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"TOPS: a reliable and simplified tool for predicting mortality in transported neonates".

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Abstract:
Background: *Illness severity scores have been used as predictors of neonatal mortality to give prognostic information to parents about their baby,to identify high risk babies for prompt action (triage) and for standardized comparisons between neonatal units for quality assessment.*
Objective:*To evaluatethe TOPS (Temperature,Oxygenation,Perfusion and blood Sugar) score predictive value for hospital death so as to institute an easy tool for assessing mortality index in transported neonates.*
Methods:*A prospective study was conducted in a tertiary teaching hospital enrolling 500 transported neonates. TOPS scoring was done at admission (temperature by digital thermometer in axilla, saturation by pulse oximeter, capillary refill time in mid sternum region, blood sugar by reagentstrip) and babies were followed for outcome.*
Results: *A mortality of 22.8% was observed. Prematurity and birth asphyxia were leading causes of mortality. Derangements in TOPS variables had significant correlation with neonatal mortality onunivariate odds ratio analysis. Hypothermia was commonly observed in transported neonates (39%).The sensitivity, specificity, positive and negative predictive values of derangements of two or more TOPS parameters in predicting mortality were 71.9%,80.8%,64.3% and 90.1% respectively. The score accuracy for mortality was confirmed (area under the ROC curve = 0.764).*
Conclusions: *Besides being useful to predict hospital death, TOPS was a simple score that can be easily applied in neonatal units.Based on these results, we recommend TOPS score to be done routinely for all the babies at admission.*
Key words:*TOPS score, transported neonates, mortality, prognosis.*

I. Introduction

Niloufer Hospital for Women & Children is a tertiary care teaching hospital that receives several sick extramural neonates delivered in the state of Telangana and adjoining states of Maharashtra, Andhra Pradesh and Karnataka. Most of them are transported without proper stabilization from referral hospitals. The care during their transport is also not satisfactory. The assessment of illness severity in neonates at admission is central to assessing risk of fatality [1]. Numerous scoring systems, predict illness severity and mortality in neonates however, none of them can be routinely implemented in developing countries [2-9].Scoring systems for the assessment of severity of neonatal illness are increasingly utilized to compare populations and quality and cost of care at different centers as well as to predict morbidity and mortality. Such systems facilitate communication about and comparison of neonates at different centers. Proposed systems have used data obtained at the beginning, during, and at the end of hospitalization to predict these various outcomes. However, it must be remembered that these systems provide generalizations about groups and that they do not allow the bedside clinician to predict outcome for an individual patient. The desirable properties of neonatal scores have been described as including: "(1) ease of use; (2) applicability early in the course of hospitalization; (3) ability to reproducibly predict mortality, specific morbidities, or cost for various categories of neonates; (4) usefulness for all groups of neonates to be described."[10] However, these properties are difficult, perhaps impossible, to achieve completely.

Birth weight has classically been considered as the most significant predictor of neonatal mortality. In developed countries, improvement of neonatal care advances in neonatal ventilation, and in particular the use of pulmonary surfactant have not only reduced preterm neonatal mortality, but also increased survival for extremely premature infants. Other factors have been found to affect morbidity and mortality, hence in present scenario birth weight alone cannot be taken as a predictor of mortality[11, 12].

Tarnow-Mordi et al published a scoring system, the Clinical Risk Index for Babies (CRIB) score that was created to predict mortality for infants born at less than 32 weeks gestation at birth and was derived using data from infants admitted to four UK tertiary neonatal units from 1988 to 1990 .It takes into account birthweight,gestational age, maximum and minimum fraction of inspired oxygen (FIO2) and maximumbase deficit during the first 12 hours, as well as presence of congenital malformations.[5]In the 1990s, Richardson et al, developed the Score for Neonatal Acute Physiology (SNAP) assessing the worst clinical status found in the first 24 hours after admission using points assigned to 26 physiological variables: the higher the score, the greater the risk of death. With the Score for Neonatal Acute Physiology Perinatal Extension (SNAPPE), 3 additional variables were added: birth weight, the Apgar score, and being small for gestational age [13].Due to the time needed to complete scoring, the authors subsequently developed a simplified version of the score, using only 6 variables (mean blood pressure, lowest temperature, Po_2/Fio_2 ratio, serum pH, multiple seizures, and urine output) to be measured within 12 hours of admission. The simplified scoring system was designated SNAP II and its perinatal extension SNAPPE II[14]. These scoring systems have been validated in studies with large numbers of patients and have been shown to be very good predictors of mortality in newborns in neonatal intensive care units (NICU). Both theCRIB and SNAP II use data collected over 12 hours andthus may reflect the effects of interventions ratherthan the underlying risk at an early time point.

A 7-variable (Apgar score at 1 minute, birthweight, presence of a congenital anomaly, and infant'sage, pH, arterial partial pressure of oxygen, and heart rateat the time of the call) model was used to generate the MINT score, which gave areas under ROC curves of 0.80 for both neonatal and perinatal death[4]. But the availability of ABG and documentation of APGAR scores for all cases is difficult to be obtained in government hospitals hence there is a need for simpler yet reliable score for prediction of mortality in a transported neonate.

Neonatal physiology is adversely affected based on **t**emperature, **o**xygen saturation, skin **p**erfusion and blood **s**ugar (TOPS) which have shown to predict the mortality in transported neonates by MathurNBet al[15]. TOPS score has an equally good prediction for mortality as SNAP II and can be used as a simple and useful method of assessment of fatality that can be assessed immediately, at admission.

The present study is therefore designed to evaluate the reliability of TOPS and forming a scoring system as it can be easily and effectively used in high flow resource constraint government hospitals to prognosticate the outcome of the babies at admission.

II. Materials And Methods

This prospective observational study was conducted for the period of six months from July to December 2015 in the Department of Neonatology at NilouferHospitalforWomen & Children, Osmania Medical College, Hyderabad,enrolling extramural (outborn) newborns.

Inclusion criteria: All the extramural neonates (<28 days) requiring admission.

Exclusion criteria: Neonates having life threatening congenital anomalies Refusal to give informed written consent.

A total of 500 babies were screenedand enrolled in the study as per the above criteria. A pre-designed proforma was used to record information at the time of admission. Ethical Committee approval was taken for the study. Written consent was taken from the attendants after explaining them the purpose of study in their own language.

The study was questionnaire based, where the receiving resident shall document the complete history, examination and clinical physiological parameters (TOPS) as observed on arrival of the baby on a data capturing sheet.

It includes:

i. **T**emperature by digital thermometer in axilla,
ii. **O**xygenation by Spo2 monitoring (radical 7 pulse oxymeter),
iii. **P**erfusion by capillary refilling time(CRT) on mid-sternum,
iv. **S**ugar by reagent strip and low reading <45mg/dlconfirmed by serum samples at laboratory [16].

Hypothermia, hypoxia, prolonged CRT and hypoglycemia were defined as <36.5°C [17], <90%[15], ≥ 3 seconds [18] and < 45mg/dl [22], respectively.

2.1Statistical Analysis:

Data was analyzed and tabulated; SPSS software version 21 was used. For continuous variables t-test, for categorical variables chi-square test and multiple logistic regression were used. Sensitivity, specificity, positive and negative predicted values, area under the ROC curve and total classification rate were calculated for validation of TOPS score. For predictors of mortality p value < 0.01 was considered significant.

III. Results

A total of 500 babies were enrolled in the study, out of which 307 (61.4%) were males and 193(38.6%) were females.Mean age of neonate was 30hrs, weight at admission was 2265g and gestational age was 35wk at admission.Out of 500 babies, 360 (72%) were discharged, 114 (22.8%) had expired and 26 (5.2%) left against medical advice. Hence the correlation of TOPS score on mortality was done on 474 babies. Out of 114 deaths 70 (61%) were male babies and 44 (39%) were female babies, comparable with admission magnitudes.

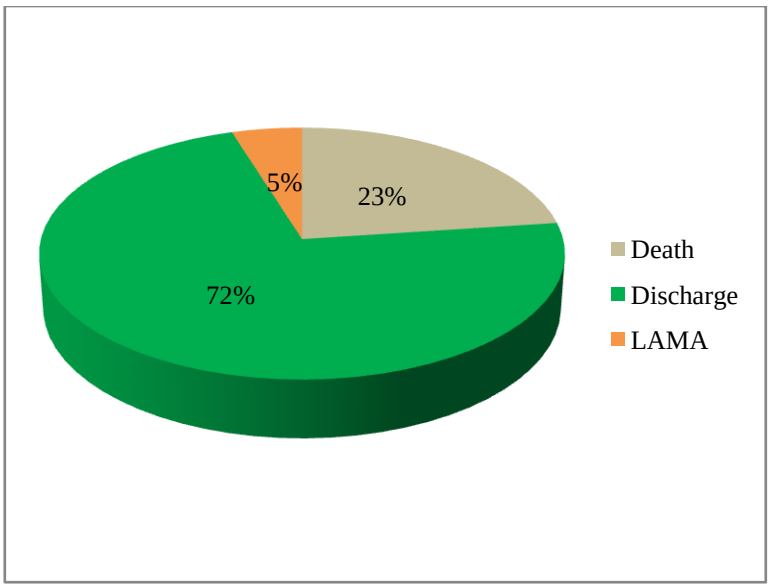

Figure 1. Outcome of study population

Descriptive analysis at admission of weight and gestational age of babies who died and those who survived, as well as the respective standard deviations, and minimal and maximal values, are shown in Table 1.

Table 1: Mean, minimal value, maximum value and standard deviation (SD) of weight at admission and gestational age in the patients that survived and in the ones who died

Statistics	Weight (g)		Gestational age (weeks)	
	Death	Survival	Death	Survival
Mean	1843.16	2398.25	32.64	35.95
Minimal	500	900	22.0	27.0
Maximum	3900	4000	37	40
SD	837.4	597.2	4.60	2.09

The demographic characteristics of the admissions are presented in Table 2. Common indications for referral were birth asphyxia in 190 (38%), prematurity in 154 (30.80%), meconium aspiration syndrome in 139 (27.80%), neonatal jaundice in 74 (14.80%) and sepsis in 68 (13.60%) babies.

Table 2: Demographic profile of study population and its significance

Parameter	**Deaths(n=114)**	**Discharged(n=360)**	**P-value**
Age (Hours) at admission	18.22	35.75	0.029
Weight (gms) at admission	1843	2398	0.0001
Gestational Age (weeks)	32.64	35.95	0.0001
Diagnosis (number)*			
Sepsis (68)	7	61	0.0034
Birth Asphyxia (190)	57	133	0.0001
Meconium Aspiration Syndrome (139)	28	111	0.6804
Low Birth Weight (154)	65	89	0.0264
Congenital heart disease (8)	2	6	0.8547
Neonatal Jaundice (74)	2	73	0.1245
Others (61)	22	81	0.0315

*Babies had more than one diagnosis

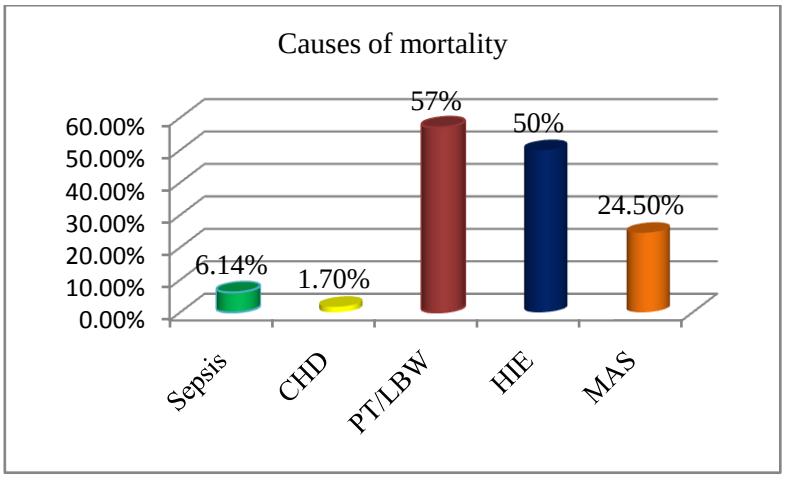

Figure 2: Causes of mortality among the expired neonates

Derangements in TOPS variables had good correlation with neonatal mortality as depicted by univariate odds ratio analysis.Prolonged capillary refill time (CRT) indicating poor perfusion was the strongest predictor of mortality with highest odds ratio. Though pulse oximetry has its limitations but saturation must be noted in every neonate as hypoxia was observed as a significant predictor of mortality.

Table 3: Odds ratio of TOPS variables for predicting mortality

Predictor Variable	Univariate odds ratio (95% CI)	p-value
Skin Temperature	3.2529	0.0080
<36.5°C	(1.36 – 7.77)	
Saturation	11.9985	<0.0001
<90%	(7.36 – 19.55)	
Blood Sugar	2.59	0.01
<45mg/dl	(0.86 – 4.63)	
CRT	29.76	<0.0001
≥3 seconds	(13.44 – 65.87)	

Hypoxia was found in 141 (28.2%) babies. Hypothermia was found in 195 (39%) babies. Severe hypothermia(< 32° C) was found in17 babies (3.4%) of which 14 (82%) expired. Hyperthermia was found in 43 (8.6%) babies. Prolonged capillary filling time was identified in 55 (11%) babies. Hypoglycemia was found in 30 (6%) babies. Hyperglycemia was identified in only 3(0.6%) babies and none of them died.There was no derangements in TOPS score in 253 neonates, out of which 13 expired (p-value <0.01). All the four parameters were abnormal in 6 neonates with 100% mortality.

Table 4: Altered parameters of transported neonate leading to mortality

Parameter*	At Admission	At Mortality
Skin Temperature(<36.5°C)	195 (39%)	83 (73%)
Saturation(<90%)	141 (28.2%)	79 (69%)
Blood Sugar(<45mg/dl)	30 (6%)	11 (9.6%)
CRT(≥ 3 sec)	55(11%)	46 (40.3%)

*Babies had more than one parameter deranged.

A score of 1 was given for each deranged parameter in TOPS i.e., hypothermia, hypoxia, hypoperfusion and hypoglycemia and a score of 2 for each normal parameter, thus every neonate gets a score ranging from 4 (minimum) to 8 (maximum). It was found that group of neonateswith scoring4 to 6 had mortality of 54.3% and those with score of 7 & 8 had 9.9%. Thus a cutoff of two or more deranged parameters in TOPS had a significant prediction of mortality with p – value <0.01.

Table 5: Scoring of TOPS and its outcome

TOPS	Outcome		Total
	Death	Discharge	
4-6	82 (54.3%)	69 (45.7%)	151 (100%)
7-8	32 (9.9%)	291 (90.1%)	323 (100%)
Total	114 (24.1%)	360 (75.9%)	474 (100%)

Fig. 3 shows the ROC curve of TOPS score. The value under the curve was 0.764 (95% CI: 0.710 – 0.817) with a standard error of 0.027. The curve is deviated upwards and to the right, so that it is located in the upper right corner of the graph. This means that, as sensitivity decreases, it is not followed by loss of specificity. Therefore, TOPS turns out to be a reliable test to predict the mortality of transported neonates. Thus it can be used effectively to triage the babies who require prompt treatment and strive for intact survival of neonates.

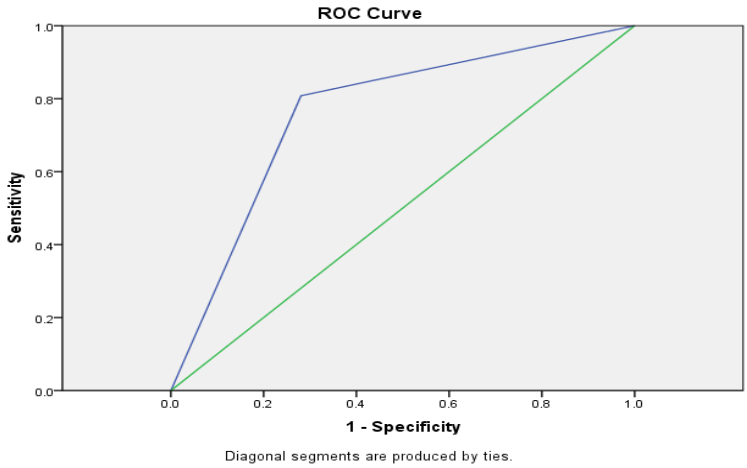

Figure 3: ROC Curve of TOPS Score

IV. Discussion

Undoubtedly, thesurvival perspective of extramural neonates does not rely only onthe quality and intensity of the available neonatal care, butalso on the state of the neonate at admission.A mortality rate of 22.8% was detected in the present study. Being one of the major referral points in Telangana and the surrounding states, this hospital caters to high risk neonates referredfromits wide catchment area. This could be the reason for witnessing higher mortality. However, mortality rate of 25-35% have also been reported in previous Indian studies among the neonates transported to tertiary care center[20-24].

Although severity of illness is a familiar medical concept, it is sometimes difficult to assess. In the context of intensive care, a rational and objective way to define and quantify severity of illness is through the development of probabilistic models predicting mortality risk.[25]The present study revealed that derangements of two or more TOPS variables had good sensitivity, specificity, positive and negative predictive values comparable to Mathur NB et al study[15].

Table 6: Comparison of TOPS Significance

Parameters	Present Study	Mathur N B et al study[15]
Sensitivity	71.9%	81.6%
Specificity	80.8%	77.4%
Positive predictive value	64.3%	72.3%
Negative predictive value	90.1%	89%
Area under ROC curve	0.764	0.89
Total correct classification rate	78.7%	81.7%

During this study, we verified that TOPS score was easily applied. This score is practical, since it uses variables that are part of the routine care of newborns, and also because they are quickly obtained. TOPS score can be easily reproduced, avoiding interpretation errors due to individual subjectivity. The quantitative expression of TOPS score as a mortality predictor was assessed through thearea under the curve of thereceiver operating characteristic curve. Thus, TOPS score confirmed its fair ability to predict hospital mortality, with an area of 0.764 under the ROC curve.

Highest altered parameter found in the study was hypothermia (39%), as shown in other related studies[15, 16].In the present study, the mortality in severely hypothermic babies was found to be 82%; similar figure of 80% was depicted in the study conducted by Mathur NB et al in 2005[26].

We found that there was 100% mortality in babies with all the four deranged parameters at admission, a similar association was found in studies conducted by Mathur N B et al study[15] and Dalal Ekta[16]. It reinforces the fact that once the irreversible cellular injury sets in any extent of heroic efforts taken to revive the baby becomes futile. Hence a meticulous neonatal transport is of utmost importance and need of the hour in neonatal care to reduce neonatal mortality.Because of the obvious ethical issues involved, we want to emphasize that the present scoring system is not sufficiently accurate to identify those patients who cannot be saved.

V. Conclusion

Illness severity scores for newborns are complex, cumbersome and require expensive equipment. Most of the referral cards do not have proper history like APGAR score and resuscitation done to newborn hence the scores in which this information is required cannot be applied.TOPS score comprises following features that are necessary for an efficient predictive score of mortality: (1) reliability, (2) easy application, (3) applicability early in the course of hospitalization and (4) usefulness for all groups of neonates to be described.Because of these features, TOPS seems to be the score of choice for the assessment of neonatal units, especially in countries where advanced diagnostic and therapeutic resources are limited.

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