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Research Article

Prediction Models for Admission of Infants Under 6 Months of Age Presenting with Non-specific Complaints

Michael Zhang[1,3*] Marie-Louise Ratican[2,3] Valerie Astle[3], Nicholas Marriage[3], Jonathan Ash[3], Haddijatou Hughes[3]

[1]*School of Medicine and Public Health, University of Newcastle, NSW, Australia*
[2]*Queens University Belfast, UK*
[3]*Emergency Department, John Hunter Hospital, NSW, Australia*

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Abstract

Objective

When young infants are brought to ED for assessment with non-specific complaints, it may be difficult to distinguish those with mild illness from those with serious underlying infection requiring admission. We hypothesize that prediction models for admission can be derived from the features manifested by the infants presenting to the ED.

Methods

This retrospective observational study examined a primary outcome of admission rate in infants under 6 months presenting to a mixed ED in the 2013-14 period. Clinical data of eligible patients were extracted from electronic medical record to construct statistical models of risks for admission.

Results

Around 30% of infants with non-specific complaints were admitted for further management in the hospital. Multivariate modelling based on clinical data created a Combined model (AUC 0.965) that explained the variation of admission of these infants better than the SPOC model (AUC 0.702), Clinical model (AUC 0.862) and Flow model (AUC 0.925) ($p < 0.001$).In the Combined model, the biggest predictors for admission were necessity for blood test (OR 20.52, 95% CI 11.32 – 32.17), arrival by ambulance (OR 7.99, 95% CI 3.23 – 19.75) and maximum body temperature (OR 1.82, 95% CI 1.31 – 2.53) of the presenting infants. In contrast, the infants waiting longer periods of time to be seen by ED doctors were more likely to be discharged.

Conclusions

Prediction models with excellent accuracy can be built on the features of young infants presenting with non-specific complaints. They could be used to guide decision making on the management of this group of patients in the ED.

Keywords: Prediction Models; Admission; Infants; Non-specific Complaints;

Introduction

Each day a wide variety of patients attend Emergency Departments (ED) with a diverse range of complaints. After careful assessment, a clinical decision must be made to either discharge them to the care of their general practitioners (GP), or to admit as an inpatient for further management. When considering young infants presenting with non-specific complaints, these decision making processes may not be easy. A variety of factors contribute to this, and different approaches can be observed across different EDs with variable admission rates as a result. The admission rates vary significantly in rural versus metropolitan hospitals [1], paediatric versus general EDs [2,3], between speciality and general clinicians [2,3], and in crowded departments [4].

Some attempts have already been made to identify patterns of admission in the ED. Simple models developed for adult patients using information at triage such as triage category, age, other demographics, arrival mode and, primary complaints were found to be accurate in predicting the likelihood of admission from ED [5-7].Other approaches based on historical information, physiological parameters, and therapy modalities had been utilized to construct prediction models for paediatric risk of hospital admission [8-11]. A more refined model for admission was developed by controlling

***Corresponding Author:** Michael Zhang, Paediatrician / Emergency Physician, School of Medicine and Public Health, University of Newcastle, NSW, Australia, Email: michael.zhang@hnehealth.nsw.gov.au

3 care characteristics such as annual patient volume, presence of paediatric emergency subspecialists and presence of residents [10].

However similar prediction models for admission of young infants presenting with non-specific complaints are yet to be developed. This study was intended to explore different risk factors associated with this targeted infant population and subsequently to construct useful prediction models on their risk of admission.

Methods

This project was a retrospective observational study which took place in an Emergency Department in a regional hospital in the Hunter New England Local Area Health Network, New South Wales, Australia. The Emergency Department consists of a combined adult and paediatric ED, and has annual attendances of more than 70,000, one third of which are children. Most of the clinical specialities and sub-specialities are available in this hospital, and it serves as a referral centre for the surrounding suburban hospitals.

Lists of electronic medical records on all infants aged less than 6 months presenting to this ED over a two year period between 2013 and 2014 were scanned for subjects meeting a pre-defined inclusion criteria. ICD-10 diagnostic codes entered by ED staff on the electronic record system at either the time of patient discharge or admission, supplemented by ED triage notes, were used for subject selection.

The inclusion criteria were based on the ED discharge diagnoses that were not apparent to clinicians about their specific underlying pathologic diagnoses. The examples included diagnoses of fever of unknown origin, viral infections, and vague symptomatic diagnoses such as unspecified fever, irritability, lethargy, feeding intolerance, seizures, jaundice, respiratory difficulty, sole vomiting, rash, and so on. The infants were excluded if they were given clear systemic diagnoses such as cardio-respiratory arrest, bronchiolitis, gastroenteritis, conjunctivitis, allergy, gastro-oesophageal reflux, constipation, eczema, failure to thrive, and so on. Also excluded were surgical problems, trauma, carer stress and social problems. On the other hand, the infants diagnosed with serious infections such as sepsis, meningo-encephalitis, urinary tract infections (UTI), and pneumonia were included in this project. Although this group of patients had a clear diagnosis, they often presented with vague symptoms and their clinical manifestation could be very similar to the rest of the infants fulfilling the inclusion criteria. It challenges many clinicians to differentiate them correctly and thus formed a major rationale to have both groups included in this project.

Clinical records including observation sheets, progress notes, and medication charts were reviewed and the relevant data were entered into a standardized research spread sheet designed for this project. Notably a Standard Paediatric Observation Chart (SPOC) used in this ED categorizes vital signs into colour coded zones for visual cues of abnormal signs. Infants with vital signs at the markedly abnormal range, at least one "red zone" or two "yellow zones", would be regarded as high risk for sepsis, according to the pre-existing local "Paediatric Sepsis Pathway", and trigger a Sepsis Alert response to initiate a septic workup to measure inflammatory marker levels and perform body fluid cultures. These records and additional information such as microbiology results and radiology reports were also transcribed into the spread sheet. The final diagnoses were determined by the order of body fluid culture results, inpatient team entry and ED clinicians' notes.

Statistical Analysis

All the relevant variables were determined at the beginning of the study. The categorical variables were analysed in the forms of percentage and were compared by chi square test. The continuous variables were evaluated with means and standard deviation if in normal distribution, or median and interquartile range if in skewed distribution. Similarly the normally distributed continuous variables were compared by student t test and the ones with skewed distribution compared by rank sum or median test. Standardized methods and statistical software to develop and validate regression models were adopted to derive models in this project [12]. All statistical models were checked for the diagnostics and model fit. Statistical significance was determined at the level of p values less than 0.05.

Ethics

This project was approved by the Hunter New England Local Area Health Ethics Committee.

Results

Patient population

Of the 3298 infants under 6 months of age presenting to this ED, 968 (29.35%) met the inclusion criteria for this study. The admission rate for the included patients was 33.6% (95% CI 30.59 – 36.55 %) (Table 1).The admitted infants (median age 2.1, IQR 1.07 – 3.67 months) were slightly younger than the discharged ones (median age 2.43, IQR 1.20 – 4.17 months, $p = 0.025$) and just over half were male in both groups.

More infants in the admitted group (16.31%) were brought to ED by ambulance, compared to the discharged group (4.35%). Admitted infants were also noted to have been given much higher triage Categories, and were seen by ED doctor's earlier ($p < 0.001$). They stayed in ED longer (median 5.32 hours) than the discharged infants (median 2.92 hours) ($p < 0.001$).

Evaluation before admission

A much larger proportion of admitted infants (47.13%) met the sepsis alert criteria than the discharged group (6.78%). Of the infants meeting the criteria, none in the discharged group had a full septic work up, in contrast to 10.8% of the admitted infants. Only 1 patient had CSF collection before being discharged home from ED. LPs were performed on 125 (38.82%) of admitted infants, but 17 (13.6%) were unsuccessful.

In the admitted infants, more had blood tests taken (86.46%) than urinalysis (60.06%) and chest x-rays (37.38%). Abnormalities were found in 36.89% of the chest x-rays in this group. Urine leucocytes were positive in 44.26% and nitrite positive in only 11.6%. Mode of urine collection was not specified in 65.84% of the samples taken, however the most common mode of collection when specified was a clean catch sample (56.5%).

	Admitted N = 325	Discharged N = 643	P value
Demographics			
Age, months	2.1 (2.6)	2.43 (2.97)	0.025
Male	176 (54.15)	350 (54.43)	0.935
Arrival by Ambulance	53 (16.31)	28 (4.35)	< 0.001
Triage Categories:			
Cat. 1: Resuscitation	8 (2.46)	0 (0)	
Cat. 2: Emergency	65 (20.00)	21 (3.27)	
Cat. 3: Urgent	197 (60.62)	332 (51.63)	
Cat. 4: Semi-urgent	53 (16.31)	283 (44.01)	
Cat. 5: Non-urgent	2 (0.62)	7 (1.09)	< 0.001
Time first seen by doctor	0.60 (1.25)	1.23 (1.78)	< 0.001
Clinical Features			
Fever	156 (48.30)	53 (8.56)	< 0.001
Laboratory Tests			
Urinalysis Performed	191 (60.06)	156 (24.41)	< 0.001
CXR Performed	120 (37.38)	10 (1.56)	< 0.001
Blood Test performed	281 (86.46)	38 (5.91)	< 0.001
Blood culture performed	260 (80)	26 (4.04)	< 0.001
Lumbar puncture performed			
No LP	197 (61.18)	638 (99.84)	
Failed LP	17 (5.28)	0	
Successful LP	108 (33.54)	1 (0.16)	< 0.001
Septic work-up needed	148 (47.13)	32 (6.78)	< 0.001
Septic work-up performed	16 (4.92)	0	< 0.001
Management			
Time to be seen by ED doctor (hours)	0.60 (1.25)	1.23 (1.78)	< 0.001
Intravenous fluid therapy			
No IV fluid _baseline	188 (57.85)	641 (99.69)	
IV bolus + maintenance fluid	61 (18.77)	1 (0.16)	
IV maintenance fluid only	76 (23.38)	1 (0.16)	< 0.001
Antibiotics IV administered	205 (64.06)	3 (0.47)	< 0.001
Length of stay in ED (Hours)	5.32 (3.15)	2.92 (2.18)	< 0.001
Disposition from ED:			
Paediatric ward	316 (97.23)	-	
Paediatric ICU	8 (2.46)	-	
Retrieved to other hospital	1 (0.31)	-	< 0.001
follow-up plan			
ED review	0	15 (2.35)	
LMO review	177 (54.97)	304 (47.57)	
Paediatric clinic review	83 (25.78)	46 (7.20)	
No follow up specified	62 (19.25)	274 (42.88)	< 0.001
Re-presentation to ED	16 (4.97)	39 (6.11)	0.471

Table 1 Characteristics of infants under 6 months in two groups
Continuous variables are expressed as mean and standard deviation or median and interquatile range; categorical variables as number and percentage. BP, blood pressure; sBP, systolic blood pressure; SpO_2, percutaneous oxygen saturation; SPOC, standard paediatric observation chart; SG, specific gravity; CXR, chest X-ray; WCC, white cell count; CRP, C reactive protein; ED, emergency department; IV, intravenous; Cat., category

Risk Factors for Admission

Nearly half of the admitted patients were febrile in comparison with less than 10% of the discharged infants. The range of body temperature was also higher, with each degree rise in body temperature carrying a 4.2 (95% CI: 3.46 – 5.25) times higher risk of admission (Table 2). This is higher than the risks associated with each unit increase in the capillary return time (OR 3.38), maximum pulse rate (OR 1.07), and maximum respiratory rate (OR 1.11). Infants with higher oxygen saturation had lower risk of being admitted (OR 0.68). Systolic blood pressure was not checked in many infants, and the difference was not significant between two groups in which it was measured.

Sick infants in need of admission were more likely to have some diagnostics tests: full blood examination (OR 101.68), chest x-ray (OR 37.55) or urinalysis (OR 4.66). The risk was even greater in the patients having lumbar puncture done (OR 401.25).

White cell count in blood analysis was higher in the admitted group (median 11.50, 95% CI: 8.40 – 15.80, vs. median 9.75, 95% CI: 7.10 – 12.30; p = 0.008). Neutrophil count was also higher (median 4.60, 95% CI: 2.20 – 7.80, vs. 2.40, 95% CI: 1.50 – 3.90; p < 0.001), along with CRP (median 6.50, 95% CI: 2.00 – 31.60, vs. 0.75, 95% CI: 0.20 – 6.50; p = 0.016). However, the same was not found with serum lactate level (median 2.30, 95% CI: 1.70

	Odds Ratio	95% CI	P value
Demographics			
Age (Months)	0.909	0.838 - 0.985	0.025
Male	0.989	0.757 - 1.292	0.935
Arrival by Ambulance	4.28	2.649 - 6.914	< 0.001
Triage Categories:			
Cat. 1 / 2: Resuscitation / Emergency	12.167	2.349 - 63.017	0.003
Cat. 3: Urgent	2.077	0.427 - 10.096	0.365
Cat. 4: Semi-urgent	0.655	0.133 - 3.242	0.605
Cat. 5: Non-urgent _ baseline			
Clinical Features			
Highest Body Temperature ('C)	4.26	3.463 - 5.245	< 0.001
Fever	9.976	6.986 - 14.245	< 0.001
Maximum Heart Rate (/min)	1.065	1.055 - 1.075	< 0.001
Capillary Return Time (Seconds)	3.376	2.265 - 5.031	< 0.001
Lowest sBP	0.989	0.949 - 1.028	0.555
Maximum Respiratory Rate (/min)	1.11	1.090 - 1.131	< 0.001
Lowest S_pO_2 (%)	0.684	0.627 - 0.746	< 0.001
SPOC Positive	12.259	8.04 - 18.69	< 0.001
Laboratory Tests			
Urinalysis Performed	4.656	3.491 - 6.210	< 0.001
Urine leucocytes positive	2.978	1.830 - 4.846	< 0.001
Urine nitrate positive	9.778	2.254 - 42.420	< 0.001
CXR Performed	37.552	19.324 - 72.973	< 0.001
Blood Test performed	101.678	64.411 - 160.507	< 0.001
WCC	1.079	1.007 - 1.157	0.008
Neutrophils count	1.336	1.140 - 1.564	< 0.001
CRP	1.074	1.014 - 1.138	0.016
lactate	1.380	0.614 - 3.101	0.933
Blood culture performed	94.923	58.893 - 152.995	< 0.001
Lumbar puncture performed	401.248	55.724 - 2889.255	< 0.001
Management			
Antibiotics IV administered	377.913	118.825 - 1201.917	< 0.001
Time staying in ED (Hours)	1.799	1.649 - 1.962	< 0.001

Table 2 Univariate determination of predictors for admission of infants under 6 months
Cat., category; sBP, systolic blood pressure; SpO_2, percutaneous oxygen saturation; SPOC, standard paediatric observation chart; CXR, chest X-ray; WCC, white cell count; CRP, C reactive protein; ED, emergency department; IV, intravenous;

– 2.90, vs. median 2.00, 95% CI: 1.30 – 2.75, p > 0.05). The risk of admission associated with intravenous antibiotics was 377.9 times higher (95% CI: 118.83 – 1201.92).

Risks Prediction Models Construction and Validation

Multivariate models were constructed by stepwise forward selection of significant variables. The simplest models using local paediatric sepsis alert criteria had moderate discrimination with a pseudo R^2 0.168 and a concordance index of 0.702 (Table 3). A similar model based on specific clinical signs was generated by manual selection of these variables resulting in better discrimination with c statistics of 0.862 and pseudo R^2 0.33. The patient flow model including the transport mode, time to be seen by doctor and time stayed in ED examined the admission process from a different perspective. Incorporating the variables from different perspectives allowed creation of a combined model, showing these significant predictors: transport mode, highest body temperature, respiratory rate, whether blood tests were done, time seen by a doctor and time spent in ED (Table 4).

The combined model had an excellent discrimination with Area under ROC of 0.965 (Figure 1). The sensitivity of this model was 91.56%, the specificity 89.37%, and a negative predictive value 94.06%, based on the admission rate of about 30%. It could correctly classify 90.25% of the infants presenting with non-specific complaints potentially requiring admission. Overall performance of this model was further supported by a low Brier score of 0.0665

Goodness of fit test by decile of model prediction resulted in satisfactory Hosmer-Lemeshow statistics (Figure 2). Further internal validation was performed with 700 bootstrap iterations.

	Odds ratio	95% CI	P value
Patient flow model (n=953)			
model χ^2 575.71 , p < 0.001			
pseudo R^2 0.473			
Ambulance	7	3.67 - 13.36	< 0.001
Time to doctor	0.25	0.2 - 0.31	< 0.001
Time in ED	3.15	2.72 - 3.66	< 0.001
Clinical signs model (n=777)			
model χ^2 347.58 , p < 0.001			
pseudo R^2 0.333			
Temperature (max, °C)	2.34	1.8 - 3.04	< 0.001
HR (max)	1.02	1.01 - 1.04	< 0.001
Capillary Return Time (seconds)	2.38	1.52 - 3.72	< 0.001
Respiratory rate (max, /minute)	1.06	1.03 - 1.08	< 0.001
SpO_2 Room Air (min, %)	0.75	0.67 - 0.84	< 0.001
SPOC model (n=786)			
model χ^2 177.57, p < 0.001			
pseudo R^2 0.168			
SPOC positive	12.26	8.04 - 18.69	< 0.001
Laboratory model (n=335)			
model χ^2 274.88, p < 0.001			
pseudo R^2 0.596			
Leucocytes in urinalysis	2.36	1.06 - 5.26	0.036
Lumbar puncture done	15.95	2.01 - 126.89	0.009
CXR performed	4.25	1.25 - 14.51	0.021
Blood Test performed	7.05	2.48 - 20.06	< 0.001
Blood Culture performed	6.68	2.35 - 18.99	< 0.001

Table 3 Preliminary models to predict admission of infants with non-specific complaints

	Odds ratio	95% CI	P value
Ambulance	7.99	3.23 - 19.75	< 0.001
Time to doctor	0.53	0.40 - 0.70	< 0.001
Time in ED	1.80	1.50 - 2.16	< 0.001
Temperature (max, °C)	1.82	1.31 - 2.53	< 0.001
Respiratory rate (max, /minute)	1.06	1.03 - 1.10	< 0.001
Blood Test performed	20.52	11.32 - 37.17	< 0.001

Table 4. Final combined models to predict admission of infants with non-specific complaints

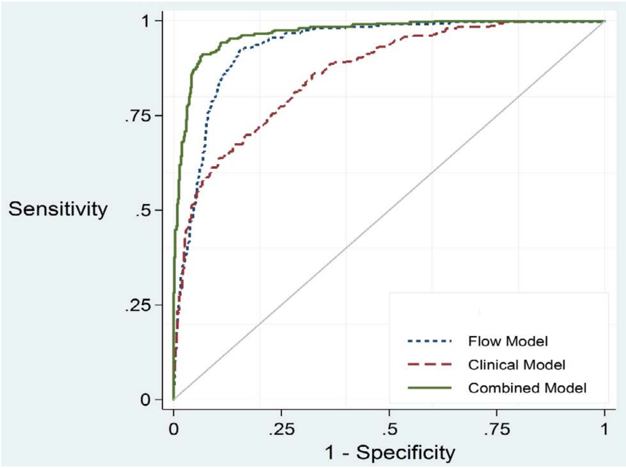

Figure 1. Receiver Operator Curve to compare the discriminability of Flow model (AUC 0.925), Clinical model (AUC 0.862) , and Combined model (AUC 0.965) (p < 0.001).

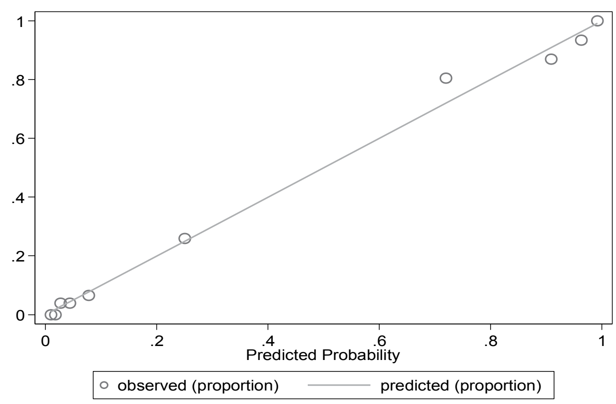

Figure 2. Calibration curve for Combined model of paediatric admission. Perfect model prediction is represented by the diagonal line in ideal situation. The Combined model is shown to be a good fit to the actual probability, Hosmer-Lemeshow $\chi^2(10)$ = 9.42, p = 0.49

Over fitting of the model was then corrected by a shrinkage factor of 0.991, which was applied to the slope of the combined model. The final model with bias corrected estimates fitted better on the calibration plot (Figure 3). However this model may slightly overestimate the probabilities near the extremes of the spectrum.

A scoring system was developed by taking advantage of the predictors in the combined model (Figure 4). Each characteristic of an infant corresponds with a score on the diagram. The total score can then be matched easily with a value on the probability scale.

Discussion

The combined model in this study hopes to address the difficulty of predicting the need for admission, when faced with infants presenting with non-specific complaints. Infants noted to be more unwell by their careers were often brought to ED via ambulance. This transport mode was strongly associated with probability of admission and was included in the final model. Infants arriving by ambulance were also more likely to be given higher triage categories. However, triage categories were excluded from this model given the co-linearity with ambulance transport.

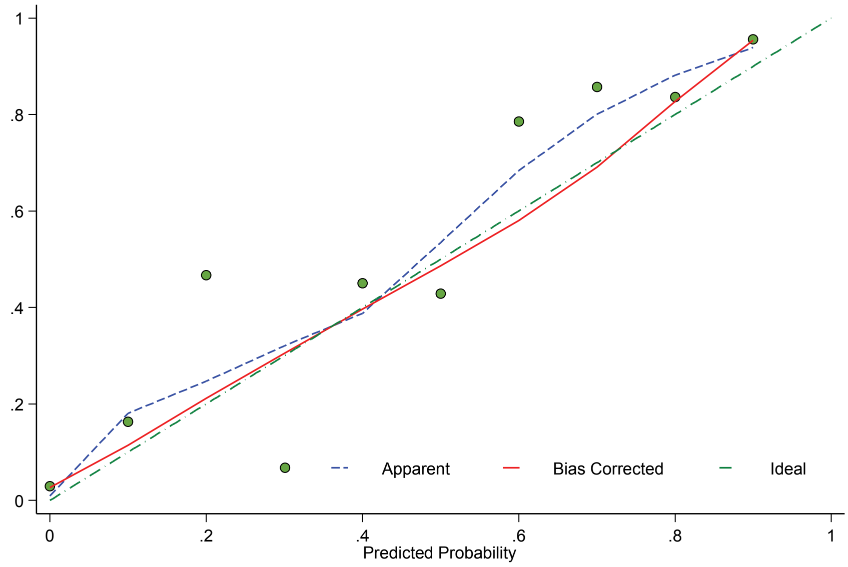

Figure 3. Internally validated combined model by bootstrapping with shrunken estimates from bias-correction of model slope were plotted along with a smooth nonparametric estimator. The models fit appeared satisfactory (mean absolute error 0.089).

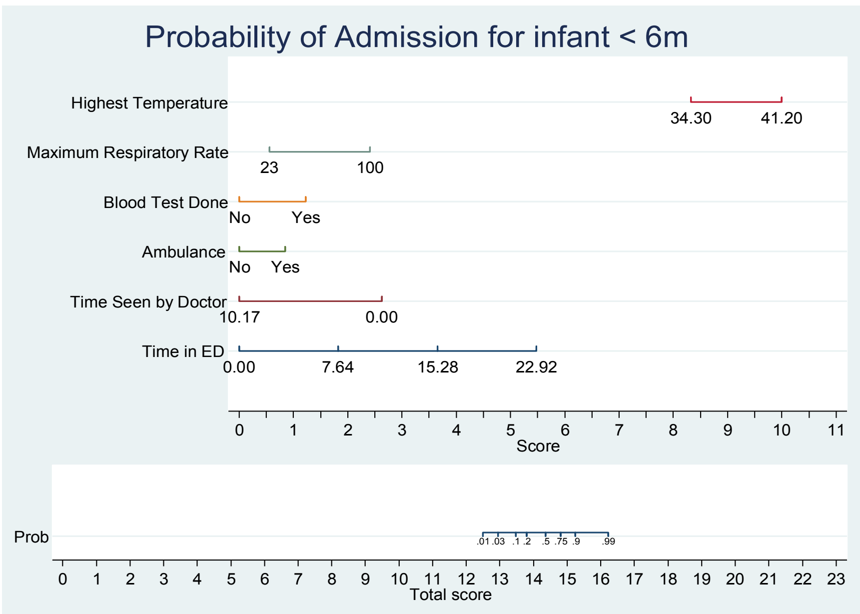

Figure 4. Scoring system to predict likelihoods of infants being admitted from ED based on some clinical features and administrative information.

Time to be seen by an ED doctor was shown to be inversely related to the risk of admission in this model. A similar pattern was observed in a study observing older children in Triage categories 3 and 4 [13]. On the other hand, with other factors controlled, the infants remaining in the ED for a longer period of time were more likely to be admitted. This could be explained by sicker infants requiring a longer time period to be evaluated, and the time taken awaiting the formal admission process by the inpatient team.

The underlying pathological process diagnosed by clinicians will impact the management of these infants. However patient factors other than the specific disease entity can also have a significant influence, as previously observed in a study regarding children with UTI [14]. Risk of admission was noted to be higher in patients of young age, male gender and higher co-morbidity status, along with those suspected of having complicated UTI and sepsis. It should also be considered that treatment modalities initiated by physicians such as oxygen therapy or intravenous fluids, in addition to disease severity signs displayed by the patient, can influence decision to admit. This was observed in a study examining predictors for admission in infants with bronchiolitis [15].

When presented with infants with non-specific complaints and hence unclear diagnoses, physicians may feel they are left without the additional information they need to commence appropriate management strategies. They hence often opted to order blood tests in the infants they had a higher level of concern about or deemed to appear unwell looking. This highly significant independent predictor was found to be positively related to the likelihood of being admitted to hospital in the combined model.

The combined model also indicated febrile infants to have a higher risk of admission. This has also been demonstrated in a study on children with peri-orbital cellulitis [16]. Another significant predictor in the combined model was faster respiratory rate, a surrogate marker for respiratory distress and other related physiological changes in sick infants.

Limitations

Young infants are vulnerable to some serious conditions warranting admission to hospital. There are many factors which could contribute to their increased risk, and not all of them were considered in this study. Among them, prematurity status and body weight changes are significant factors which were not included. Indeed it has been demonstrated that variables such as low body mass index lead to higher risk of being admitted from ED [17].

As a retrospective chart review, missing data on some patients was inevitable. List wise deletion of the relevant patients reduced the statistical power of this study.

Being a single centre study, the findings may not be generalized to other EDs with different skill mixes and management protocols. Previously exemplified by a study indicating that the standardized admission rate for bronchiolitis was 45% lower in Paediatric ED than in the general ED [2].

A better designed multicentre prospective study in the future could help to solve the limitation issues mentioned above.

Conclusions

Whilst the admission rate is thought to be reflective of the acuity and severity of patient presentations to the Emergency Department, the decision to admit is often a multifactorial process surrounding the evaluation of the patient. The process can be more complex in young infants with non-specific complaints. Altered clinical signs as a manifestation of underlying pathology, carers' and clinicians' approaches to the infants' condition and time taken to manage their condition in ED are incorporated into an internally validated model. The proposed prediction model could assist clinicians in clinical decision making when considering young infants with similar non-specific complaints. A previously developed model was proposed as a measure to compare decision-making performance in different EDs [18]. Thus it is proposed the scoring system derived from this study could also be useful as a bench marking measure and institutional comparisons.

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