Use of Sepsis Screening Tests to predict severe Bacterial Infections in Infants beyond Neonatal Age

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ABSTRACT

A single-centre prospective case control study was done to find out the role of conventional sepsis screening tests for diagnosing serious bacterial infections in infants beyond neonatal age group. Sepsis screening tests and blood culture were performed in 41 admitted infants between 1 month to 1 year of age with suspected septicemia and in 24 healthy children of this age group (controls). 9 cases (21.90%) were blood culture positive (proved sepsis). There was statistically significant difference between µ ESR and TLC (p<0.001). µ ESR, CRP and toxic granules in neutrophils had 100% sensitivity, 100% negative predictive value and 80% accuracy. All these tests are simple, low cost, easily available and rapid in nature which helps physician in deciding about appropriate management at the earliest.

Key words: *Sepsis, Infant, Culture, Screening test*

INTRODUCTION

Infections are the leading cause of mortality in infants especially in developing countries like India.[1] Sepsis is a serious medical condition that is characterized by a whole-body inflammatory state (SIRS) and the presence of a known or suspected infectious agent.[1,2]

Sepsis can have varied clinical presentations, more so in children and young infants. A high index of clinical suspicion is required on the part of the clinician so as it can be diagnosed at its earliest and most of the dreaded complications can be prevented. Since, the outcome of infants with sepsis depends on early diagnosis and adequate treatment; there arises a need for certain diagnostic tests which predicts the presence of infection. CRP, µ ESR, TLC, presence of toxic granules and band cell in neutrophils and I: T ratio are simple and rapid diagnostic tests evaluated both in single and in combination for their efficacy in early diagnosis of bacterial infections. When at least two of these parameters are positive, it gives the sensitivity and specificity of 93 and 88 percent respectively.[3,4]

Clinical diagnosis of a severe bacterial infection in infants is a difficult task due to its protean manifestation. So we have planned this study to evaluate the role of sepsis screening tests (micro-ESR, serum CRP, white cell count and toxic granules and Band cell in neutrophils both in single and in combination) for diagnosing serious bacterial infections in infants beyond neonatal age group and compare these tests with the blood culture for the diagnosis of serious bacterial infections.

MATERIAL AND METHODS

The Study was done at Department of Pediatrics, Dr S.N. Medical College, Jodhpur. This single-centre prospective case control study was conducted over a period of six months after approval from the institute's ethical committee

Inclusion Criteria:

Infants aged 1-12 months having suspected septicaemia, meningitis, consolidation (pneumonia) and urinary tract infection. Healthy children in this age group served as controls.

Exclusion Criteria:

1. Patient already on antibiotic therapy.
2. Conditions which alter ESR apart from infection like anaemia, congenital cyanotic heart disease, congestive cardiac failure.

Sepsis screening tests (CRP, TLC, micro ESR, band cells, toxic granules, and I/T ratio) and blood culture were performed in 41 admitted infants between 1 month and 1 year of age with suspected septicemia, meningitis, consolidation (pneumonia) and urinary tract infection and in 24 healthy children of this age group who served as controls. Sensitivity and specificity of these tests to diagnose bacterial infection were calculated by comparing these with the gold standard test of blood culture.

RESULTS

A total of 65 children one month to one year of age were enrolled in the study. Out of 65 children 9 cases had blood culture proven septicemia, 32 were cases of blood culture negative probable septicemia and 24 children were healthy control without any evidence of infection. Following are the salient observations from the present study.

51% children in case group and 29% in control group were of age group 1-3 months. Male and female distribution of cases and control group ($X^2 = 0.31$, p= > 0.7) were matched. Out of 41 cases 9 (21.90%) were

blood culture positive (proved sepsis) and the remaining blood culture negative subjects were considered probable sepsis. Important signs observed were pyrexia in 100% culture proved cases and 93.75% of probable cases followed by irritability, refusal to feed, respiratory distress & convulsions.

Among 41 cases of sepsis group meningitis was present in 7(17.07%) cases while consolidation in 5 (12.19%) cases. Culture proved UTI was present in 3 (7.31%) cases. Blood culture was positive in 9 (21.90%) cases. In 5 (54.44%) cases coagulase positive staphylococcus aureus was grown followed by 2 (22.22%) coagulase negative, staphylococcus aureus, 1 (11.11%) Klebsiella and in 1 case (11.11%) pseudomonas was grown. Culture proved urinary tract infection was present in 7.31% of cases and organisms grown were E.Coli and Klebsiella.

Raised CRP level were found in large number of infants with proven sepsis (77.77%) and in probable sepsis (59.37%). The difference in CRP of proven sepsis and probable sepsis was statistically not significant. Raised micro ESR, abnormal TLC, Toxic granules in polymorpho- nuclear cells was observed in 66.66% cases of proven sepsis. Highest sensitivity for single test was observed for CRP (>1.2μg/ml) (77.77%), followed by equal sensitivity of 66.66% for abnormal TLC, raised Micro-ESR and Toxic Granule. Least sensitivity was observed for I/T ratio and Band cells (33.33% each). I/T ratio (>0.2) showed highest specificity (87.50%) followed by Band cells (78.12%). CRP Abnormal TLC, Micro-ESR and Toxic Granule have shown specificities of 40.62%, 31.25%, 21.87%, and 75.75% respectively.

Positive predictive value was highest and equal for I/T ratio and Toxic granules (42.85%). Positive predictive value was almost similar for other parameters. Negative predictive value was highest for Toxic granule 89.28% followed by CRP 86.66%. Least negative predictive value was observed with micro-ESR. Accuracy was highest with I/T ratio (75.60%) followed by toxic granules (73.80%).

Among two tests combination, a combination of micro-ESR and CRP had a sensitivity of 83.33% and specificity of 88.23% with negative predictive value of 93.75%. Combinations of micro-ESR+TLC have shown maximum Specificity of 90.47% and negative predictive value of 94.70% respectively. A similar accuracy was observed with combination of micro-ESR +CRP and micro ESR+TLC i.e. 86.95% and 86.20% respectively.

When three tests were combined, a combination of micro-ESR, CRP and Toxic Granule had 100% sensitivity, negative predictive value and 80% accuracy. A combination of abnormal TLC, micro-ESR and CRP had a specificity of 90%.

DISCUSSION

The presence of severe bacterial infection in infants may not be quite revealing as it does in older children. The clinical manifestations are protean and often subtle. Moreover, certain viral infections and metabolic conditions may mimic a child with severe bacterial infection. So there is a need for a test or group of tests which can detect the condition pretty early when clinical features are not helpful and which could also indicate the presence of infection when blood culture results are not contributing. Some of the simple, rapid haematological tests like micro-ESR, CRP, blood counts and peripheral smear examination have been evaluated for their usefulness in predicting septicaemia in neonates and infants up to 3 months of age by many investigators[5]. There are very few studies which have evaluated these tests in invasive bacterial infections in infants up to 1 year of age. In this study we have evaluated the role of these tests both individually and in union in predicting the presence of serious bacterial infections like septicaemia, meningitis, pneumonia and urinary tract infection in infants beyond neonatal age group (i.e. 1 month to 12 months).

In our study septicaemia was seen predominantly (73.17%) in male children in both sepsis and probable sepsis group. St. Geme[6] et al and Washburn TC et al[7] also observed that male infants are two to six times more likely to develop sepsis than females. Higher infection rate in males has been reported by other authors too like Gluck et al (1966)[8] and Singh M (1985).[9]

Among culture proven septicemia 33.33% cases each were LBW, had Failure to thrive (FTT) and were placed in PEM grade III. FTT was present in 37.50% of probable group of sepsis. Misra et al[10] studied 128 children of which 50 were controls and 78 were cases of suspected septicemia. 54% were of PEM III, 30% LBW and 34% FTT.

In our study CRP had a maximum sensitivity of 77.77%. Micro ESR, TLC and toxic granules in neutrophils had 66.66% sensitivity. I/T ratio had maximum specificity of 87.5% followed by band cells with 78.12%. I/T ratio also had maximum positive predictive value of 42.85%. Toxic granules, CRP and I/T ratio had negative predictive value of 89.2, 86.6 and 82.3 respectively. Borna et al[11] reported that CRP had the best sensitivity (79%) and negative predictive value (97%), but poor positive predictive value (36%), and its specificity was 85%. Lacour et al[12] also found that in detection of severe bacterial infection in infants up to the age of 36 months CRP had a sensitivity of 89% and a specificity of 75%. Okolo AA et al[13] observed that mini-ESR alone yields, a sensitivity of 96.9%, specificity of 90% and a predictive value of 94%. Mc Carthy et al[14] observed that the risk of bacteraemia was increased threefold and the risk of pneumonia was increased twofold in children with a TLC count >15000/cu mm. Virendra Kumar et al[15] had observed a

very high sensitivity of 95% and a specificity of 89% for toxic-granules. Walliullah et al[16] observed. In our study Combinations of micro-ESR+TLC have shown maximum specificity of 90.47% and negative predictive value of 94.70% respectively. A sensitivity of 75% was observed with combination of these two tests. A similar accuracy was observed with combination of micro-ESR +CRP and micro ESR+TLC i.e. 86.95% and 86.20% respectively. Anita Sharma et al[17] had reported a sensitivity of 80% and specificity of 88.9% with CRP and toxic-granules in neonates with septicaemia. Misra et al[12] had observed a combination of micro-ESR and abnormal TLC as the best among two test combination When three tests were combined, a combination of micro-ESR, CRP and toxic-granule had 100% sensitivity, 100% negative predictive value and 80% accuracy. Micro-ESR and CRP had a specificity of 90%. Anita sharma et al[17] also observed that the above three tests had the highest.

To conclude, the study indicates that along with a meticulous clinical examination, a collective and maximum use of few screening tests like micro-ESR, CRP, Total Leucocyte Count and peripheral blood smear examination is a definitive aid to the diagnosis of sepsis in view of the limitations of the gold standard i.e. blood culture. Though these tests cannot replace the culture studies but because of their simlicity, low cost, easy availability and rapid nature they help the treating physician in deciding about appropriate management at the earliest.

Table 1: Sepsis Screen in Sepsis group and Control group

Parameters		Sepsis group		Total (41) (%)	Control Group
		Proved	Probable		(n=24) (%)
		(n=9)(%) (b)	(n=32)(%) (a)		(A)
Micro-ESR:	>15mm/hr.	6 (66.66)	25 (78.12)	31 (75.6)	3 (12.50)
	<15mm/hr.	3 (33.34)	7 (21.88)	10 (24.4)	21 (87.5)
CRP:	>1.2 mg/dl	7 (77.77)	13 (40.63)	20 (48.78)	3 (12.5)
	<1.2 mg/dl	2 (22.23)	19 (59.37)	21 (51.22)	21 (87.5)
Toxic Granules in Polymorphs	Present	6 (66.66)	8 (25)	14 (34.15)	1 (4)
	Absent	3 (33.33)	24 (75)	27 (65.85)	23 (96)
TLC	[< 5000 & >15000]	6 (66.66)	22 (68.75)	28 (68.3)	6 (25)
	N [5000-15000]	3 (33.34)	10 (31.25)	13 (31.7)	18 (75)
I/T ratio	(> 0.2)	3 (33.34)	4 (12.5)	7 (17)	0
	(<0.2)	6 (66.66)	28 (87.5)	34 (83)	(100)
Band Cell	Present	3 (33.34)	7 (21.88)	28 (68.3)	0
	Absent	6 (66.66)	25 (78.12)	13 (31.7)	(100)

A - Control group (n=24), a - Probable (n=32), b- Proved (n=9)

Table 2: Sensitivity, specificity and predictive value of various tests used for diagnosis of culture and probable sepsis

Parameters		Blood Culture		Sensiti-vity %	Speci-ficity %	PPV %	NPV %	Accuracy %
		(+)	(-)					
CRP (> 1.2μg/ml)	+ -	7 2	19 13	77.77	40.62	26.92	86.66	48.78
I/T ratio(> 0.2)	+ -	3 6	4 28	33.33	87.5	42.85	82.35	75.60
TLC [< 5000 & >15000	+ -	6 3	22 10	66.66	31.25	21.24	76.92	39.02
Micro-ESR (mm/Ist hr)	+ -	6 3	25 07	66.66	21.87	19.35	70	31.70
Toxic Granule in Polymorphs (+/-)	+ -	6 3	08 24	66.66	75.75	42.85	89.28	73.80
Band Cell	+ -	3 6	07 25	33.33	78.12	30	80.64	68.29

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