotics started in view of suspected sepsis at admission to NICU and CoNS growth in their single blood culture were probably false positives. The reasons for their NICU admission in this study were variable like prematurity, low birth weight, low APGARs, meconium stained liquor, transient respiratory distress, poor feeding and poor activity.

A retrospective study reported true CoNS infection is unlikely in infants with BW >2000 g and gestation >34 weeks and total central lines required for care, lethargy and gastric residuals predicted true CoNS infection.[17] Six neonates (13.3%) had worsening of clinical condition in the form of poor activity, respiratory distress needing oxygen and poor peripheral circulation and positive CRP they needed treatment with vancomycin (4 CoNS) and meropenenem (2 contaminants other than CoNS). These 4 neonates with CoNS probably had true infection and their blood culture growth was true positive, while that of 2 neonate who had clinical sepsis, their blood culture with contaminants were false negatives due to insufficient blood volume or contamination of blood. In the contaminant group 86.6% were inborn and 88.8% were screened for EONS (1 out born) in contrast to LONS which is common with CoNS. The possible source of CoNS in these neonates is from the hospital environment at the time of delivery or at admission to NICU within three days after birth due to lack of proper hand hygiene and blood sampling. CoNS colonization of neonates in the hospital environment occurs horizontally by parents and staff and transmission of endemic strains by hospital staff can lead to their circulation for extended periods.[18]

In spite of microbiological advances, there are no consensus on definitions and practices with CoNS infection among the clinicians thus resulting in over presentation of CoNS as true pathogen.[3] Further multicentric large sample size, case control studies are needed to develop clinical predictability scoring to identify CoNS true infection so that it can be treated wisely and cost effectively which can reduce the exciting dilemma.

CONCLUSIONS

Blood culture contamination is a challenge that requires a multidisciplinary approach.

Proper clinical judgment of CoNS infection is vital to enhance the validity of a blood culture so that injudicious use of antibiotics is reduced.

Limitations

This is a retrospective study with a small sample size and hence no predictability score was developed. The study was conducted at single center which reflect the practice pattern of that center. Single blood culture in a neonate with suspected CoNS infection is suboptimal. All the study neonates suspected with sepsis were treated with empirical antibiotics which could have modified the clinical course. The antibiogram was not done due to high contaminants.

Recommendations

To obtain more than one blood culture if CONS or other contaminants are grown.

This is an interim study to assess the magnitude of blood contamination. Further studies are needed after effective implementation of strategies to reduce blood contamination by strict adherence to hand hygiene and blood sampling method**.**

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