Evaluation of Simple Clinical Signs of Illness in Young Infants (0-2 months) and its Correlation with WHO IMCI Algorithm (7 days to 2 months).

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Objective: *To evaluate simple clinical signs of illness in young infants (0-2months) and to correlate with WHO IMCI algorithm (7days-2months).* ***Design:*** *Prospective observational. Study conducted in the outpatient department and emergency room of a pediatric tertiary level hospital.* ***Methods:*** *Four hundred and ninety seven young infants (0-2months) presenting to outpatient department or emergency room were recruited. Detailed history, clinical examination including all signs in IMCI algorithm was recorded in the pre-designed proforma. The study subjects were investigated and managed according to the protocol of treating unit, which served as 'gold standard'. The diagnostic and therapeutic agreement between the gold standard and IMCI was computed. The study subjects were analyzed as one age group (0-2months) and also after de- segregating into early and late neonatal age group (0-7days and 7days-2months age).* ***Results:*** *Mean number of illnesses in 0-7days, 7days-2months and 0-2months groups were 1.97, 2.0 and 2.02 respectively. Those who required referral as per IMCI algorithm had higher proportion of co-morbidities. The referral criteria were fairly sensitive (78-85%) in predicting hospitalization with moderately high specificity (78%). Diagnostic agreement between gold standard and IMCI module was complete in 57-68%. Amongst diagnostic mismatch, under-diagnosis was found more frequently (72-82%) than over-diagnosis (17-29%). The sensitivity of algorithm to identify serious bacterial infections was quite high (96-98%) with moderately good specificity (80-92%). Jaundice was single most important complaint accounting for 47-62% of diagnostic mismatch.* ***Conclusion:*** *IMCI algorithm appears to be a promising, feasible and useful intervention strategy to triage and treat young infants in 7days-2months age group. This tool remains effective even when extended to 0-7 days age group. However a further increase in its sensitivity can be achieved by including yellowness of lower extremities/ palms/ soles as a criterion*

Key words: *Illnesses, IMCI, IMNCI, Young infants.*

INFANT mortality constitutes a major component of childhood mortality in developing countries. In India, there are about 1.8 million deaths under the age of one year(1). Out of these, 1.2 million babies die in the first month of life(1). Furthermore, in the neonatal period, the first week is even more crucial. Three-fourth of all newborn deaths occurs during the first week of life, making it the most vulnerable period of life. Any meaningful strategy to combat the childhood mortality needs to train its gun on the most vulnerable period that is the early neonatal period (0-7 days).

The signs and symptoms of several of the major childhood illnesses contributing to under-five mortality have a substantial overlap. Thus, a single diagnosis for a sick child is often

inappropriate because it identifies only the most apparent problem and can lead to an associated and potentially life threatening problem being overlooked. For effective management of these major childhood illnesses, WHO and UNICEF have developed the "Integrated Management of Childhood Illness" (IMCI) Strategy(2,3). Generic IMCI program brought to India did not initially include newborn less than one week old. The clinical experience with the field-testing of the integrated approach is largely limited to African subcontinent or older children(4-7). These studies had suggested the feasibility and utility of integrated approach in preference to vertical single disease associated program. No study has so far validated the IMCI algorithm in neonates <1 week old and there are very few published studies where IMCI algorithm has been tested in children 7 days - 2 months old(8,9) within Indian subcontinent.

Subjects and Methods

The study was conducted in the Department of Pediatrics of a tertiary care hospital at New Delhi, during April 2002 to January 2003, as a prospective observational study. Ethical clearance by the institute's committee was taken. Verbal parental consent for inclusion in the study and for follow up visit was taken in every case. The study was spread over 10 months duration to minimize the seasonal variation in morbidities. The subjects were included as they came in contact with the study team in the in-patient and out patient department. No pre-selection of cases was done.

A total of 497 young infants (0-2 months) who presented to OPD or emergency room of the treating unit for a fresh episode of illness formed the material for the present study. For the children recruited to the study, detailed history and clinical examination were recorded in a pre-designed proforma, including all signs listed in IMCI algorithm, in the same order. In addition, certain signs not included in generic IMCI algorithm but considered important for sickness in 0-2 months age group, particularly in 0-7 days age, as stated in "Child Survival and Safe Motherhood" (CSSM) Programme started in 1992 were studied(10). These signs include bleeding, cyanosis, abdominal distension, CFT >3 seconds and apnea. Information regarding yellowness of lower extremities/ palms/ soles was also noted. The treatment steps were also identified as according to the 'Assess and Classify' module of IMCI algorithm and recorded in the proforma.

The study subjects so selected were managed according to the protocol of treating unit under the supervision of the senior faculty. All relevant investigations were performed, using appropriate methods, wherever indicated. Bacterial infections were identified based on clinical picture of the patients supplemented by laboratory test including blood culture and sepsis screen. The treating unit protocol and diagnosis was considered as the 'Gold Standard' for comparison.

The study children were either admitted or sent home after initial evaluation, depending upon nature and severity of illness. Hospitalized children were discharged on recovery of the condition and other children were sent only after establishment of a definite diagnosis, which could be managed at home. The recruited infants were followed up to determine the outcome. For hospitalized subjects this was limited to their hospital stay while the out patient recruits were re-evaluated on follow up one week later. Feeding counseling was given to every child with low birth weight or feeding problems.

The study subjects were first analyzed separately as 0-7 days (group 1) and 7 days-2 months (group 2) age groups. The data was then also combined to study the utility of IMCI

algorithm for all infants up to the age of 2months (group 3). The data was entered in Microsoft Excel® and analysis was done using SPSS® software version 10.

Two categories of possible diagnosis and treatment were available for each recruited study subject, namely 'Gold Standard and IMCI algorithm'. The diagnostic and therapeutic agreement between the 'Gold Standard and IMCI' was compared. The utility of reference criteria to predict admission was also evaluated to compute sensitivity and specificity of the algorithm. Other standard statistical tests performed included Pearson's chi square test, Fischer's exact test, odds ratio, *etc*. Sample size of 120 neonates in each group was calculated to be sufficient to detect a difference of 10% in diagnostic agreement from "Gold Standard" with 90% power and alpha of 0.05.

Results

Out of total 497 infants, 293 patients were aged 0-7 days (group 1) and another 204 were between 7 days - 2 months of age (group 2). In group-1, 144 (49.1%) were recruited from OPD and 149 (50.9%) from emergency room. While in group-2, 94 (46.1%) were from OPD and 110 (53.9%) from emergency room. Of the 497 subjects, 25 (5%) expired, 401 (80.7%) improved and 71 (14.3%) were lost to follow up.

In group 1, out of 293 patients, 195 were admitted by Gold standard and 98 patients were sent home while using IMCI algorithm 174 patients would have been referred and 119 patients would have received home treatment. Similarly in group 2, out of 204 patients, 107 were admitted by Gold standard and 97 patients were sent home while IMCI would have referred 112 patients and not referred 92 patients. Sensitivity of referral criteria was assessed by comparing the referral status of the patients as per IMCI algorithm with the Gold Standard decision of either admitting or sending home after evaluation by the treating pediatrician. Sensitivity, specificity, positive predictive value, negative predictive value, odds ratio, 95% confidence interval and 'P' value as computed is given in *Table I*.

Only 25-30% of subjects in any study group had a single morbidity while most had 2 or more morbidities at presentation. Mean number of illness in group 1, group 2 and group 3 were 1.97, 2.0 and 2.02 respectively. IMCI algorithm in comparison to Gold Standard could identify relatively lower number of illnesses (1.67, 1.77 and 1.71 respectively) in the groups studied. Further, mean numbers of illness were higher in those who required referral as per IMCI algorithm (1.75 ± 0.68, 1.97 ± 0.66, 1.84 ± 0.64 vs 1.54 ± 0.44, 1.53 ± 0.6, 1.54 ± 0.56 respectively in three age groups).

Among the clinical signs listed in IMCI algorithm as predictor of serious bacterial infections, lethargy/unconsciousness and decreased movements had high specificity >90% and moderately good sensitivity (>65%). Fast breathing, severe chest indrawing, nasal flaring, grunting and temperature abnormalities had high specificity (87-99%) and moderately low sensitivity (30-40%). Convulsions and bulging fontanel had very high specificity >99% but very low sensitivity <10% in all age groups.

Other signs, not listed in IMCI but studied by us like bleeding, cyanosis, abdominal distension, CFT >3 seconds, apnea though were highly specific (>90%) had very low sensitivity (<15%) in all the age groups. Yellowness of lower extremities/palms/soles was single important sign which had high sensitivity in both age groups. The sensitivity and specificity in various groups was found to be 22.5% and 84.6% in 0-7 days, 10.2% and 92.6% in 7 days to 2 months and 18.2% and 88.7% in 0-2

TABLE I–*Validity of Referral Criteria (IMCI) as a Predictor of Hospital Admission (Gold Standard) in Study Subjects*

Parameter	Age group		
	0-7 days (n = 293)	7 days-2 months (n = 204)	0-2 months (n = 497)
Sensitivity (%)	78.5	85.0	80.8
Specificity (%)	78.6	78.3	78.4
Positive predictive value (%)	87.9	81.3	85.3
Negative predictive value (%)	64.7	82.6	72.5
Odds ratio	13.13	20.5	15.3
95% CI	7.2 - 25.2	9.5 - 45.3	9.6 - 24.6

months, respectively. After inclusion of this sign in algorithm, the sensitivity of the algorithm to predict referral increased from 78.5% to 88.7% in 0-7 days, 85% to 86.9% in 7 days to 2 months and 80.8% to 88% in 0-2 months age group and the specificity decreased from 78.6% to 74.5% in 0-7 days, 78.3% to 78.2% in 7 days to 2 months and 78.4% to 76.4% in 0-2 months age group.

Broad diagnostic agreement between the Gold Standard and the IMCI module was analyzed. Since IMCI classifies illnesses into groups rather than individual diagnosis, the diagnosis agreement between the two was analyzed by comparing illness groups. For example, serious bacterial infections were not subdivided into sepsis, pneumonia, meningitis *etc*. while analyzing the diagnostic agreement, rather on the presence of any of the individual diagnosis the patient was classified as possible serious bacterial infection. Those cases referred by IMCI, which were not hospitalized, were considered as a diagnostic mismatch. If more than one illness was recorded as per 'Gold Standard' and if any of the illness was not covered by IMCI algorithm, it was considered as diagnostic mismatch (under diagnosis) even if the patient was referred as per IMCI algorithm. Though referral in this case was considered as treatment match. This accounts for discordance between results of diagnostic agreement and treatment agreement. Comparison of diagnostic and treatment agreement between Gold Standard and IMCI module is shown in *Table II*. More than 88% of diagnosis as per Gold Standard was either totally or partly covered by IMCI algorithm. About 12% diagnoses were however not covered at all.

The predictive value of IMCI algorithm for identifying infants with bacterial infection was very high. IMCI algorithm had high sensitivity of 96-98%. Algorithm tends to over diagnose serious bacterial infection by 8-20% (in three age groups) as it classifies all febrile patients under serious bacterial infections, some of which had either environmental fever or mild URI. Algorithm performed reasonably well in identifying dehydration status although it tends to over diagnose the severity of dehydration. As per IMCI algorithm, 40-45% patients had some feeding problem and required counseling for breast-feeding. About one fourth of patients were unable to feed because of serious illness. Jaundice was single most important complaint accounting for 47-62% of cases with diagnostic mismatch (gold standard admitted the patients with severe jaundice which were totally missed by IMCI algorithm as it has no provision to

TABLE II–*Diagnostic/Treatment Agreement Between 'Gold Standard' and 'IMCI Algorithm'*

Type of mismatch	0-7 days		7 days - 2 months		0-2 months	
	Diagnostic agreement n (%)	Treatment agreement n (%)	Diagnostic agreement n (%)	Treatment agreement n (%)	Diagnostic agreement n (%)	Treatment agreement n (%)
No mismatch	168 (57.3)	205 (70)	139 (68.1)	146 (71.6)	307 (61.8)	351 (70.6)
Any mismatch	125 (42.7)	88 (30)	65 (31.9)	58 (28.4)	190 (38.2)	146 (29.4)
Under diagnosis/ treatment by IMCI	109 (87.2)	71 (80.6)	47 (72.3)	50 (86.2)	156 (82.1)	121 (82.9)
Over diagnosis/ treatment by IMCI	32 (16.8)	17 (19.4)	19 (29.2)	18 (31)	42 (17.9)	35 (23.4)

identify this sign). Other important complaints were cough (10-26%) and fever (11-23%). In 29 cases that had fever and were referred, 19 were diagnosed as environmental fever and 10 had associated URI. In our study breast fed stools were present in 7 (2.4%) cases in 0-7 days, 6 (2.9%) in 7 days-2 months age group and 13(2.6%) cases in 0-2 months age group

Discussion

Various studies in the past had shown a substantial overlap between the signs and symptoms of several of major childhood illnesses(4,5,8,11,12). The basis of propagating IMCI approach is that a single diagnosis for a sick child is often inappropriate because it identifies only the most apparent problem and can lead to an associated and potentially life-threatening problem being overlooked. The results of present study reaffirm the presence of co-existing morbidities, even in early neonatal age group (0-7 days). Nearly 70% of patients in both age groups (0-7 days and 7 days-2 months) had more than one illness. In an earlier study from India, co-existence of morbidity was seen in 75% of the infants in 7 days-2 months age group, which is quite similar to our results(8). No study is available in 0-7 days age group for comparison.

In our study, 45-50% subjects had 2 morbidities and 20-25% had 3 or 4 illnesses. Mean (± Standard deviation) number of morbidities in different age groups studied was 1.97 ± 0.93, 2.0 ± 0.8 and 2.0 ± 0.8 in 0-7 days, 7 days-2 months and 0-2 months age group respectively according to the Gold Standard. Mean number of morbidities as identified by the IMCI algorithm in our study was little less (1.67-1.77) as compared to Gold Standard. About 2.12 numbers of mean morbidities were identified as per Gold Standard assessment and 1.77 by IMCI algorithm in 7 days-2 months age group in another study from a different hospital in Delhi(8). This data supports the contention of IMCI that often diseases/morbidities co-exist and disease specific interventions or algorithms may miss some of important co-morbidities particularly due to overlapping clinical signs. Further, in our study the number of morbidities was significantly higher in those infants who had been assessed to have relatively severe condition requiring a referral. Mean number of morbidities in patients requiring referral was 1.75, 1.97, and 1.85 in 0-7 days, 7 days-2 months and 0-2 months respectively. Mean number of morbidities in patients not requiring referral was 1.53-1.54 in different age groups. Similar results were also shown in the earlier study(8).

In the present study there was total agreement of diagnosis in 57-68% (range signifies percentages in 3 groups) of total patients in different age groups. In patients having any diagnostic mismatch, under diagnosis by algorithm was commoner (72-87%) than the over diagnosis (16-29%). These results are comparable with previous study in 7 days-2 months old infants, which reported 24% mismatch and most of the mismatch was due to under diagnosis (87%).

The present study also shows that 62-67% patients were totally covered by IMCI algorithm. Of the remaining 21-26% were partially covered and only 11-12% patients were not at all covered. Similar results were seen in earlier reports(7,8).

IMCI algorithm was found to have high sensitivity >95% in all age groups and relatively good specificity (80-85%) in identifying serious bacterial infection. The algorithm also showed excellent sensitivity in picking any signs of dehydration although over diagnosed severity of dehydration. Previous studies have also shown similar results(4,8) except for one study from Bangladesh where specificity was much lower though the sensitivity was comparable.

IMCI algorithm quite efficiently identifies feeding problem in infants. About 40-45% of patients had some feeding problem and required breast feeding counseling. These were either low birth weight or top fed. About one third patient was unable to feed because of serious illness. A previous study in 7 days-2 months old infants showed that counseling for breast feeding was required in 55% of patients and about one fourth were unable to feed because of serious illnesses(8).

In our study, jaundice forms single most important cause of diagnostic mismatch particularly in 0-7 days age group. Inclusion of this sign in the algorithm result in significant increase in sensitivity with only small decrease in specificity. Other studies have not reported this as they have excluded 0-7 days age group(8). Other causes of diagnostic mismatch were mild fever in 15.2% of subjects who were unnecessarily referred for situations like environmental fever or upper respiratory tract infection. Breast fed stools were present only in 2.5% cases in our study.

Early recognition of severe illness and timely referral to the higher level of health facility is an important component of the IMCI algorithm. In the present study, the sensitivity of the IMCI algorithm in 0-7 days age group subjects was 78.5% and specificity was 78.6%. The sensitivity in 7 days to 2 months age group was 85% and specificity was 78.3%. Main reason for this relatively low sensitivity in 0-7 days age group was inability of the algorithm to pick the patients having severe neonatal jaundice requiring hospitalization. The sensitivity when two age groups are taken together (0-2 months) is 80.8 and specificity is 78.4. Specificity of the IMCI algorithm for 7 days-2 months age group in our study was much higher as compared to previous study in the similar group while the sensitivity was comparable(8,9). However, no study is available for comparison in 0-7 days age group. Positive predictive value in our study was high (85-88%) as compared to previous studies in similar age group(8,9). The positive predictive value is determined by prevalence of condition as well as by sensitivity and specificity and as the study was conducted in a setting that might have attracted more severe illnesses, it is possible that this study would overestimate the IMCI predictive value in a tertiary level health care setting. Probably, the predictive value would have been lower in a typical first level health facility. Considering that, signs and symptoms in 0-2 months age group are often

Key Messages

- Co-existence of illnesses is the rule rather than exception for sick young infants.
- The performance of proposed referral criteria and also the diagnostic and treatment agreements is within 'acceptable range' for both 0-7 days and 7 days to 2 months age group.
- Sensitivity of IMCI algorithm can be further increased if yellowness of lower extremities/ palms/soles is included in the algorithm.

subtle and non-specific, the sensitivity and specificity in our study shows that there is still considerable utility of IMCI algorithm in predicting childhood illnesses including serious bacterial illnesses. From the foregoing discussion, it can be concluded that the neonatal coverage with IMCI algorithm in 0-7 days age group can be improved by adding yellowness of the lower extremities/palms/ soles as an additional criteria for referral.

The IMCI strategy has since been expanded in India to include all neonates and renamed as "Integrated Management of Neonatal and Childhood Illnesses (IMNCI)". IMNCI includes all neonates from 0-2 months excluding birth care(13). Jaundice has been included in it as one of the referral criteria(13). Our study provides the evidential basis of above inclusion. However it is pertinent to point out that in the present study a trained doctor picked up this sign with good sensitivity. However more studies are required using peripheral health worker to really assess the impact on sensitivity and specificity with the recommended change.

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