

Original Research Article

A study of level of procalcitonin as marker of early onset sepsis in neonates

Nirali J. Mehta*, Jigar P. Anadkat, Arpita K. Patel

Department of Paediatrics, SIMMER Medical College, Surat, Gujarat, India

Received: 02 January 2024

Revised: 02 February 2024

Accepted: 06 February 2024

*Correspondence:

Dr. Nirali J. Mehta,

E-mail: drnirali@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Neonatal sepsis is one of the commonest causes of morbidity and mortality. It is one of the four leading causes of morbidity and mortality in India. The purpose of this study was to evaluate the levels of procalcitonin as a rapid diagnostic test, to identify those with infection as soon as possible, and to classify them into definitive, clinical, or no sepsis. The rise in Procalcitonin levels in the neonate with sepsis is very rapid. Hence, it can be used for the diagnosis of early onset neonatal sepsis. Objectives were to estimate the concentration of Procalcitonin for diagnosis of early onset neonatal sepsis and to compare the Procalcitonin levels amongst 3 categories of neonatal sepsis (definite, clinical and no sepsis).

Methods: This is a hospital based analytical prospective study.

Results: 104 babies with early onset sepsis were included in the study from the NICU in tertiary health care center. Procalcitonin is positive in 69 (66.35%) and negative in 35 (33.65%). Out of the total 69 neonates with Procalcitonin positive, 42 (60.8%) neonates are preterm and 27 (39.1%) are term neonates. Out of the total 35 neonates with Procalcitonin negative, 24 (68.5%) neonates are preterm and 11 (31.4%) are term neonates. There was no sepsis observed in 57 (54.8%) of cases, clinical sepsis was observed in 34 (32.6%) of cases and definite sepsis was observed in 13 (12.5%). The mean value of level of Procalcitonin in different categories of sepsis as determined from the data is 3.27 ng/ml in cases of No sepsis, 11.79 ng/ml in cases of clinical sepsis and 17.2 ng/ml in cases of definitive sepsis.

Conclusions: Procalcitonin has good sensitivity and hence can detect most cases of neonatal sepsis and good negative predictive value. Procalcitonin contributes more significantly to the diagnosis of newborn septicemia when paired with additional testing and helps in identifying the categories of sepsis in neonates.

Keywords: Neonates, Early onset sepsis, Procalcitonin

INTRODUCTION

Neonatal sepsis is one of the commonest causes of morbidity and mortality in the neonates in India compared to the developed countries. It is one of the four leading causes of morbidity and mortality in India among the neonates due to delivery and postnatal follow up in an unhealthy environment and low socio-economic state leading to maternal infection and premature delivery. There are various diagnostic tests used for rapid diagnosis

of neonatal sepsis. These rapid diagnostic tests that differentiate infected from non-infected neonates, particularly in the first few days, have the potential to make a significant impact on neonatal care. Early diagnostic tests for infection should have 100% sensitivity and specificity. However, such a test is yet to be discovered. The purpose of this study was to evaluate the levels of procalcitonin as a rapid diagnostic test, to identify those with infection as soon as possible, and to classify them into definitive, clinical, or no sepsis. This

was done in order to clearly distinguish the infected from non-infected neonates among those having the possibility of infection. The rise in Procalcitonin levels in the neonate with sepsis is very rapid. Hence, it can be used for the diagnosis of early onset neonatal sepsis.

Objectives

Objectives of current study were to estimate the concentration of Procalcitonin for diagnosis of early onset neonatal sepsis and to compare the Procalcitonin levels amongst 3 categories of neonatal sepsis (definite, clinical and no sepsis).

METHODS

Study type, location and duration

It is a hospital based analytical prospective study conducted at neonatal intensive care unit (NICU), Department of Pediatrics at SMIMER Hospital. Study was conducted for a period of 9 months and data analysis was conducted over a period of 3 months.

Sample size and sampling technique

Sample size for this study is 104. Sample size calculated by considering the proportion of neonatal sepsis cases admitted in NICU out of total number of patients admitted in NICU according to previous 1 year hospital record data. Allowable error=6%. Purposive sampling was used as sampling technique. Cases were selected randomly from the Pediatric department after applying the inclusion and exclusion criteria.

Inclusion criteria

Any one of the following 3 criteria is to be fulfilled for inclusion of neonate in the study: Neonates born to mothers with at least one of the following risk factors are included, Premature rupture of membrane (PROM) >12 hours, more than 3 vaginal examinations after rupture of membranes, Intrapartum fever (>38° C), Foul smelling liquor, Meconium-stained liquor, Maternal UTI within 2 weeks prior to delivery and Prolonged and difficult delivery with instrumentation. Neonates born in tertiary health centers and outborn neonates which were referred to our hospital within 72 hours of birth. Newborn having sepsis related clinical signs: Temperature instability, Apnea, Bradycardia, Tachycardia, Hypotension/Hypoperfusion, Feeding intolerance, Abdominal distention and Necrotizing enterocolitis.

Exclusion criteria

Exclusion criteria were; Newborn babies with gestational age <28 weeks, Neonates with birth weight less than <1000 gm, Neonates with lethal congenital anomalies, Still born and fetal deaths, Post-dated neonates, Neonates with anemia.

Procedure

Those neonates who developed signs and symptoms of neonatal sepsis within 72 hours of birth in NICU according to inclusion criteria were taken in study. The laboratory parameters were sent for evaluation of neonatal sepsis and categorized the patients into 3 categories (definite, clinical or no sepsis). Determining the level of procalcitonin for the diagnosis of early onset neonatal sepsis. To compare the levels of PCT amongst 3 categories of neonatal sepsis.

Statistical method

Descriptive Chi-square test was used for statistical analysis.

RESULTS

Total 104 babies with early onset sepsis were included in the study from the NICU in tertiary health care center. Males were 60 (57.6%) and females were 44 (42.4%). 81 cases were low birth weight (<2.5 kgs) and 23 babies were of normal weight (>2.5 kgs). 66 cases are preterm (<37 weeks) and 38 cases were term neonates (>37 weeks of gestation).

Table 1: Distribution of cases according to sex (n=104).

Sex	N	%	90%CI
Male	60	57.6	49-65
Female	44	42.4	34-50
Total	104	100.0	-

Table 2: Distribution of cases according to birth weight (n=104).

Birth weight (kg)	N	%	90%CI
<2.5	81	77.8	70-83
>2.5	23	22.2	16-29.6
Total	104	100.0	-

In view of clinical presentation in the neonates, 84 (80.7%) had developed respiratory problems, 35 (33.6%) had developed general signs and symptoms, 13 (12.5%) developed gastrointestinal tract related problems, 12 (11.5%) babies had CNS related problems, 11 (10.5%) babies had cardiovascular problems, 4 (3.8%) babies had hematological problems and 44 (42.3%) babies had multisystem involvement (i.e. >1 system involvement). Among 104 babies, Procalcitonin is positive in 69 (66.3%) with (90% CI, 58.2-73.5) and negative in 35 (33.65%) with (90% CI, 26.4-41.7). Out of the total 35 neonates with Procalcitonin negative (<0.5 ng/ml), 24 (68.5%) neonates are preterm and 11 (31.4%) are term neonates. Out of the total 69 neonates with Procalcitonin positive (>0.5 ng/ml), 42 (60.8%) neonates are preterm and 27 (39.1%) are term neonates. Among 104 cases blood culture was positive in 13 (12.5%) of babies and

negative in 91 (87.5%) of babies. The neonates with blood culture positive are marked as Definite sepsis. The neonates with either 2 clinical signs positive along with 1 laboratory parameter abnormal or vice versa with blood culture negative is marked as Clinical sepsis. The

neonates with no signs of sepsis or abnormal laboratory parameters are marked as No sepsis. Among the 104 cases, there was no sepsis observed in 57 (54.8%) of cases, clinical sepsis was observed in 34 (32.6%) of cases and definite sepsis was observed in 13 (12.5%).

Table 3: Comparison of procalcitonin levels in different categories of sepsis.

Parameters	PCT level (ng/ml)	Total cases	No sepsis	Clinical sepsis	Definitive sepsis	P value (Chi square test)
Negative	<0.5	35	34	0	1	<0.00001
Weakly positive	0.5-2	16	9	5	2	
Positive	2-10	30	10	17	3	
Strongly positive	>10	23	4	12	7	

Table 4: Clinico-laboratory correlation of procalcitonin positivity in early onset sepsis.

Parameters	True positive	False positive	False negative	True negative	Total
Procalcitonin (>0.5 ng/ml)	46	23	1	34	104

Out of the 57 neonates with no sepsis, 34 had negative PCT (<0.5 ng/ml), 9 had weakly positive PCT (0.5-2 ng/ml), 10 had positive PCT (2-10 ng/ml), 4 had strongly positive PCT (>10 ng/ml). Out of the 34 neonates with clinical sepsis, 5 had weakly positive PCT (0.5-2 ng/ml), 17 had positive PCT (2-10 ng/ml), 12 had strongly positive PCT (>10 ng/ml). Out of the 13 neonates with definitive sepsis, 1 had negative PCT (<0.5 ng/ml), 2 had weakly positive PCT (0.5-2 ng/ml), 3 had positive PCT (2-10 ng/ml), 7 had strongly positive PCT (>10 ng/ml). There is statistically significant ($p<0.00001$) association found between the categories of sepsis and Procalcitonin levels, which suggest that if the Procalcitonin level is negative then the chances of patient falling in no sepsis category is more and if the procalcitonin level is high then the chances of patient falling in clinical or definite sepsis is more.

Table 5: Comparison of mean procalcitonin levels in different categories of sepsis (n=104).

Categories of sepsis	Mean procalcitonin level (ng/ml) $\pm$ SD	P value (ANOVA test)
No sepsis	3.27 $\pm$ 14.63	0.002
Clinical sepsis	11.79 $\pm$ 14.63	
Definitive sepsis	17.2 $\pm$ 15.57	

Among the 104 cases, compared with blood culture, clinical signs and symptoms and laboratory parameters, Procalcitonin is true positive in 46 cases, false positive in 23, false negative in 1 and true negative in 34. Among the different categories of neonatal sepsis, the mean procalcitonin levels in case of no sepsis is 3.72 ng/ml $\pm$ 14.63, in clinical sepsis is 11.79 ng/ml $\pm$ 14.63 and in definitive sepsis is 17.2 ng/ml $\pm$ 15.57. The p value is 0.002 (as calculated with ANOVA test), which suggests strong significance between procalcitonin values with different categories of sepsis.

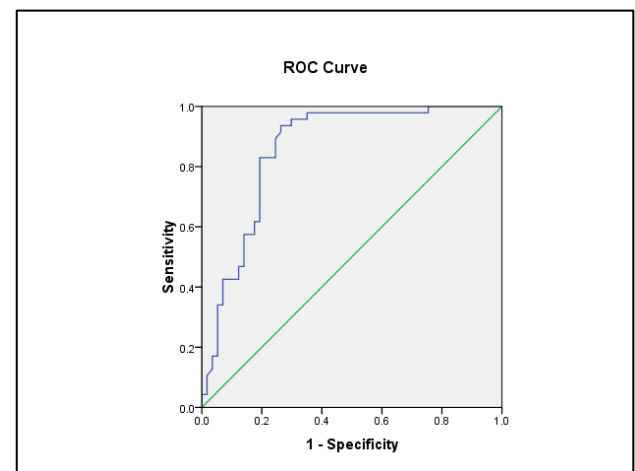


Figure 1: Receiver operating characteristic curve for estimating cut-off value of procalcitonin.

AUC represents the degree or measure of separability. It tells how much the model is capable of distinguishing between classes. By analogy, the Higher the AUC, the better the model is at distinguishing between patients with the disease and no disease. Here in this AUC for Procalcitonin is 0.857 which indicates the model is a good predictor. By a cut-off value of 1.115 ng/ml, Procalcitonin predicted risk of development of sepsis with sensitivity 95.74% and specificity 65.92% in neonates with early onset sepsis. It shows that people with procalcitonin levels above 1.115 ng/ml have a 95.74% chance of developing sepsis.

DISCUSSION

Early diagnosis of neonatal septicemia helps the clinician in instituting antibiotics therapy at the earliest thereby reducing mortality in neonates. Early identification of an infected neonate also helps in avoiding unnecessary treatment of a non-infected neonate. In the present study

an attempt has been made to estimate the level of Procalcitonin in the diagnosis of early onset neonatal

sepsis with optimum sensitivity and specificity.

Table 6: Receiver operating characteristic curve analysis.

Test result variable(s)	AUC	P value	Cut-off value	Sensitivity	Specificity
Procalcitonin	0.857	<0.0001	1.115 ng/ml	95.74%	65.92%

Table 7: Comparison of cut-off value, sensitivity and specificity of procalcitonin in different studies and its significance.

Authors	Cut-off value of procalcitonin (ng/ml)	Sensitivity (%)	Specificity (%)
Mishra et al²	2.5	82	87
Ramsthaler et al³	2	86.96	94.39
Pamela et al⁴	0.5	57	85
Present study	1.115	95.74	65.92

Table 8: Comparison of mean procalcitonin values in different categories of neonatal sepsis.

Authors	Mean Procalcitonin value (ng/ml)			P value
	No Sepsis	Clinical Sepsis	Definitive Sepsis	
Daynia et al⁵	0.4	2.55	7.0	<0.0001
Park et al⁶	0.21	15.64	56.27	<0.001
Gupta et al⁷	0.433	52.22	27.95	0.001
Present Study	3.27	11.79	17.2	0.002

Here for the convenience of the study we have categorized the patients in no sepsis, clinical and definite sepsis. In the present study, the procalcitonin cut-off value as determined from the ROC curve is found out to be 1.115 ng/ml which showed sensitivity of 95.74% and specificity of 65.92%. In comparison to other studies, our study has much more sensitivity than other studies and is near to the study Ramsthaler et al.³ The specificity in our study is quite low as compared to other studies.

In the present study the mean Procalcitonin value in different categories of sepsis i.e no sepsis, clinical sepsis and definitive sepsis is much higher as compared to the mean Procalcitonin value in the study Daynia et al and less as compared to the study Park et al and Gupta et al.⁵⁻⁷ In all the studies Procalcitonin proved to be a good marker for the diagnosis of neonatal sepsis and also the level of Procalcitonin was higher in patients of Definitive sepsis as compared to Clinical sepsis and least in No sepsis patients. However, in the study Gupta et al the mean Procalcitonin level was more in case of clinical sepsis as compared to definite sepsis.⁷ The level of Procalcitonin also helps in categorizing the patients in different categories of sepsis.

Limitations

Since there are no standard definitions for the categorization of sepsis with regard to clinical and laboratory criteria, we attempted to follow the categorization of sepsis as mentioned in other studies reviewed by us. The study was limited to one tertiary care center catering to urban population with relatively small

sample size hence the results of this study cannot be generalized for other settings and still more studies are required for the significance of this test.

CONCLUSION

Procalcitonin testing for sepsis is expensive but has been demonstrated in numerous trials to be a good indicator, particularly for detecting early-onset sepsis, but financial gains of avoiding antibiotic expenses could compensate. Procalcitonin has good sensitivity and hence can detect most cases of neonatal sepsis and good negative predictive value, which will lead to decrease in the number of patients treated unnecessarily. Procalcitonin contributes more significantly to the diagnosis of newborn septicemia when paired with additional testing and helps in identifying the categories of sepsis in neonates.

Recommendations

This study corroborates the utility of procalcitonin as an early diagnostic marker in early onset sepsis in neonates.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

- Aggarwal R, Sarkar N, Deorari AK, Paul VK. Sepsis in the newborn. Indian J Pediatr. 2001;68(12):1143-7.

2. Jeeva SM, Ramesh A, Ashok KD, Vinod KP. Sepsis in the newborn. *Indian J Pediatr.* 2008;75:261-6.
3. Verganano S, Sharland M, Pkazembe A. Neonatal sepsis: an international perspective. *Arch Dis Child Fetal Neonatal.* 2005;90:220-4.
4. National Neonatal Perinatal Database, Report 2002-03. Available at: https://www.newbornwhocc.org/pdf/HRRC-Report_2002-03.pdf. Accessed on 20 November 2023.
5. Singh M. *Care of the Newborn.* 6th ed. India: Sagar Publishers; 2004.
6. Betty C, Inderpreet S. Early Onset of Neonatal Sepsis. *Indian J Pediatr.* 2005;72:23-6.
7. Tallur SS, Kasturi AV, Shobha D Nadgir, Krishna BVS. Clinicobacteriological Study of neonatal septicemia in Hubli. *Indian J Pediatr.* 2000;67(3):169-74.
8. Raghavan M, Mondal GP, Bhatt V, Srinivasan S. Perinatal risk factors in neonatal infections. *Indian J Pediatr.* 1992;59:335-440.
9. Roy I, Jain A, Kumar M, Agarwal SK. Bacteriology of neonatal septicemia in a Tertiary care Hospital of Northern India. *Indian J Med Microbiol.* 2002;20(3): 156-9.
10. Nawshad ASM, Azad MAK, Mahbul H, Darmstadt GL. Clinical and bacteriological profile of neonatal septicemia in a tertiary level Pediatric Hospital in Bangladesh. *Indian Pediatr.* 2002;39:1034-8.
11. Gerdes JS, Polin R. Early diagnosis and treatment of neonatal sepsis. *Indian J Pediatr.* 1998;65:63-71.
12. Abida M, Hasani SE, Khan HM, Ahmed AJ. Nosocomial infections in newborn. *Indian Pediatr.* 2001;38:68-71.
13. Kilbride HW, Powers R, Wirtschafter DD, Sheehan MB. Evaluation and development of potentially better practices to prevent neonatal Nosocomial bacteremia. *Pediatrics.* 2003;111:e504-18.
14. Kuruvilla KA, Pillai S, Jesudason M. Bacterial Profile of Sepsis in a Neonatal unit in South India. *Indian Pediatr.* 1998;35:851-8.
15. Bhattacharya S. Blood culture in India: a proposal for a national programme for early detection of sepsis. *Indian J Med Microbiol.* 2005;23:220-6.

Cite this article as: Mehta NJ, Anadkat JP, Patel AK. A study of level of procalcitonin as marker of early onset sepsis in neonates. *Int J Contemp Pediatr* 2024;11:277-81.