

FUNCTIONAL AND BEHAVIORAL RESPONSES AS MARKER OF ILLNESS, AND OUTCOME IN INFANTS UNDER 2 MONTHS

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ABSTRACT

Value of abnormal findings on 11 functional and behavioral items were studied for identification of serious illness, presence of bacteremia and prediction of the outcome (recovery or death) in infants upto 2 months of age. All the items were graded on a 3 point scale (0,1 and 2) in the ascending order of severity. A total of 116 infants who were being evaluated for suspected sepsis were enrolled. The assessment was completed before detailed history and physical examination. Significant associations were observed between presence of serious illness and six items by χ^2 -test and/or Pearson's correlation and multiple stepwise regression analysis. These were decreased activity, abnormal quality of cry, presence of pallor, fast breathing, decreased consolability, and consciousness level. The sensitivity of the six item model was >90% and negative predictive value 95%. The negative predictive value of several individual items was also above 90%. Consciousness level was the most important predictor of the outcome followed by poor feeding, hydration, color, consolability and abnormal expression (combined multiple $R=0.51$). A total score of 7 or more on above six items had a sensitivity of 80%, and negative predictive value of 97% for death. In conclusion, behavior and functional responses (as mentioned above) were fairly useful in predicting the outcome and/or the severity of the illness. These items may be combined to develop a scale to help in therapeutic decision making.

Keywords: Bacteremia, Behavioral responses, Infants.

During physical examination, the young child with a potentially serious illness may not manifest specific findings suggestive of the illness. Experienced physicians often find an overall 'subjective' assessment of the severity of underlying illness useful in final decision making. Most of this assessment is based on evaluation of behavioral and functional response of the child such as irritability, abnormal cry, poor feeding, lethargy, drowsiness, refusal to play, pallor, and rapid or irregular breathing(1-3). In the last decade several studies have aimed at enlisting these signs for an objective assessment of febrile as well as a febrile sick children(1 -5). Based on these signs, observation scales formally quantifying this assessment have been devised to evaluate severity of illness in febrile children(5,6). Such scales have proved valuable in older infants and children(2-5) but may not be completely predictive of severe illness in very young febrile infants(6).

The objective of this study were to determine value of certain abnormal functional and behavioral symptoms (Table I) in (i) identification of serious illness; (ii) prediction of the outcome of the illness (recovery or death); and (iii) in discriminating bacteremic infants from those without bacteremia in infants upto 2 months of age.

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TABLE I—Variables Used for Infant Assessment, and their Grading

Variables	Impairment grading		
	Nil (0)	Mild-Moderate (1)	Severe (2)
1. Feeding	Feeding well	Feeding, but not well ^a	Not feeding at all
2. Spontaneous activity level	Normal	Reduced, less than normal ^b	Not playful/active at all
3. Quality of cry	Strong, normal content	Whimpering or sobbing	Weak or moaning or not crying
4. Facial expression	Normal, contented, Alert look	Anxious/dull	Frowning, expression of pain
5. Eyes movements	Looks around, Makes eye contact	Closed/opens briefly	Not interested in looking around/does not open
6. Consolability	Contented, no cry on for longer period	Irritable ^c /cries off and on	Continued cry
7. Consciousness level	Awake Asleep Wakes up on stimulation	Less alert ^d , opens eyes and on, wakes up with difficulty	Altered, obtunded/does not wake up/coma
8. Color	Pink extremities	Pale ashen/mottled	Pale/cyanotic
9. Hydration	Normal	-	Dehydrated
10. Respiratory efforts	Normal, no distress	Fast breathing	Labored and fast breathing
11. Temperature	Upto 38°C	38°-39°C	>39°C

a – fed slowly or took less amount than usual.

b – has been moving arms and legs less than usual.

c – more fractious and difficult to settle than usual.

d – less alert than usual.

Material and Methods

A total of 116 infants upto 2 months of age who were evaluated for suspected sepsis were enrolled in this prospective study. They had presented with either

history of fever or one or more of the following symptoms: poor activity and feeding, breathing problems, seizures, loose stools, abdominal distension or skin and soft tissue infection to Pediatric Emergency of Nehru Hospital,

PGIMER, Chandigarh during a two year period. All the infants were assessed for abnormal response on 11 functional and behavioral items. Each item was given an arbitrary score of 0,1 and 2 in the ascending order of the severity (*Table 1*). These items were chosen on the basis of literature and personal experience. Initial assessment was performed by a resident doctor, while the infant was seated on the parent's lap. Items that required observation only were assessed first followed by those which needed interaction with the infant. Every attempt was made to place the child in a state of quiet wakefulness prior to the assessment. After the observation, the history and physical examination were performed.

After clinical assessment, all the infants had a standard set of investigations carried out (blood counts, micro ESR, hematocrit, culture). Lumbar puncture for CSF cell count, biochemical analysis and culture, and chest X-ray were done routinely for all babies upto 4 weeks of age, and thereafter whenever indicated by history or physical examination. Stool culture was done only in those who had diarrhea. Screening for urinary tract infection could not be performed due to the practical difficulties in the emergency area. An earlier study⁽⁷⁾ had shown that only one half of the patients with UTI have abnormal urinalysis and an unacceptably large number of cases yield indeterminate results from culture of a bag specimen. Illnesses requiring hospitalization or intravenous fluids, oxygen therapy such as bacteremia, meningitis, pneumonia, empyema, cellulitis, osteomyelitis, septic arthritis, necrotizing enterocolitis

and gastroenteritis were grouped as serious illness. All the infants were followed up in the hospital to record the final diagnosis and outcome of the illness.

Data Analysis

Contingency table analysis (k^2 test) were done in order to determine those items which had significant association with bacteremia, serious illness and outcome. Pearson's correlation analysis was also performed between observation items score on one hand and score on severity of illness, and the outcome. Multiple stepwise regression (MSR) analysis was done to recognize a minimum number of observation variables (as identified by A.²-test or Pearson's correlation analysis) which when put together will identify at least 95% of all severely ill febrile children.

Sensitivity, specificity and positive and negative predictive value of the variable identified as significant from above analysis were determined for the severity of illness and the outcome.

Results

At the end of the initial history and physical examination a specific diagnosis was arrived at in 26 (22%) of 116 infants studied. In another 40 (28%) infants with localizing signs, a definitive diagnosis could be made after relevant bedside investigation, *viz.*, X-ray chest, lumbar puncture or complete blood count. The remaining 50 infants were categorized as possible sepsis; of these nine had bacteremia. The details of the diagnostic categories and bacterial isolates have been communicated in a previous paper. Score on functional and

behavioral variables in different diagnostic categories are shown in *Table II*.

Severity of Illness

It is apparent from *Table II* that mean scores on the 10 item scale were significantly higher in infants whose final diagnosis indicated a serious illness (10 ± 4) as compared to those with nonspecific illness (5 ± 3) ($p < 0.0001$). The mean age of infants in both the groups was similar (serious illness 27.7 ± 20.5 days, nonspecific illness 26.2 ± 18.3 days.). On Pearson's correlation analysis, except hydration and temperature, all the items showed a significant correlation with presence of severe illness. These items were feeding ($r=0.28$), spontaneous activity level ($r=0.40$), quality of cry ($r=0.29$), facial expression ($r=0.34$), eye movements ($r=0.21$), consolability

TABLE II - Mean±SD Scores on 11 Behavioral and Observation Variables in Different Diagnosis Categories.

Diagnostic category	Mean±SD Score
1. All those with bacteremia or positive culture (n-15)	11±4
2. Pneumonia/empyema	9±3
3. Bronchiolitis (n-14)	9±2
4. Meningitis (n-12)	12±4
5. Localized infections, soft tissue joint (n-10)	9±5
6. Non-specific illness (no focus, negative investigation) (n-33)	5±3
7. Miscellaneous and noninfective illness (n-12)	6±4

$p < 0.0001$ by ANOVA.

($r=0.37$), consciousness ($r=0.48$), color ($r=0.27$), and respiration ($r=0.35$) ($p < 0.05$ for all). Most of these variables showed a significant intercorrelation.

MSR analysis identified six items which added 1% or more to multiple R, hence these were most predictive of severe illness (*Table III*). Out of these six items, three items, viz., spontaneous activity, color and respiration alone had a combined multiple R value of 0.56. The specificity, sensitivity and positive

TABLE III- Results of Multiple Regression Analysis

Variables	Multiple R	R ²	Partial R ²
<i>Serious illness</i>			
Spontaneous activity	.44	.19	.034
Color	.50	.25	.069
Respiration	.56	.32	.088
Quality of cry	.57	.33	.016
Consciousness	.58	.33	.017
Consolability	.59	.34	.012
<i>Outcome</i>			
Consciousness	.43	.19	.146
Feeding	.45	.20	.025
Hydration	.47	.22	.20
Color	.48	.23	.013
Consolability	.49	.24	.016
Facial expression	.51	.26	.012
<i>Bacteremia</i>			
Consolability	.59	.35	.429
Facial expression	.65	.42	.173
Color	.68	.46	.088
Hydration	.69	.48	.036

predictive value of the 6-item model for serious illness were 93%, 42% and 26%, respectively. The negative predictive value of the model was 95%, *i.e.*, if an infant was not impaired on any of the six items, the probability of the child having a serious illness was only 5%.

Outcome

Of 116 infants, 15 (9%) died. The mean \pm SD score in these infants was 12 ± 4 , as compared to 8 ± 3 in those who survived. A significant correlation was also seen between a poor outcome and abnormality on several observation variables individually. These were feeding ($r=0.30$), cry ($r=0.30$) facial expression ($r=0.24$), eyes movements ($r=0.28$), consolability ($r=0.20$), consciousness level ($r=0.46$), and color ($r=0.31$). Contingency table analysis using χ^2 test, also showed a similar significant association between the outcome and abnormality on the above seven observational variables. Of the seven items, only three items, *viz.*, consciousness level, feeding and consolability were picked up as the most predictive on MSR. However, when all the eleven variables were entered in the MSR, three more variables hydration, color, and facies were added to the model (*Table III*).

These six-variables were further analyzed for their ability to predict mortality (*Table IV*). An impaired consciousness level with a total score of >7 on the above six-variables had a sensitivity, specificity, and a positive and negative predictive value of 80%, 89%, 52% and 97%, respectively for mortality.

Bacteremia

Out of 50 infants categorized as

possible sepsis without a focus, 9 had bacteremia. A significant correlation was seen between presence of bacteremia and total score on 11 variables ($r=0.398$). The mean \pm SD score in bacteremic infants was 11.0 ± 3 in contrast to 7 ± 4 in non-bacteremic infants ($p < 0.01$, t-test). A score >10 had a sensitivity, specificity and positive and negative predictive value of 66.6%, 84%, 43% and 92.0%, respectively. Individually, a significant correlation was observed between bacteremia and quality of cry ($r=0.355$), consolability ($r=0.592$), consciousness level ($r=0.305$) and feeding ($r=0.359$). Contingency table analysis also showed a significant association between the above variables and bacteremia (*Table V*). However, the balance of sensitivity, specificity and predictive values of these variables individually was not satisfactory, except that for consolability (*Table V*).

On multiple stepwise regression, in which all the eleven items were entered, a four items model was identified as significant predictor of bacteremia (*Table III*). A score of 5 or more on these 4 items identified 8 of 9 (88.8%) cases of bacteremia with a specificity of 68.5%, and a positive and negative predictive value of 42% and 96%, respectively.

Discussion

The ability of the pediatrician to gain a sense of the well being of the child by observing the child prior to the physical examination is critical in the evaluation of febrile children. The present report has focused on 11 items on history and observation variables with defined three point scales for each item that may help in prediction of serious illness and out-

TABLE IV—Sensitivity (Sn), Specificity (Sp), and Predictive value (PV) Expressed as Percentages, of Selected Observation Variables for Outcome of the Illness in 113 Infants upto 2 Months of Age

Variable	Individual score	Outcome		Sn	Sp	Predictive value (PV)	
		Death (n-15)	Alive (n-98)			+ve	-ve
Feeding	2	11	24	73*	75	31	95
	1	3	61	93 ⁺	13	7	93
	0	1	13				
Cry	2	9	15	60	85	37	93
	1	4	53	87	31	16	94
	0	2	30				
Facial expression	2	10	26	67	73	28	93
	1	4	63	93	9	14	90
	0	1	9				
Eye movements	2	4	9	27	91	31	89
	1	10	45	93	45	21	98
	0	1	44				
Consolability	2	7	14	47	86	33	86
	1	6	69	87	15	13	88
	0	2	15				
Consciousness level	2	4	4	27	96	50	89
	1	10	3	93	64	29	98
	0	1	63				
Color	2	4	4	27	96	50	90
	1	6	27	67	68	24	93
	0	5	67				

All the variables included in the table were significant at least at 0.05 level by χ^2 -test.

*Sn, Sp, and PV are calculated for a score of 2 vs <2.

⁺ Sn, Sp, and PV are calculated for a score of ≥ 1 vs 0.

come. The sensitivity, specificity and predictive value of the individual observation items were studied. Out of these, six items individually had significant association with presence or absence of serious illness and the outcome. Others did not perform as well as these items. These six items were spontaneous activity, cry, consolability, respiration and

consciousness level and color. However, only four items, viz., consolability, facial expression, color and hydration were specific and predicted bacteremia. The actual sensitivity and predictive values of individual items may not be relevant in another study sample with less number of infants with severe illness, but the value of functional and behavioral

TABLE V— Scores Obtained by 50 Infants Without a Focus of Illness on Selected Observation Variables with Respect to Presence or Absence of Bacteremia, and Sensitivity (Sn), Specificity (Sp) and Positive (+ve) and Negative (-ve) Predictive Value (PV) of the Observation Variables.

Variable and score	Number of infants			λ^2 value	Sn	Sp	+ve PV	-ve PV
	Blood culture							
	+ve	-ve						
Consolability	0	0	12	21.5				
	1	2	23					
	2	7	3	17.2	77*	90	64	9
Color	0	3	28					
	1	6	10	3.0	67*	72	35	9
	2	0	1					
Cry	0	0	17	6.4				
	1	6	13					
	2	3	8	4.5	33*	79	27	8
Feeding	0	0	6	4.9				
	1	4	24					
	2	5	8	2.8	55*	79	38	8
Consciousness level	0	1	21	4.1				
	1	8	15	7.1	89*	53	31	9
	2	0	2					
Total of all items	≥ 10	6	6		67	84	50	9
	< 10	3	33					

responses stands out in evaluation of seriousness of illness and possible outcome.

Interestingly, these findings are similar to studies of this nature in older children and in different population groups. Hewson *et al.*(3) in their study of 682 infants under 6 months of age found analysis of baby's functioning as the most important part of assessment of presence of serious illness. Out of 28 symptoms and 46 signs, they found that symptoms of drowsiness (increased sleeping), decreased activity, and weak cry had a positive predictive value of over 50% while individual signs of decreased arousal (decreased aware-

ness, poor eye fixation), poor peripheral circulation (generalized pallor, cold calves) and respiratory compromise had predictive values of more than 65% for serious illness.

In early studies on this subject, authors used a global assessments of febrile infants and found it fairly accurate in identifying infants with serious bacterial infections(1,8-10). In these studies, resident doctors assessed infants as ill, questionable ill or well(8), and gave their impression of the likelihood of sepsis as strong, ambivalent or negative(1,10); or noted them as ill versus not ill(9). The residents were found to base

their assessment on five factors; level of activity, feeding pattern, irritability, responsiveness and ability to be consoled(1,9). Combining data from these four studies, only 0.6% of 326 infants who appeared well were bacteremic compared with 26 (12%) of 209 infants who did not appear well(1,8-10).

A 6-item acute illness observation scale (AIOS), developed by McCarthy *et al.*(5) on children 3 months to 2 years old, has found a wide acceptance. The items used are quality of cry, reaction to parent stimulation, state variation, color, hydration and response (talk, smile) to social overtures. Using these items only 2.7% of patients with a score of <10 had a serious illness. The authors have subsequently demonstrated that incorporation of AIOS in assessment of febrile children three months to two years improves the sensitivity of history and physical examination in detecting serious illness in a hospital emergency room as well as a private practice(11). On the other hand, Dagan *et al.*(12) presented data to show that irritability, lethargy and poor feeding were equally common among infants assessed as 'at

low risk' on 'high risk' (on basis of laboratory data), and infants who had serious bacterial illness (SBI).

Adaptation of the AIOS for infants 4-8 weeks old did not discriminate among infants with or without SBI. Baker *et al.* (13) found it unreliable in a study of 49 infants (1-2 months old, temperature >38.2°C); 22 had serious illness (meningitis -15, UTI - 4, pneumonia and sepsis one each). Of 27 infants with score <10, 40.7% had serious illness whereas of 14 infants with score >16, 42% had serious illness. The study was extended to 126 febrile infants aged 4-8 weeks(14). Of 91 infants who scored <10, 20 (22%) had a SBI. On the other hand, of 20 infants who had a score >16 indicative of serious illness, only 9 (45%) actually had a serious illness. Of the 12 infants with a positive blood, urine, stool, or CSF culture only 4 (33%) infants had a AIOS score of 16 or more.

In conclusion, nine observation items were found fairly useful either as the predictor of serious illness or the outcome of sick infants less than 2 months. A scale combining these 9 items may be a useful tool in assessing

TABLE VI—Sensitivity (Sn), Specificity (Sp), Positive and Negative Predictive Value (PV) of a Score ≥ 10 on a 9 Items Scale for Outcome and Bacteremia.

	Score		Sn	Sp	+vePV	-vePV
	>10	<10				
<i>Outcome</i>						
Dead (n-15)	13	2	86	55	24	97
Alive (n-98)	40	58				
<i>No focus of illness (n-48)</i>						
Bacteremia (n-9)	6	4	67	84	46	92
No bacteremia (n-39)	7	36				

severity of illness and prediction of outcome in sick infants <2 months of age. A score of >10 on these 9 items was sensitive (*Table VI*). However, this will need further evaluation for its validity and practical applicability in therapeutic decision making(15). The findings also illustrate the need to teach resident doctors and parents the importance of behavioral and functional responses of infants as indicators of illness. The tendency for parents to mention more graphic symptoms (such as vomiting, cough, convulsions and diarrhea) and overlook behavioral and functional responses (such as increased sleepiness, decreased activity, and weak cry) has been shown(3).

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