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RESEARCH ARTICLE
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A STUDY ON DIAGNOSIS OF NEONATAL SEPSIS IN SEPSIS SCREEN POSITIVE NEONATES BY SIMULTANEOUS TWO SITE BLOOD CULTURE SAMPLE- A PROSPECTIVE COHORT STUDY CONDUCTED AT MGMH, WARANGAL

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ABSTRACT

Background

Neonatal sepsis is a life-threatening condition characterized by systemic infection and inflammatory response in newborns. It remains a major cause of morbidity and mortality in neonates, particularly in low and middle-income countries. Early and accurate diagnosis is essential for the timely initiation of appropriate antibiotic therapy and to improve survival rates.

Materials And Methods

The present prospective cohort study was conducted on 336 neonates admitted to NICU, Department of paediatrics, Mahatma Gandhi Memorial Hospital, Warangal, for a period of 18 months. All the patients fulfilling selection criteria were explained about the details of the disease and a written informed consent was obtained before enrolment. A detailed clinical history and physical examination was carried out on patients, the clinical data of each patient was recorded in the pre-coded clinical proforma designed for the study. The blood culture samples were labeled as sample 1 and sample 2. All the data was documented and analyzed by subjecting to statistical analysis.

Results

Out of 336 babies samples collected over 18 months - Majority of babies had Both cultures negative i.e. 172 babies (51.19%) followed by 75 babies (22.32%) with both positive culture, 49 babies (14.58%) with 2nd culture positive, and finally 40 babies (11.90%) with 1st culture positive. Distribution of cases according to culture grouping VS various risk factors was assessed. Age at time of sampling of blood culture (less than 72 hours and more than 72 hours of age), PROM, Prolonged labor, assisted ventilation, delayed enteral feeds , type of feed (breast milk vs formula

feeds) carried statistical significance. Details of various micro –organisms grown in blood culture are - Both blood cultures negative did not yield any organism in 172(51%). In 38(50.66%), blood culture was positive for klebsiella, 18(24%) Acinetobacter, spp 8(10.6%) Escherichia coli, 5(6.6%), candida albicans, 3(4%), enterococcus 3(4%), pseudomonas, 0(0%). MRSA, 0(0%) citrobacter culture samples. The high positivity of klebsiella is observed in the study followed by acinetobacter, Escherichia coli, candida, enterococcus and pseudomonas. Results showing gram negative organisms are common cause for sepsis in neonatal age group.

Conclusion
From this study, The study reveals that using two simultaneous blood culture samples from different sites significantly improves the diagnostic accuracy for neonatal sepsis, reducing false-negative results and enabling early intervention. In conclusion, this study recommends simultaneous dual-site blood culture method enhances diagnostic precision for neonatal sepsis, allowing for better detection, timely intervention in sepsis screen positive neonates and overall improvement in neonatal mortality and morbidity outcomes.

Key Words: Neonatal Sepsis, Sepsis Screen, Dual Site Blood Culture

INTRODUCTION

Diagnosing neonatal sepsis is notoriously challenging due to the non-specific nature of its clinical manifestations, which can overlap with other neonatal conditions. Symptoms such as temperature instability, respiratory distress, lethargy, and poor feeding are common but not exclusive to sepsis, making clinical diagnosis difficult. The gold standard for the diagnosis of sepsis is the isolation of pathogens from blood cultures. Blood cultures can have a low sensitivity due to the small volume of blood typically drawn from neonates and the intermittent or low-level presence of bacteria in the bloodstream. To address these challenges, the sepsis screen is often employed.

Sepsis screen include: Complete Blood Count (CBC): White blood cell count, immature to total neutrophil ratio (I/T ratio), Erythrocyte sedimentation rate (ESR). C - reactive protein (CRP). Given the limitations of traditional single-site blood culture, simultaneous two site blood culture sampling has been proposed as an enhanced diagnostic method. This approach involves collecting blood samples from two different anatomical sites at the same time. The rationale behind this method includes: Increased Sensitivity: By obtaining a larger overall volume of blood and potentially capturing bacteria from different sites, the likelihood of detecting a bloodstream infection increases. Reduced Contamination: If the same pathogen is isolated from both sites, it is more likely to be a true pathogen rather than a contaminant. Conversely, differing results can help identify contamination.

MATERIALS AND METHODS

The present prospective cohort study was conducted on 336 neonates admitted to NICU, Department of paediatrics, Mahatma Gandhi Memorial Hospital, Warangal, for a period of 18 months. All the patients fulfilling selection criteria were explained about the details of the disease and a written informed consent was obtained before enrolment.

They were informed of their right to withdraw from the study at any stage. A detailed clinical history and physical examination was carried out on patients. The clinical data of each patient was recorded in the pre-coded clinical proforma designed for the study. The blood culture samples were labeled as sample 1 and sample 2. The data was recorded and noted down in the master charts. All the data was documented and analyzed by subjecting to statistical analysis.

Inclusion Criteria

- Neonates of >30 weeks to 28 days of life, admitted to NICU.
- Presence of atleast one clinical feature with 2 or more risk factor for sepsis,
- Foul-smelling liquor or presence of 3 or more risk factors.
- Risk factor for sepsis (prolonged rupture of membranes, foul smelling liquor, maternal fever within 2 weeks of delivery/during labour, multiple vaginal examinations, delayed cry, dai handling, APGAR<4 at 1 minute, prematurity, previous hospital stay and history of faulty feeding).
- Patients willing to give consent, Patients willing to participate

Exclusion Criteria

- Patients who already received antibiotics before blood culture sampling.
- Neonates with local sepsis.
- Patients who were not willing to give consent, Patients not willing to participate.

Sample Size

The study was conducted on 336 neonates.

Procedure

The prospective cohort study was carried out at the NICU, Department of paediatrics at Mahatma Gandhi Memorial Hospital, Warangal. Prior to the procedure, the resident physician or staff should prepare a skin patch around the intended veni-puncture site that is about 5 cm in diameter and use sterile gloves. Thoroughly clean this region with 70% isopropyl alcohol, then povidone-iodine, and finally alcohol once again. Apply povidone-iodine in concentric circles that radiate outward from the center. Before taking a sample, the skin needs to air dry for at least a minute. A blood culture vial holding five to ten milliliters of culture media should be filled with no more than one milliliter of blood, two samples are collected from two different sites, one after the other. Only fresh venipuncture sites should be used for culture collection due to the high risk of contamination associated with samples taken from indwelling lines and catheters. Before any blood cultures are declared sterile, they must be monitored for a minimum of 72 Hours. With the use of enhanced bacteriological methods like BACTEC and BACT/ALERT blood culture systems, it is now feasible to identify bacterial growth in as little as 12 to 24 hours.

Statistical Analysis

The collected data was entered into Microsoft Excel Worksheet-2010 and data was taken into IBM SPSS Statistic for windows, version 24 (IBM Corp., Armonk, N.Y., USA) software for calculation of frequency, percentage, mean, standard deviation and probability value.

Qualitative data was represented in the form of frequency and percentage. Association between qualitative variables was assessed by Chi Square test with continuity correction for 2 x 2 tables and Fisher's exact test for all 2 x 2 tables, where P value of chi square test was not valid due to small counts.

Quantitative data was represented using mean and standard deviation. Analysis of quantitative data within the groups was done using paired t test if data passes 'Normality test'. One Way Analysis (ANOVA) was used to compare more than two groups.

A **'P'** value of <0.05 was considered statistically significant.

RESULTS

Among the study population two site simultaneous blood culture sample was sent in all 336 cases.

Group	Number of Babies(N)	Percentage (%)
1st culture positive	40	11.90
2nd culture positive	49	14.58
Both cultures positive	75	22.32
Both cultures negative	172	51.19
Total	**336**	**100**

Table 1: Distribution of Cases According to Results of Blood Culture

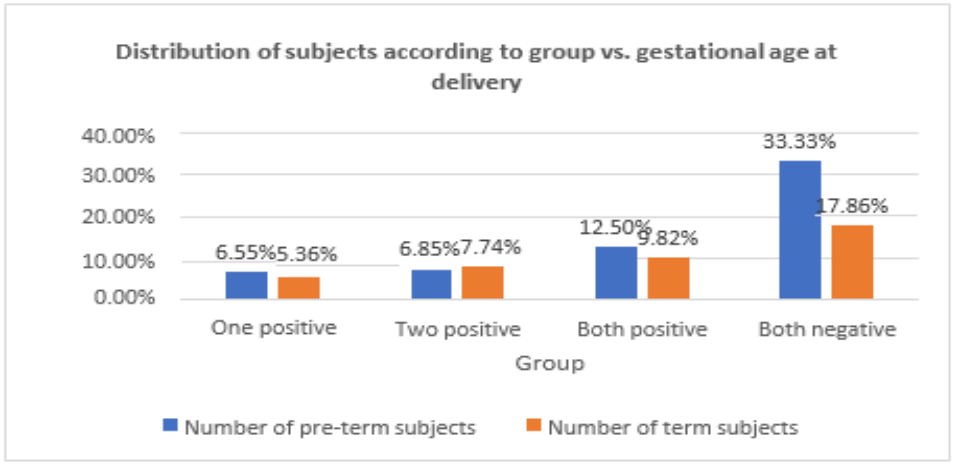

Figure 1: Distribution of Cases According to Term Versus Preterm

P value 0.1044 - statistically not significant

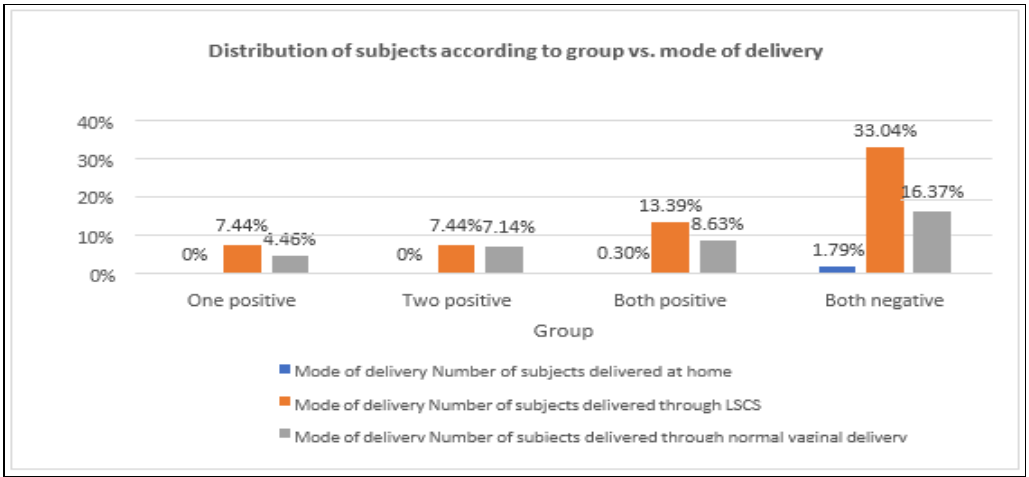

Figure 2: Distribution of Cases According to Group vs Mode of Delivery

P Value - 0.2376 - Statistically not Significant

Group	Age at the Time of Blood Culture		P-Value
	<72 Hours (N %)	>72 Hours (N %)	
1st culture positive	19 (5.65 %)	21 (6.25 %)	<.0001 Highly Significant
2nd culture positive	20 (5.95 %)	29 (8.63 %)	
Both cultures positive	41 (12.20 %)	34 (10.12 %)	
Both cultures negative	129 (38.39 %)	43 (12.80 %)	
Total	**209 (62.20 %)**	**127 (37.80 %)**	

Table 2: Distribution of Cases According to Group vs. Time of Sampling Blood Culture

Group	PROM as a Risk Factor		P-Value
	Absent (N %)	Present (N %)	
1st culture positive	24 (7.14 %)	16 (4.76 %)	0.8938 Highly Significant
2nd culture positive	27 (8.04 %)	22 (6.55 %)	
Both cultures positive	44 (13.10 %)	31 (9.23 %)	
Both cultures negative	94 (27.98 %)	78 (23.21 %)	
Total	**189 (56.25 %)**	**147 (43.75 %)**	

Table 3: Distribution of Babies According to Group vs. PROM as Risk Factor

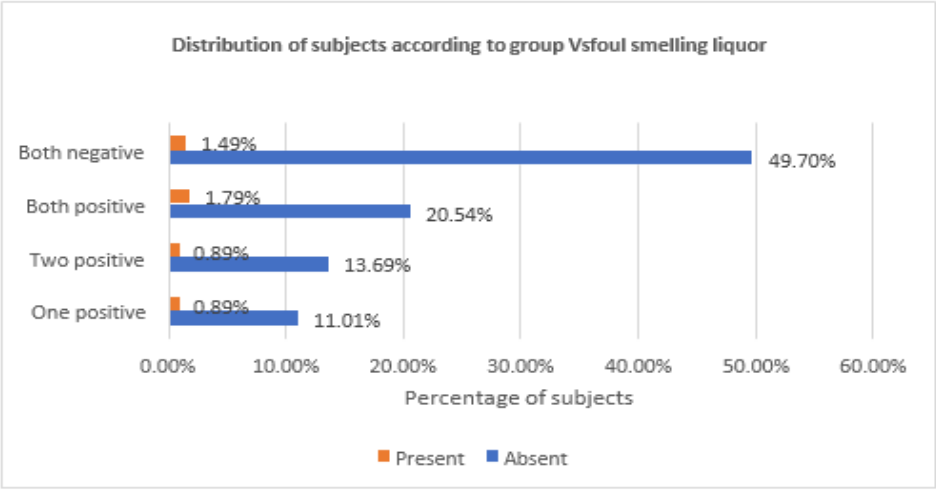

Figure 3: Distribution of Babies According to Group vs. Foul Smelling Liqour as Risk Factor

P Value - 0.304 - Insignificant

Group	Prolonged Labour		P-Value
	Absent (N %)	Present (N %)	
1st culture positive	35 (10.42 %)	5 (1.49 %)	0.05 Significant
2nd culture positive	45 (13.39 %)	4 (1.19 %)	
Both cultures positive	55 (16.37 %)	20 (5.95 %)	
Both cultures negative	139 (41.37 %)	33 (9.82 %)	
Total	**274 (81.55 %)**	**62 (18.45 %)**	

Table 4: Distribution of Cases According to Group vs. Prolonged Labour as Risk Factor

Group	Assisted Ventilation		P-Value
	No (N %)	Yes (N %)	
1st culture positive	30 (8.93 %)	10 (2.98 %)	0.0388 Significant
2nd culture positive	39 (11.61 %)	10 (2.98 %)	
Both cultures positive	48 (14.29 %)	27 (8.04 %)	
Both cultures negative	103 (30.65 %)	69 (20.54 %)	
Total	**220 (65.48 %)**	**116 (34.52 %)**	

Table 5: Distribution of Cases According to Group vs Assisted Ventilation as Risk Factor

Group	Delayed Enteral Feeds		P-Value
	No (N %)	Yes (N %)	
1st culture positive	24 (7.14 %)	16 (4.76 %)	**0.0002 Significant**
2nd culture positive	32 (9.52 %)	17 (5.06 %)	
Both cultures positive	39 (11.61 %)	36 (10.71 %)	
Both cultures negative	60 (17.86 %)	112 (33.33 %)	
Total	**155 (46.13 %)**	**181 (53.87 %)**	

Table 6: Distribution of Cases According to Group vs Delayed Enteral Feeds as Risk Fator

Group	**Type of Feeds**		**P-Value**
	Top Feed (N %)	**Breast Feed (N %)**	
1st culture positive	5 (1.49 %)	9 (2.68 %)	0.0062 Significant
2nd culture positive	2 (0.60 %)	17 (5.06 %)	
Both cultures positive	5 (1.49 %)	22 (6.55 %)	
Both cultures negative	6 (1.79 %)	25 (7.44 %)	
Total	**18 (5.36 %)**	**73 (21.74 %)**	

Table 7: Distribution of Babies According to Group vs. Type of Feed

Organism	**1st Culture Positive**	**2nd Culture Positive**	**Both Culture Positive**
Klebsiella pneumoniae	14	16	38
Acinetobacter	9	14	18
E.coli	6	2	8
Candida albicans	4	8	5
Enterococcus	3	1	3
Pseudomonas	1	7	3
MRSA	2	0	0
citrobacter	1	2	0
Total	**40**	**49**	**75**

Table 8: Distribution of Cases According to Organisms vs. Group

Details of various micro –organisms grown in blood culture are - Both blood cultures negative did not yield any organism in 172(51%). In 38(50.66%), blood culture was positive for klebsiella, 18(24%) Acinetobacter, spp 8(10.6%) Escherichia coli, 5(6.6%), candida albicans, 3(4%), enterococcus 3(4%), pseudomonas, 0(0%). MRSA, 0(0%) citrobacter culture samples.

The high positivity of klebsiella is observed in the study followed by acinetobacter, Escherichia coli, candida, enterococcus and pseudomonas. Results showing gram negative organisms are common cause for sepsis in neonatal age group.

DISCUSSION

At admission, 336 neonates, history was obtained using a systematic proforma, underwent a thorough clinical examination, and sepsis screen and simultaneous two site blood samples were sent. 75 babies (22.32%) with both positive culture, 49 babies (14.58%) with 2nd culture positive, and finally 40 babies (11.90%) with 1st culture positive. 26(7.7%) babies were detected with sepsis by simultaneous two site blood culture sampling, increasing the yield of culture .In a similar prospective study conducted on 475 neonates by taking two blood cultures increased the culture yield by 7.6% by P. Thomar et al.

A prospective study by Struthers et al. 141 aimed to decrease the use of antibiotics by distinguishing pathogenic from contaminant CONS. After 48 hours of life, 100 pairs of cultures were taken from two percutaneous sites in 69 neonates suspected of having sepsis. Additionally, they regarded both positive CONS cultures as infections and one positive culture as a contaminant.

They distinguished between pathogenic CONS in 16 neonates with both positive cultures and contaminant CONS in 5 neonates with growth in just one of the two cultures. On the other hand, a sizable percentage of the isolates in our investigation were classified as contaminants.[3-9]

CONCLUSION

The study reveals that using two simultaneous blood culture samples from different sites significantly improves the diagnostic accuracy for neonatal sepsis, reducing false-negative results and enabling early intervention. This method is particularly beneficial for neonates with severe clinical presentations or those at higher risk due to prematurity, need of assisted ventilation, prior NICU admission. The mode of delivery, especially cesarean sections, had implications for neonatal sepsis, with a notable prevalence in such cases due to possible exposure to nosocomial infections. The term of delivery and age at the time of blood culture were critical factors, with neonates delivered at term and older showing a lower incidence of sepsis. Maternal and neonatal factors were found to have significant associations with the incidence of neonatal sepsis. Preterm infants, those with low birth weight, and those born after prolonged labor, premature rupture of membranes have less number of both culture positives in present study, may be due to advent of elective LSCS, intrapartum antibiotics, maternal education, improved hand hygiene, antenatal registration with regular follow up and better medical services. Assisted ventilation, delayed enteral feeds showed significant correlation with neonatal sepsis. In conclusion, this study recommends simultaneous dual-site blood culture method enhances diagnostic precision for neonatal sepsis, allowing for better detection, timely intervention in sepsis screen positive neonates and overall improvement in neonatal mortality and morbidity outcomes.

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