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Bacteriological Profile of Neonatal Sepsis in VLBW Babies and Their Growth and Development at 6month Follow Up – A Study Done at Tertiary Care Hospital, South India

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ABSTRACT: Background: Globally, neonatal septicaemia is an important cause of neonatal mortality and morbidity. This study evaluates the distribution of microorganisms causing sepsis, emergence of multi drug resistant bacteria and also the short-term growth and neurodevelopmental outcomeamongVery Low Birth Weight (VLBW) neonateswithculture proven blood stream infection.
Methods: Single centre prospective cohort study. VLBW Neonates with clinically suspected sepsis were subjected to blood cultures using standard protocol. Our study included 109 VLBW babies with blood culture-proven sepsisascases and genderandgestationalage-matched blood culture sterile VLBWnewbornsascontrols.Weight, length,head circumference measurements anddevelopmental assessment were done regularly on follow up till 6months corrected gestational age(CGA).
Results: Klebsiella pneumoniae, E. colifollowed by Candida and CoNS were themostcommonorganismsisolatedfromVLBWinfa ntswithsepsis. Mortality was highest in Acinetobacter sepsis. Neurodevelopmental impairment was highest in sepsis due to Pseudomonas. Developmental delay was seen in 26% cases and 2% controls. The mean weight(5830±210gms), length(53.6±7.3cm), head circumference (41.91cm) at 6months CGA and themean mental quotient (77±13 vs.84±9),mean motor quotient (73±13vs.82±10),meandevelopmentalquotient(76.3 ±12.2vs. 83.8±9.8) were significantly lower in the culture-positive group compared to thecontrolgroup.

Conclusions: Gram negative organisms predominated in the neonatal septicaemia. Our findings suggest that sepsis significantly affects mortality, growth and neurodevelopmental outcomes in VLBW neonates. Therefore, preventive measures for sepsis in VLBW neonates is crucial, and those with culture-positive sepsis will require close monitoring and follow-up evaluations.

KEYWORDS:bacteriological profile, culture positive sepsis, neurodevelopment follow up, outcome, vlbw neonate.

I. INTRODUCTION

Recent years witnessed tremendous improvement in survival of VLBW infants duetoadvancesinneonatalandperinatalcare.
Knowledge of epidemiology of bacterial isolates and their antibiograms in hospital settings is necessary for the prompt empirical anti-microbial therapy of neonatal sepsis. Also, prematurity is now the leading cause of neurological morbidities. Among preterm infants, survivorsof <32wks are at higher risk of facing neurodevelopmental abnormalitiesinseveral developmental domainswith significantimpactonqualityoflife.Approximately40 %ofpreterminfantscandevelopmildtomoderateneuro developmentalimpairment.

VLBW neonates are more prone to infection during their hospital stay due to multiple interventions and prolonged hospital stay. Earlyrecognitionoftoneabnormalities, provision of early intervention services will dramatically reduce the burden of cerebral palsy and improve the outcome. Because of the paucity of data on VLBW babies with neonatal sepsis inmiddle- and low-income countries, this study is taken up to evaluate the distribution of microorganisms causing sepsis and the emergence of multi drug resistant bacteria and also to evaluate growth and neurodevelopmental outcomeamongVLBWneonateswithculture-positivesepsis. This will also be

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ausefultoolinestimatingthelong-termprognosisofVLBWbabiesandhelp incounsellingparents.

II. AIMS AND OBJECTIVES

To study the bacteriological profiles and antibiograms of blood culture isolates of VLBW babies and tostudythe growth and neurodevelopmentaloutcomeofVLBWneonateswith culture-positivebloodstreaminfection,comparedtoculture-negativecontrolsmatchedforgestationalageandsexat 6monthscorrectedgestationalage and also to assess the other risk factors which are associated with adverse neurodevelopmental outcomes.

III. MATERIALS AND METHODS

Thisprospective,cohortstudywasconducted inNICU,GovernmentGeneralHospital,Kakinada,An dhraPradesh, India over two yearsfrom October 2018 to September 2020. Basedonpreviousstudies,assumingsurvivalwithoutn eurodevelopmental impairment of 50% in the study group and 75% amongcontrols, 96 cases, and 96 controls were required for an α of 0.05 and power of 80%. Anticipating a loss of 15% during follow-up, 109 casesand 109controlswereenrolledinthestudy. Babies with a birth weight below 1500g with blood culture-proven sepsiswereincludedascases and genderandgestationalage-matched blood culture sterile VLBWnewbornswereselectedascontrols. Babies with Majorcongenitalmalformations/geneticsyndromes, culturespositive forcontaminants, deathwithin72hoursofadmission were excluded.

The demographic details, history of illness, examination findings, treatment provided and complications during the course such as IVH, NEC, BPD, ROP, mortality were recorded during the hospital stay. After discharge, these infants were followed up in high-risk follow-up clinicsat6,10,14 weeks andevery month till 6 months corrected gestational age. At each follow-up visit, the infant'sweight, length, and head circumference were measured to assess the growth. These parameters were compared with the help of Fenton's chart for gender and age and at the end of 6 monthsby usingstandardWHOageandgendergrowthcharts.

Initial Amiel-Tison assessmentwas done using a goniometer and documented at every visit, followed by DASII at6monthsCGAtoassessthedevelopmentalquotient(DQ).Asignificantneurodevelopmental delay was considered as a mental/motor/developmental quotient ofDASIIscoresoflessthan70 (-2SDbelowthe mean).

IV. STATISTICAL ANALYSIS

Statistical analysis of the descriptive data was done by using SPSS softwareversion 15.0. Continuous data were presented as mean with standard deviation andcomparison between groupswascarriedoutusingunpairedstudent'st-test.Thecategorical outcomes were expressed as percentages and compared across groupsusing Chi-square/ Fisher's exact t-tests. P-value < 0.05 was considered statisticallysignificant.Multiplelinearregressionanal ysesofpredictorvariablesandthe neurodevelopmental outcomeweredone.Ethical clearance was obtained from institutionalethics committee. Written and informed consent was obtained from a legallyaccepted representative (LAR).

V. RESULTS

During the study period, 181 VLBW babies with clinically suspected sepsis were admitted to NICU.Of them,72wereexcludedfrom thestudy. The remaining 109 VLBW babies who were blood culture positivewere included in the study as cases. 109 gestational age and gender-matched VLBWbabieswhowerebloodculture-negativewereenrolled as controls. Among these, 39 blood culture positive cases and 17 culture negative controls expired during the hospital stay. 5 babies in the culture-positive group and 2 culture-negative controls were lost to follow up. So, a total of 65 culture positive cases and 90 culture-negative controls completed follow-uptill6monthsCGAandwereincludedintheanalysisfo rneurodevelopment.

Consort diagram of the study

Characteristics of population:

Males constituted 46.8%and47.7% of case groups and control groups respectively. Mean birth weight was 1259 gm (SD- ±127) and mean gestational age was 31.7 weeks (SD±2.88). Overall,78%, were <34weeks which constitute the predominant cohort and 19.3% of mothers received complete course of antenatal steroids in this study. Infants in theculture-proven sepsis had severe grades of IVH (2 infants in Grade-IIIand 1infantinGradeIV).

21 infants(19.3%)inthecontrolgroup and 48 infants (44.0%) in the culture-positive group hadNEC with 4(3.7%)neonates in the culture-positive group and 1 neonate (0.9%) requiring surgery.

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NeonatalsepsisisanindependentriskfactorforIntraventricularhemorrhage and Necrotizingenterocolitis. The meandurationofmechanicalventilationintheculture-positivegroup was 7.33 (±4.76) andin the culture-negativegroup was 4.44 (±2.29) and the difference was statistically significant(P=0.0001). There was no statisticallysignificant difference in ROPamongthegroups(P=0.596). Culture-provensepsisinfantshad significantlyhighermortalitycomparedtoculture-negativeinfants(35.7%versus15.5%)(p=0.0009). The characteristics of the population are tabulated here.

Characteristics of population		Culture positive cases (Total- 109)	Culture negative controls (Total- 109)	p value
Gender	Male	51	52	0.89
	Female	58	57	
Gestational age (weeks)	<32 w	51	49	0.837
	32-36w	47	46	
	>36w	11	14	
	Mean	31.78 (±2.89)	31.66 (±2.87)	
Birth weight (gms)	<1200	47	51	**0.003**
	1200-1500	62	58	
	Mean	1284.62 (±128)	1234.22 (± 126)	
Mode of delivery	Vaginal (SVD/ AVD)	94	92	0.74
	LSCS	15	17	
Septic screen	Positive	72	42	
	Negative	37	67	
IVH	Nil	97	100	0.49
	Grade I – II	9	9	
	Grade III - IV	3	0	
Necrotizing enterocolitis	Nil	61	88	**0.0001**
	Stage 1	38	19	
	Stage 2,3	10	2	
BPD	Present	4	0	0.13
Mechanical ventilation	Need	63	34	
	Mean duration (days)	7.3 (±4.76)	4.44 (±2.29)	**0.0001**
Retinopathy of prematurity	Nil	88	91	0.596
	Stage 2	11	11	
Mortality		39	17	**0.0009**

Table 1: Characteristics of the population

Different types of organisms isolated from blood culture positive VLBWneonates and their contribution towards mortality andmorbidity at 6monthsCGA were tabulated in Table 2. Klebsiella pneumonia (27.5%) was the mostcommon Gram-negative organism isolated from the blood culture. The mortality washighestin sepsisduetoAcinetobacter(58.3%)followedbyKlebsiella(40.0%),CoNS(40.0%)andPseudomonas(40.0%).Neurodevelopmentalimpairmentamong survivorswas highestin sepsiscausedby Pseudomonas (66.6%), followed by S.aureus(40%) and E.coli(36.3%).

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Table2: Different typesofindividualorganisms isolated, associated mortality and developmental delay inbloodculturepositiveVLBWneonates

Nameoftheorganism	**BLOODCULTUREpositivity**		
	n	**Mortality**	**DQ<70inSurvivors**
Klebsiellapneumoniae	30	12(40.0%)	3(16.6%)
E.coli	15	4(26.6%)	4(36.3%)
Candida	14	5(35.7%)	2(22.2%)
CoNS	10	4(40.0%)	1(16.6%)
Acinetobacter spp.	12	7(58.3%)	0(0.0%)
Staphylococcusaureus	7	2(28.5%)	2(40.0%)
Pseudomonas	5	2(40.0%)	2(66.6%)
Enterococcusspecies	6	0(0.0%)	2(33.3%)
MultipleOrganisms	10	3(30.0%)	1(14.3%)
Total	109	39	17

FOLLOW UP PROFILE

70 newborns from the culture-positive group and 92 babies from theculture-negative group were discharged and enrolled for follow-up. 5 babies inthe culture-positive group and 2 babies in the culture-negative group were lostto follow up. 65 babies in the culture-positive group and 90 babies in theculture-negativegroupcompletedtheirfollow-uptill6monthscorrectedgestationalage. The mean weight (in grams) at discharge was 1520±138 and 1608±141and at 6months CGA was 5830±210 and 6620±230 in culture-positiveand controlgroupsrespectively. The mean length (in cms) at discharge was 39.81±8.6 and 42.78±9.7 and at 6months CGA was 53.60±7.3 and 59.54±7.5 in culture-positiveand controlgroupsrespectively. The mean Head circumference (in cm) at discharge was 29.5 and 29.46and at 6months CGA was 41.91 and 42.36 in culture-positiveand controlgroupsrespectively. During follow up, at the end of 6 months, there was a statistically significant difference in weight (p – 0.0001), length (p – 0.01), head circumference (p- 0.009). Their growth parameters are presented in Table 3.

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Table3: Growth parameters at discharge and on 6months CGA follow up

Anthropometric parameter		Culture positive cases	Culture negative controls	p value
Mean Weight (gm)	At discharge	1520 (±138)	1608 (±141)	0.03
	At 6months follow up	5830 (± 210)	6620 (± 230)	0.0001
Mean Length (cm)	At discharge	39.81 (±8.6)	42.78 (±9.7)	0.04
	At 6months follow up	53.60 (±7.3)	59.54 (±7.5)	0.01
Mean Head circumference (cm)	At discharge	29.5	29.46	
	At 6months follow up	41.9	42.36	0.009

Developmental delay at the age of 6 months corrected gestational age is depicted in Table 4.

Table 4: Developmental assessment on 6 months CGA follow up

Developmental assessment	Culture positive cases	Culture negative controls	p value
Developmental Quotient <70	17 (26%)	2 (2%)	<0.00001
Mean mental age (months)	4.63(±0.77)	5.24 (±0.55)	<0.00001
Mean mental Quotient	77.7 (±13.1)	84.8 (±9.2)	<0.00001
Mean motor age (months)	4.39 (±0.75)	4.47 (±0.61)	<0.0001
Mean motor Quotient	73.46 (±13.1)	82.7 (±10.1)	<0.00001
Mean developmental age (months)	4.52 (±0.7)	4.86 (±0.39)	0.0001
Mean developmental Quotient (DASII)	76.3 (±12.2)	83.8 (±9.8)	<0.001

After6monthsoffollow-up,17/65 (26.2%) of culture-positive group and 2/90(2.2%)of culture-negativegroup had developmental delay.Cerebral palsy (CP) was reported in 7 (3.2%) of sepsis group and 1 (0.4%) control. Among the sepsis group, 4 out of 7 infants withcerebral palsy patients were infected with gram-negative organisms and 2were infected with gram-positive organisms and one had fungal sepsis intheirneonatalperiod.

Gestational age, birthweight,antenatal steroidadministration,modeof delivery,theextentofresuscitation,sepsisscreen,IVH, necrotizingenterocolitis,mechanicalventilation,BPD andretinopathy of prematurity were set as predictable covariates. Multivariateanalysisresultsofdefinedcovariatesand mentalagehasnotshownstatistical significance (r2 = 0.1202, P = 0.7702). Hence, an infant's mentalageat6monthsCGAwasnotalteredorinfluenced bycovariates.Developmental age (r2= 0.2102, P=0.2601) and developmental delay (r2=0.1159, P=0.7937) at 6 months of age were also not significantly influencedbycovariates. However,motorageat6monthsCGAwas significantly influencedbycovariates(r2=0.2966,P=0.0433).

There was a significant difference noted in neurodevelopment between the two study groups (p<0.00001).

VI. DISCUSSION

The incidence of VLBW births is a major public health problem with significant medical and financial impact due to the concomitant increase in long term complications. The present prospective, cohort study focusedon finding the bacteriological profile of NICU and generating evidence for growth faltering and neurodevelopmental impairment among VLBWinfantswithsepsisincomparisonwithVLBWinfantswithoutsepsis.

109VLBWbabieswhoreblood culturepositivewereincludedinthe studyascases with109 cultures negative VLBW babies as controls. The case and control cohorts were identical for gestational age and gendereliminatingbiasin neurodevelopment.3-to-10-fold higher incidence of infections is seen in preterm neonates in comparison to full-term normal birth weight infants[1].

Inthepresentstudy, thespectrumoforganismsisolatedfrombloodculturepositiveVLBWneonateswaspredominantlyGram-negative.Klebsiellapneumoniae,(30cases-27.5%)standsouttobethemostcommon organism isolated from the blood culture from our units contributing tomortality as well as neurodevelopmental impairment followedbyE.coli, CandidaandCoNS. Various Indian studies by Sharma et al[2], Jyothi et al.[3] reported that Klebsiella is the most predominantorganism in NICU followed by fungus and CoNS. In the present study, CoNS was isolated from both EOS and LOS cases. Candida species was the most commonfungalpathogenisolatedfrominfantswithsepsis.Infantswithlowergestational age had a higher incidence of sepsis. Our results were consistent

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with studies conducted by Kaufman et al[4] and Stoll et al[5].

In our NICU, more so in the extramural unit, Carbapenem-resistant Klebsiella and E. coli were isolated as majority cases had received multiple courses of empirical antibiotictreatment before admission. The growth of Multidrug-resistant(MDR) organismsportendsagrimoutcomeconcerningbothmortalityandneurodevelopmental impairment. These particular cohorts of organisms havebecomenotonlyatherapeuticchallengebutalsoathreattoexistingneonatesduetotheriskofcross-infection.This also requires prolonged treatment with higher antibiotics like ColistinandTigecyclinewhichaddscost to existingtreatment. A study done by Siddiqui et al showed Klebsiella pneumoniae (37.5%) to be the most predominant pathogen in both early-onset (23.1%) and late-onset (46.7%) sepsis with increasing antibiotic resistance, even to amikacin (76.5%), cephalosporins (78%) and carbapenems (60%) thus emphasizing the need of antibiotic susceptibility testing[6]. Mukherjee et al reviewed the emergence of a more invasive and highly pathogenic hypervirulent K. pneumoniae (hvKP) pathotype which greatly limits the available therapeutic options in neonates with a compromised defence system[7]. Infectionscausedbycarbapenem-resistantEnterobacteriaceae(CRE),especiallymetallo-β-lactamase(NDM)-producingEscherichiacoli,havebecomeaglobaltherapeutic challengeinclinicaland publichealthsettings. Mostoftheneonateswith MDR hadrefractorysepticshockandmultiorgandysfunction especially when there was a delay in isolation of the organism.

In the studies done by LJ. Schlapbach et al.[8]and Divyen KShah et al.[9]– CoNS was the most common organism causing neonatalsepsis, especially inmostindustrializedcountries.Preterm infants often require central venous accessalong with compromised host defence. Group B Streptococcus was considered as an important agent associated with early- onset sepsis, but the recent studies show a decreasing trend in the incidence of this pathogen[10]. Group B Streptococcus was not isolated from any neonate in our study.

Inthepresentstudy,themortalitywashighestinsepsisduetoAcinetobacter (58.3%) followed by Klebsiella (40.0%), CoNS (40.0%), and Pseudomonas (40.0%). Neurodevelopmental impairment among survivorswashighestinsepsiscausedbyPseudomonas (66.6%),followedbyS.aureus(40.0%),and E.coli(36.3%). Culture-proven sepsis infants had significantly higher mortality comparedtoculture-negativeinfants(35.7%versus15.5%).Kaufman D et al.[4] and Stoll BJ et al[5] study results regarding mortality were in agreement withour results. Singh et al. also have reported similar observation with mortality among the culture-positive and culture-negative newborns being 41.2% and 17.5% respectively[11]. In our NICU, infants with gram-negative sepsis had shown ahigher mortality rate. However, Stoll BJ et al., reported that newborns withgram-positiveandfungalsepsishadhighermortalityin their study[5].

65 cases and 90 controls were included intheanalysisforneurodevelopment after completed follow up till 6months CGA. At 6 months follow up, 52 (80.0%) infants in culture-positive cases and 67(74.4%) in the culture-negative group had length less than 10th centile**.** At the end of 6 months of age 36 (55.37%) infants in the sepsisgroup and 29 (32.2%) infants in the control group had poor postnatal headgrowth with a head circumference less than 10th centile. This difference isstatisticallysignificant(pvalue=0.009).Underdeveloped headcircumferencecorrelateswithlowercognitivefunctionlaterinlife,implyinganassociationbetween postnatalheadgrowthandneurodevelopmentaloutcome.Both these findingsareinagreementwiththeStoll et al. study[5].

Even though there is growth faltering inboththegroups'catch-up growth was much lower in the culture-positive group. Multipleetiologicalfactorsinfluencethegrowth.Thepresentstudyshowsthatsepsis is an additional factor adversely affecting growth. Laxman Singh etal. in their study found that weight, length, and head circumference weresignificantly lower at 6months of follow-up in infants with culture-positivesepsis compared to controls[11]. Pawar J et al. in their study did not find anysignificant difference in weight, length, and head circumference between culture positive groups and culture negative groups at 9-15 months of CGA[12].

Regarding the impact of perinatal infection on neurodevelopment, there is abundant literature emphasizing the causative role ofbacterialproductssuchaslipopolysaccharidesanden dotoxinsinwhite matterinjuryofprematureneonates.Also, thedevelopingpretermbrainisvulnerabletosystemicinflammatorymilieucharacteristicofsepsisaswellascytotoxicandischemicinjuryfromhypotensionandreducedcerebralbloodflow[7].Approximately40%ofpreterm infantscandevelopmildtomoderateneurodevelopmentalimpairment. In our study, at 6month CGA,there

was a significant difference in neurodevelopment between the two groups (p<0.00001). Similarly, a study by Robaina et al.[13]in Cuban very low birth weight infants had reported an increased risk of neurodevelopmentaldisorder in VLBW infants with sepsis (47.4 vs 17.1%; p=0.005). After correcting with other risk factors such asmale sex, BPD, mechanical ventilation, and hyperbilirubinemia, the risk ofsepsiswasshownas significant(odds ratio4.0;CI95%1.1-14.3;p=0.03).

Also, A multicentre Swiss cohort study by Schlapbach et al.[8] reported thatneurodevelopmental impairment (NDI) wasobservedin 34% ofinfantswith proven sepsis compared with 23% uninfected infants (OR: 1.85 [95%CI:1.12–3.05];P=.016).However,NDIwasnotassociatedwithsuspected sepsis (p-value > .05). BPD, retinopathy,ultrasonography of pathologic brainand sepsispredicted the risk of NDI(P<.0001). Separate long-term follow-up studies on preterm infants were published by Wheater M et al.[14]found a causal and strong relationship between cerebralwhitematterdamageandneonatalsepsisatanearlyage.

Themeandevelopmentalquotient(76.31±12.29vs83.81±9.81)motorquotient(73.46±13.13vs82.72±10.17)andmentalquotient(77.72±13.11vs84.81±9.24) was significantly lower in the sepsis group. (P<0.001). Theseresults are comparable to study done by Singh et.al.[11] where D.Q (77.41±12.49vs.84.41±9.21), Mental Quotient (78.89±13.13 vs. 85.61±9.38), and MotorQuotient (74.56±13.43 vs. 83.22±10.07) were significantly lower in theculture-positivegroupcomparedtotheculture-negativegroupintheirstudy. Themean mental age (4.63±0.77 vs.5.24±0.55),mean motor age(4.25±0.80vs.4.32±0.74),andmeandevelopmentalage(4.01±0.42vs. 4.95±0.52) in months were also lower in the culture-positive group.Singh[11]et.al.showedsimilarresultsintheirstudy. Cerebral palsy was reported in 8 (3.6%) infants in the present study.The incidence of cerebral palsyandneurodevelopmentalimpairmentwasloweri nthepresentstudycompared to previous studies by Schlapbach et al.[8] and Stoll et al[5]. In thepresent study,the cerebral palsy rate was more with gram-negative sepsisas compared to gram-positive sepsis whereas Schlapbach et al[8] reported a higher rate ofCPamong infantsinfectedwithGram-positiveorganisms.

Several biological studies confirmed neonatalsepsiscandamagemicrogliaresultinginactivationandexcitotoxicity by reactive oxygen and nitrogen speciesleading to a free radical attack thereby causing death of the vulnerablepre-myelinatingoligodendrocytes. A systematic review of 17 studies on VLBW infants with neonatal sepsis and variable follow up periods from 6-60 monthsconcludedthattheseinfantshavetwicetheriskofneurodevelopmental impairment compared to their non-sepsis counterparts[15]. Hence the long-term neurodevelopmental follow-up in VLBW infants with sepsis is crucial for the early identification ofdevelopmental delay so that targeted interventions can minimizelong-lastingimpairmentsinpromotingintactsurvivalofVLBWneonates. Non-modifiable risk factors which include low birth weight, extremeprematurity, BPD and IVH mayinterferewithbraindevelopmentwhichsubsequentlyaffectsneurodevelopment.Incontrasttotheabove-mentionedriskfactors,sepsis isapreventablecondition.Forbetterneurodevelopmentaloutcomesin VLBWneonates, nosocomial infections are to be prevented by strict adherence to institutional protocols such as minimizing central venouscatheter use, removal of the catheter when no longer used, proper skin care,and earlyenteralfeeding.

VII. LIMITATIONS

FewVLBWnewbornsinthecontrolgroupeventhoughculture-negative had sepsis screen positive. Hence the possibility of sepsiscannot beruled outinthesebabies. The impact of sepsis without meningitis and with meningitis was notassessedseparately.

Althoughgrowthandneurodevelopmentwereassesseduptosixmonths of CGA, a long-term follow-up study is required at least up toschoolagetodeterminetheimpactofsepsisonbehavioralandcognitiveoutcomes

VIII. CONCLUSION

Thepresentstudy concludesthatKlebsiella pneumoniae, E. colifollowed by Candida and CoNS were themostcommonorganismsisolatedfromVLBWinfantswith highest mortality due to Acinetobacter. Neonatalsepsisisanindependentriskfactorforintraventricularhaemorrhage and Necrotizingenterocolitis. Neonatalsepsissignificantlyprolongedthedurationof mechanicalventilation, lengthofNICUstay and caused increased mortality. A lower developmental quotient at 6months corrected age was reported in culture-positive sepsisinfantscomparedtoculture-negativeinfants,hencetheseinfantsneed to befollowedupafterdischargeforplanningearlyinterventionservices.Neonatalsepsis significantly impactsneurodevelopment negativelyand also impairsthesomaticgrowth.

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Conflicts of interest – None

Future directions

A large, multicentre, long-termfollow-up cohort study with a highersample size is warranted to know that how sepsis and other risk factorsimpactontheneurodevelopmentaloutcome of VLBW neonates.

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