Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 11591 - 11608
Received 05 March 2021; Accepted 01 April 2021.

Prediction of Mortality in NICU of Tertiary Care Rural Hospital by using SNAPPE II (Score For Neonatal Acute Physiology With Perinatal Extension-II)

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ABSTRACT

Background: Neonatal mortality is topic of concern for many healthcare faculties. Score for Neonatal Acute Physiology with Perinatal Extension-II (SNAPPE II) score is objectified in this study to predict the mortality and morbidity of the neonates in neonatal intensive care unit (NICU). This study aimed at the prediction and correlation of mortality and morbidity of neonatesusing SNAPPE II score.

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Methodology: In the present prospective observational study, 50 neonateswith weight less than 1500 grams admitted in the NICU fulfilling the inclusion criteria were selected. The SNAPPE II score within 12 hours after arrival to the NICU was evaluated and noted. Each patient was evaluated underthe nine parameters of SNAPPE II and analyzed using the chi^2 test for each component**.**

Results: The results are showing significant association between the gestational age (p=0.001), mean arterial pressure (p=0.001), urine output (p=0.008), APGAR(<7) (p=0.012), low weight (p=0.002), ventilator support (p=0.001), inotropes (p=0.001), duration of study (p<0.00001) and total score (p=0.001). The value of ROC (Receiver Operating Characteristics) curve was 0.94 predicting the mortality of neonates weighing less than1500grams.

Conclusion: The mortality in neonates was inversely proportional to gestational age, low mean arterial pressure anddecreased urine output. Low APGAR indicated poor outcome in very low birth weight neonates. The less weight of neonates specifically extremely low birth weightshave significant association with higher mortality. A short duration of stay has highest mortality with RDS (Respiratory Distress Syndrome) as most common cause of death. Hence, the overall performance of SNAPPE II score was good with AUC (Area Under Curve) 0.94 (good discrimination) and reasonable agreement between observed and expected mortality.

Keywords: Mortality, Neonate, SNAPPE II, Rural, Tertiary Care, NICU

Introduction

From the inception of modern medicineneonatal mortality is topic of concern for many healthcare faculties.Efforts are beingmade to tackle the fragile issue of neonatal mortalitywith an attempt to bringfruitful outcome.On the journey to accomplish this target we have received substantial success in the form of statistical improvement in outcome.

Data published by WHO and supported by UNICEF[1]reflects reduction of neonatal mortality to 19 deaths per 1000 live births globally in 2016.Most of the credit goes to realization of the problems and its solution in form of trained staff, allocation of dedicated infrastructure, newer technologies and equipment to address the issues in setup. Documentation remains the mainstay to compare the outcome from various parts of the world.

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The risk markers which are available routinely, such as birth weight, gestational age and sex, do not accurately capture and clarify the degree of disease severity. The use of prognostication scoring systems has resolved this question in NICUs. During recent years many of such scoring systems have evolved focusing on severity and prognosis of patients like Clinical Risk Index for Babies (CRIB), CRIB II , Pediatric Risk of Mortality score III (PRISM III)[2],Score for Neonatal Acute Physiology (SNAP), SNAP II, SNAP with perinatal extension (SNAPPE II). Such scoring systems help to predict patient morbidity and mortality and help to improve the outcome evaluation between various hospitals and units.

In 1993, the neonatal acute physiology (SNAP) score for newborns of all birth weights was established and a score was validated to predict mortality, a physiology-based score using 34 parameters and laboratory test results that are commonly available by Richardson et al [3][4]. SNAP was a newborn disease severity score of the first generation, which was difficult to use because of its number of products and unavailability. An updated version of SNAP score known as SNAP II was validated by Richardson et al in 1998. To make SNAP II simpler, the number of things and the length of the first 12 hours of admission were reduced to six, to mitigate the impact of early care. Three perinatal variables were applied to the SNAP II score including birth weight, APGAR ratings, and small gestational age [5]and were referred to as SNAP II with perinatal extension (SNAPPE-II). The aim and objective of the research was topredict mortality of neonates in NICU by using SNAPPE II (Score for Neonatal Acute Physiology with Perinatal Extension-II) and to study correlation of SNAPPE II score and mortality.

Materials and Methods

1. **Setting:** The present study was conducted at the Department of Pediatrics, Acharya VinobaBhave Rural Hospital, Jawaharlal Nehru Medical College, Sawangi(Meghe),Wardha.
2. **Ethics Committee Permission:** The study was initiated only after obtaining permission from the Institutional Ethics Committee with reference no ‘DMIMS (DU)/IEC/2018-19/7481’.
3. **Study Design:** It was a prospective observational study of consecutively selected newbornsweighing less than 1500 gramsadmitted in the NICU of this hospital, fulfilling the inclusion criteria.

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4. **Selection Of Study Population:**

Inclusion Criteria:

All newborns coming to NICU with birth weight less than 1500 grams.

Exclusion Criteria:

1. Neonates discharged against medical advice and referred patients

2. MajorCongenital malformations

3. Newborns getting admitted to out-born section of NICU

5. Sample Size: 50

6. Study Duration: It was conducted for a period of two years from 1st August2018 to 31stJuly 2020.

7. Methodology: The information that was collected onNICU admission (after taking written consent from parents) includes name, age, IPD no, sex, stay, date and time of birth weight, gestational age, APGAR score at 5 minutes, place and type of parturition, postnatal age at admission, type of delivery, diagnosis, nature of outcome (survival /non-survival). All the subjects were enrolled with necessary investigations and their SNAPPE II score was evaluated within 12 hours after arrival to the NICU. The SNAPPE II score evaluation was done as per recommendation of Richardson et al [3].The outcome at discharge was determined as non-survival or survival. All this information was recorded inpredesigned proforma.

8. Ethical Consideration: Informed Consent was taken from parents of all new borns included in this study. This consent procedure was reviewed and approved by the Ethics committee of the Datta Meghe Institute of Medical Sciences(DU).

9. Sample Collection:

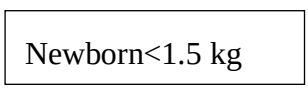
Population proportion was 0.3

Sample proportion was 0.21

Powerof90% with 5% alpha error

Sample size = 50

Study Flow Chart



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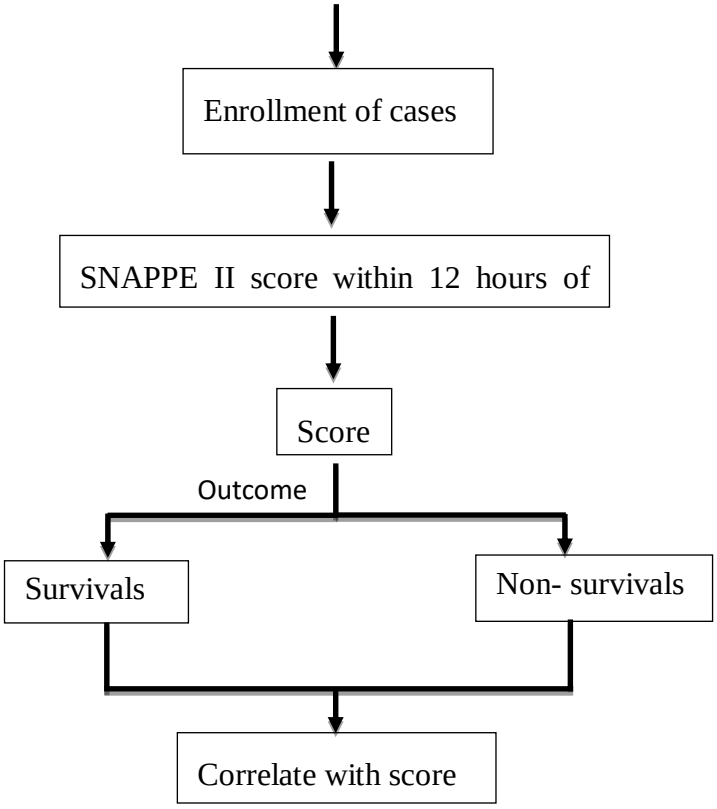

SNAPPE-II score has 9 parameters.Each patient was evaluated undereach of the parameter.

Results:

In this study, the data of 50 newborns with weight less than 1500 gram without any congenital anomaly were included.

Table 1: Gestational Age and Outcome &Score

Gestational age		Outcome		
	Death (score)	Score	Discharge	Score
≤ 30 wks(15)	12 (80%)	59.33	3 (20%)	37.33
≥ 31 wks(35)	9 (25%)	44.33	26 (75%)	19.57
Total	21 (42%)		29	

The chi^2 value was 10.52, p value 0.001illustratingthe mortality in newborns was inversely proportional to gestational age.

Table 2: MAP and Outcome and Score

Mean blood	Outcome

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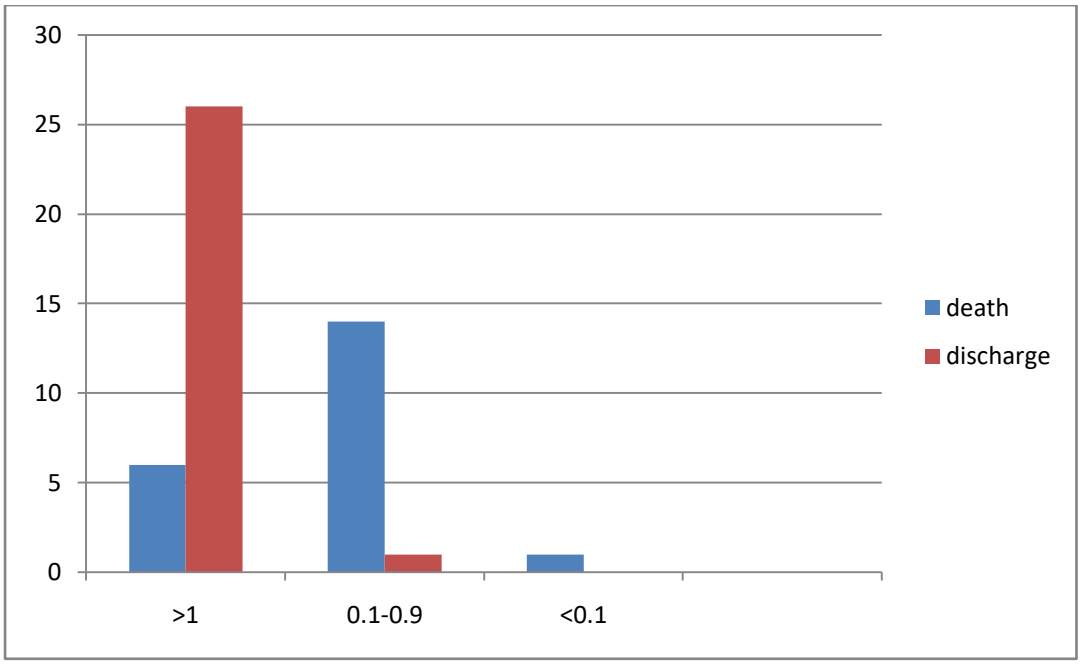
pressure (mm Hg)	Death	Score	Discharge	Score
>30	3	43	21	16.42
20-29	12	55.5	6	33.33
<20	6	69.8	2	43
Total= 50	21		29	

The chi^2 value was 16.64 and p value 0.001illustratinglow mean arterial pressure was related to high mortality.

Graph 1: Urine Output and Outcome Score



The association of decreased urine output i.e. oliguria (0.1-0.9 ml/kg/hr) and anuria (<0.1 ml/kg/hr) was significantly associated with increased mortality with chi^2 value 7.07 and p value 0.008

Table 3: APGAR Score and Outcome and Score

APGAR	Outcome			
	Death	Score	Discharge	Score
>7	15	16	28	21.14
<7	6	72.5	1	39

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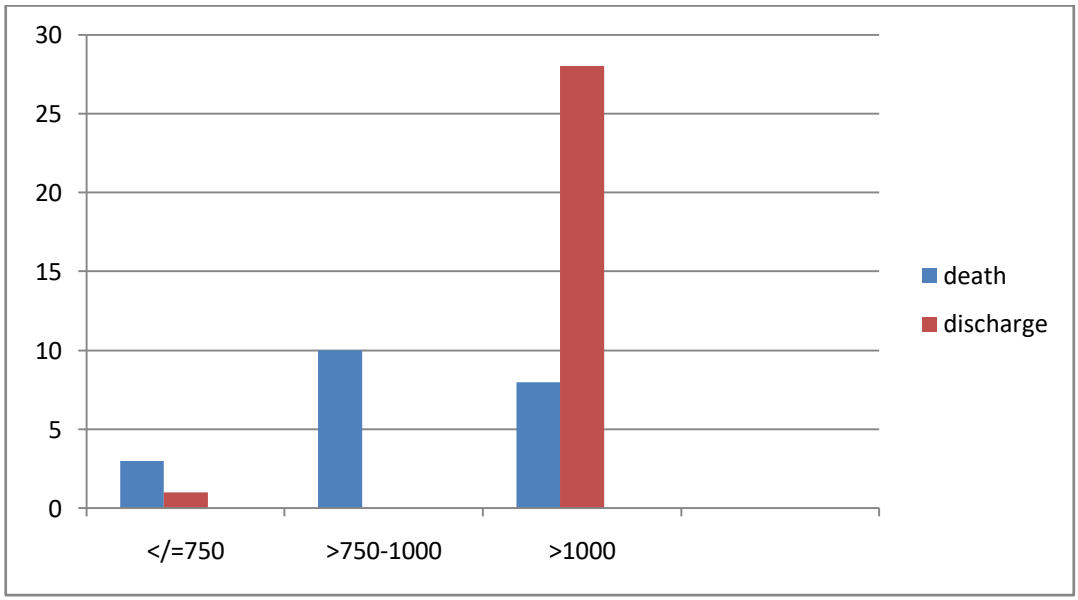
Low APGAR (<7) indicated poor outcome in very low birth weightneonates with chi^2 6.3, p value 0.012.

Graph 2: Weight and Outcome and Score



The less weight of neonates, specifically extremely low birth weights, had significant association with higher mortality with chi^2 9.23, p value 0.002.

Table 4: Ventilator Support and Outcome &Score:

Ventilator support (n)	Outcome			
	Death	Score	Discharge	Score
No(18)	0	0	18	16.94
Yes (32)	21	57.85	11	29.63
Total (50)	21		29	

The ventilator mortality in the current study was found to be 65.62% with chi^2 20.37, p value 0.001.

Table 5: Inotropes and Outcome &Score

Inotropic support (n)	Outcome			
	Death	Score	Discharge	Score
Yes (33)	21	57.8	12	30
No (17)	0	0	17	15.94

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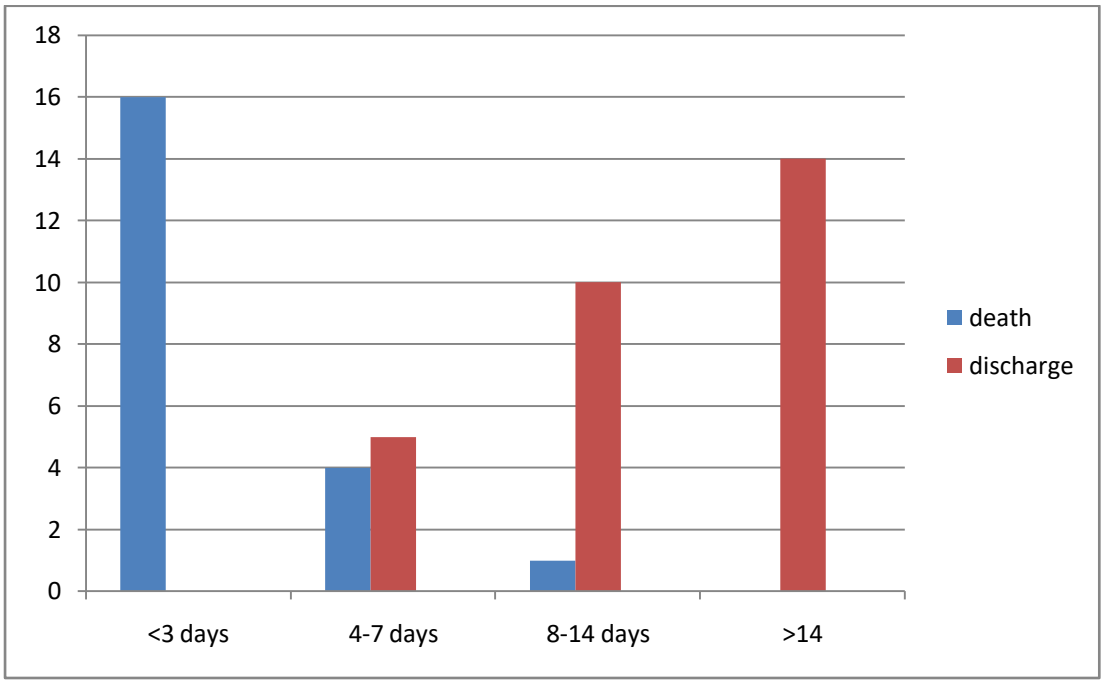
Total (50)	21		29	

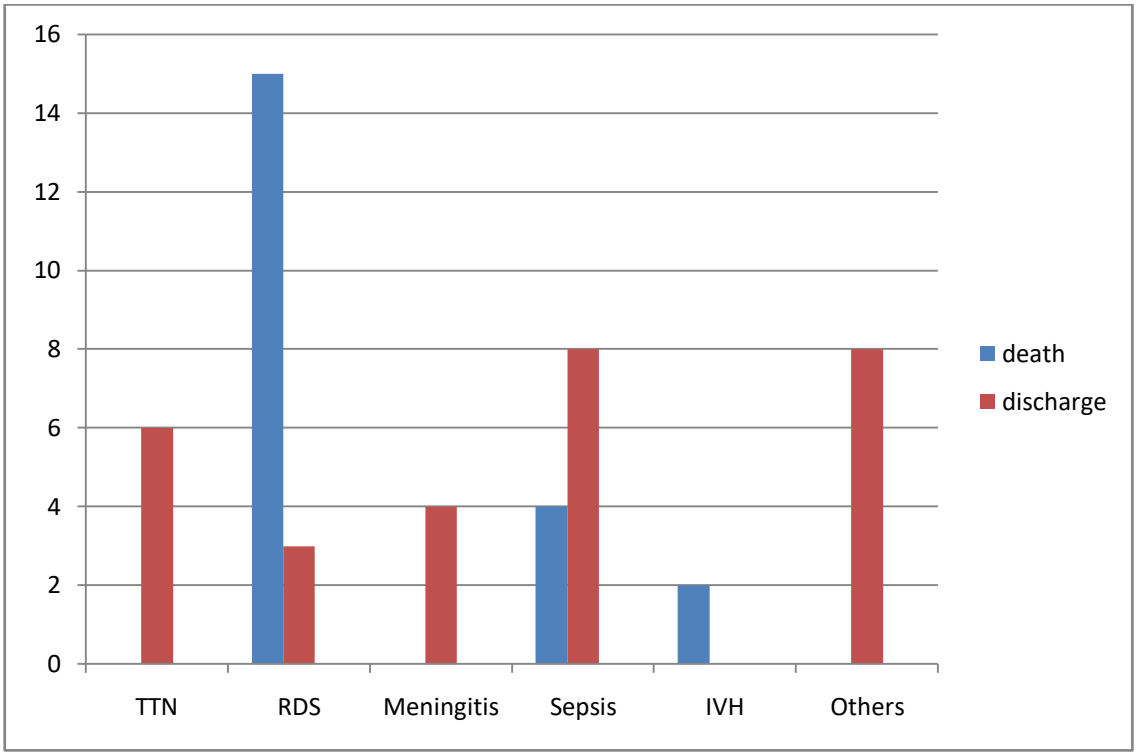
Themortality of neonates on inotropic support was 63% with chi^2 18.65, p value 0.001.

Graph 3: Duration of Stay and Outcome &Score



A short duration of stay has highest mortality. More the duration of stay, less was the mortality with chi^{2}29.6388p-value < 0.00001.

Graph 4:Diagnosis and Outcome &Score



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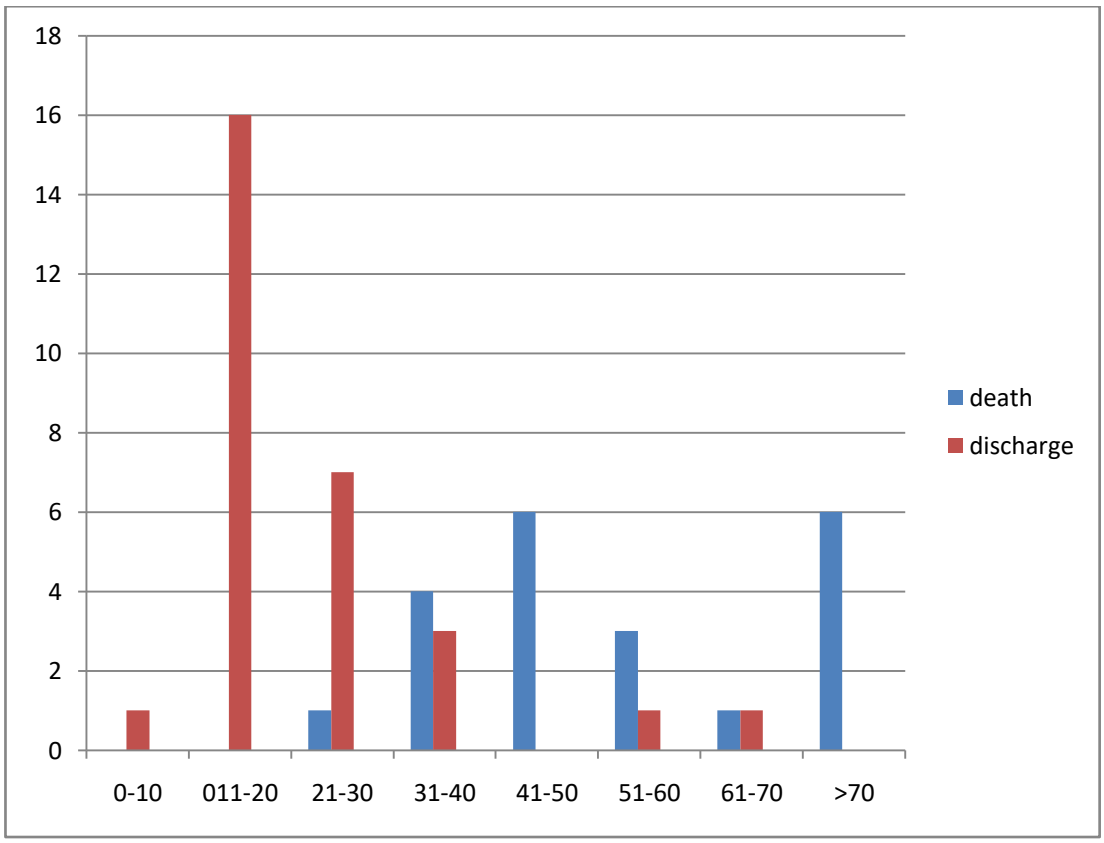
The most common cause of death in the study was respiratory distress syndrome.

Graph 4: Total Score and Outcome and score



Higher the score, more was the mortality in the neonates with chi^{2}value 29.44 and p-value 0.001.

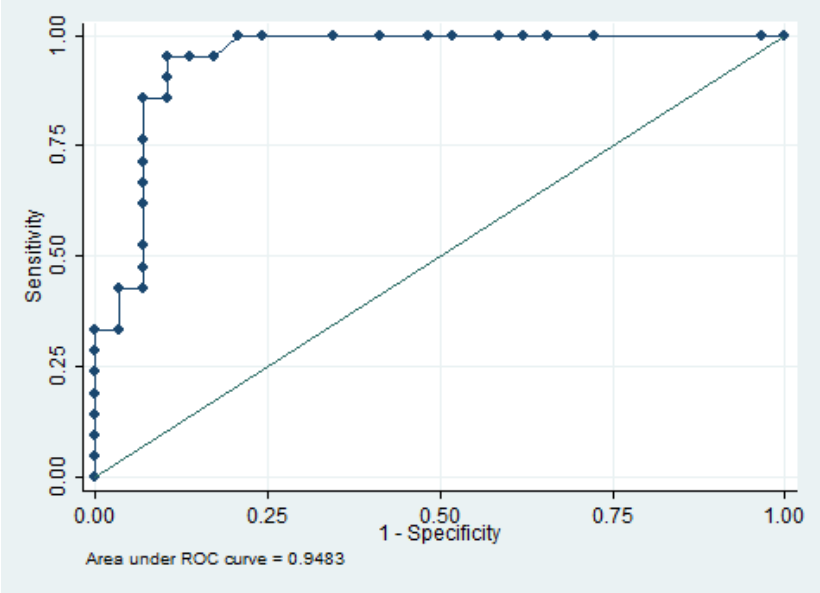


Figure 1: ROC Curve

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The value of ROC curve was 0.94 in the study. This was significantto predict mortality ofneonates weighing<1500g. The standard error of mean was 0.032 and confidence interval was 0.887 - 1.0in 50 neonates. A cut-off score of>/= 34 predicted mortality of these neonates with sensitivity 95.24%andspecificity 89.66%.The corresponding positive likelihood ratio was 9.20 and negative likelihood ratio was 0.0531.

Discussion:

Total 50 neonates were includedin this study according to the inclusion and exclusion criteria. Out of 50 newborns, 21 (42%) died and 29 (58%) survived. The cut off score was 34 with sensitivity of 95.24%andspecificity 89.66% predicted the mortality. A ROC curve was obtained, area under curvewas 0.94, which was found to be significant. Also, it was observed, that there were no cases who had any episode of seizure.

In this study, there were 24 (48%) male and 26 (52%) female neonates with ratio of 0.9:1.Sundaram V et al (2009)[6], Remirez MNM (2014) [7] and Mia RA et al (2005) [8]included more male neonates in their respective studies indicatingthe distribution of male and female neonates was not skewed in significant proportion in any of the studies indicating almost similar number of admissions in the NICU for management of neonatal illnesses.

In the present study, there were 11(22%) deaths in male neonate and 10 (20%)in female neonates. Gender as a contributor in mortality was not noted due to systemic neonatal illnesses. Mia RA et al (2005)[8] found 16 (36%) male deaths and 12 (33%) female deaths and by Radfar et al(2018) [9]found that 8(7%) deaths were in male neonates andsimilar mortality figures were observed by Thimoty J et al(2009)[10].

In this study,for the gestation ≤30 weeks, deaths were 12 (80%) out of 15 with average score of 59.33 and discharged neonates were 3 with average score of37.33 against babies born≥31 weeks. In the study by Samanta M et al (2020)[11], 5 (22%)newborns died out of22, from 32-36 weeks, 9 (19) newborns died out of 47 and when the gestation was >37 weeks, 10 (14%) died out of 67 neonates admitted for clinical suspicion of neonatal sepsis. Also, Thimoty J et al (2009)[10] found the mortality of preterm babies was 12 (46%) and in term babies was 3 (21%) with the inclusion of newborns of all gestational age showing significant association in prematurity and increased neonatal mortality. Similar findings were noted by Mia RA et al (2005) indicating lower gestational age with higher mortalityamong the newbornsas compared to survived neonates.

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It was observed that when MAP was <20 mm of Hg, 6 neonates died out of8 with average score of 69.8, the score in discharged neonates was 43. Similarly,when the MAP was 20-29 mm of Hg there were 12 deaths out of 18 with average score of 55.5. thesimilar MAP ranges had 6 discharges with average score of 33.33.Low MAP (<20 mm of Hg) in 3 neonates associated with 100% mortality and if the MAP was 20-29 mmHg, 12 (85%)out of 14 neonates diedwhile a MAP of>30 mmHg had only 6 (3.5%) deaths in a study by Radfar M et al (2018)[9].Samanta M et al (2020)[11], studied MAP as a risk factor for mortality and observedthat when it is <20 mm of Hg,20-29 mmHg and > 29 mm Hg the chance of mortality washigher for lower mean arterial pressure. In thisstudy, neonates were included after the diagnosis of severe septicemia as babies may not be very sick at admission to NICU and critical illness would start later in the course of NICU stay. Helal NF et al (2013)[12] observed that low MAP was significantly associated with death and organ dysfunction and Ashrafzadeh et al (2019)[13] observed low MAP associated with mortality(p value 0.021).

In the above study, the hypothermia was associated with high death rates in the neonates. When the temperature was $>96^0$ F, there were 19 (76%) discharges however not correlated with neonatal outcome because p value was >0.05.Similar non-significant findings were noted by Sundaram V et al (2009)[6] but Radfar M et al (2018)[9] found insignificant temperaturein expired neonates. Neonates are unable to maintain body temperature due to immaturity of hypothalamus, poor energy source and inadequate insulation to preserve heat leading to imbalance between the heat loss and production ultimately causing hypothermia. Persistent hypothermia is harbingerof shock and refractory shock with the high probability of fatal outcome.

In the current study, it was observed that higher pO_2 / FiO_2 ratio had more discharge (83.3%) and lower SNAPPE II scores. As pO_2/FiO_2 ratio decreased, the mortality in the neonates increased.The condition of the lungs affected the ventilation, when the ratio started to decrease and yet the p value was insignificant. Also, Sundaram V et al (2009)[6]supported the insignificance. Similar but not the same report was found by Aryana GK et al (2016)[14]with no better ratio (3.75) in survived neonates. A significant association of pO2/Fio2 ratio <2.5 reported by Radfar M et al (2018)[9]. In the current study, the insignificant result is probably because of two deaths when pO_2/fiO_2 ratio was >2.5.

No significant association was observed in the presence of acidosis in this study supported byAryana GK et al (2016)[14]. ButAshrafzadeh et al (2019)[13]observed no co-relation between serum pH and mortality (p value 0.701) but Rachuri S et al (2019)[15] suggested pH

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as a variable to be used as an independent parameter to predict mortality with significant statistical correlation which is further supported by Radfar M et al (2018)[9] and Sundaram V et al (2009) [6].

This study shows urine output and patient outcome is significantly associated with increased mortality supported by Radfar M et al (2018) [9] but contradicted by Helal NF et al (2013)[12], Aryana GK et al (2016)[14] and Ashrafzadeh et al (2019) [13] in their respective studies.Renal functions are very sensitive during neonatal period leading to alteration of secretion and filtration of toxic products making it a common association of critically ill neonates.In this study, the lower score of APGAR suggested more deaths supported by Kadivar M et al (2007) [16] and Gagliardi L et al (2004) but Samanta M et al(2020)[11] and Aryana GK et al (2016) found it to be insignificant in their respective research.

In this study, the less weight of neonates specifically extremely low birth weights, had significant association with higher mortality. The weight of newborns can correlate with the mortality as showed in the study by Radfar M et al (2018)[9]. Thimoty J et al (2009) showed that weight <1.5 kg had mortality of 72.2%[10] with improvement if the weight was >1.5 kg (24.13%).

In this study, it was observedthat there was no association between SGA and non-SGA neonates in the final outcome. Gagliardi L et al (2004)[17] concluded a significant risk of mortality with small SGA.Samanta et al (2020)[11]concluded that SGA neonates had more chance ofacquiring sepsis in both culture proven and culture negative categories. While estimating the validity of mortality in VLBW and ELBW infants score, Brattli SL et al (2004**)** [18] concluded gestational age of the babies offeredgood discrimination. Radfar M et al (2018)[9] and Ashrafzadeh M et al (2019)[13] found contradictory results.

The mortality in the current study was found to be 65.62% and similar report of 65% was found by Sultana SN et al (2020)[19]. There was not much difference in the mortality in a study on neonatal mechanical ventilation by Nagesh NK et al (2016)[20], the mortality rate was 52%.In the current study the mortality rate had been more in the last 2 years because of the increased referrals of critically ill neonates as the data compared with previous study from the same center, conducted during 2015-2017 by Damke S et al[21], had reported the mortality of 55%.

In the current study, mortality of neonates on inotropic support was 63%. Helal NF et al (2013)[12] mentioned the use of inotropic support to sustain circulation in cases ofneonatal

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sepsis. Those neonates were evaluated with SNAPPE II score, around 20% were on vasoactive drug support.

The sepsis rate in very low birth weight babies was 30% in the current study with most common cause of death was RDSfollowed by sepsisand IVH which proved fatal with 100% mortality in the study. Turhan EE (2015)[22] found sepsis and Jain K et al (2019)[23] found prematurity as the most common cause of death

In current study, short duration of stay has highest mortality. Richardson DK et al (1993)[3] reported similar findings. ButMuktan D et al (2019)[24] contradicted with no such correlation.Harsha et al (2015)[25]and Vasudevan A et al (2006)[26]supported the finding that length of stay has no correlation with SNAPPE-II score. Multiple reasons cited for the contrasting results of the score and length of stay like variability in gestational age, in probabilities of birth weight and type of illness.

The range of scores and neonatal outcome whether death or discharged revealed inverse correlation. Helal NF et al (2013)[12] found significant higher scores in babies who died v/s in those who discharged. Harsha SS et al (2015)[25]concluded that SNAPPE-II score is better predictor of mortality irrespective gestational age as compared to morbidity. The mortality figures in the current study were high because of unique geographical location of the place which caters to rural population and excessive referral to ICUs.

The value of ROC curve was 0.94 in the study. This was significant to predict mortality of neonates weighing <1500gram. The standard error of mean was 0.032 and confidence interval was 0.887 - 1.0 in 50 neonates. A cut-off score of≥34 predicted mortality of these neonates with sensitivity of 95.24% and specificity 89.66%.The corresponding positive likelihood ratio was 9.20 and negative likelihood ratio was 0.0531.

The results of current study match exactly with the ROC score ofUcar S et al (2014)[27], cut-off33 associated with higher mortality. Dammann O et al (2009)[28] studied the predictors of death by assessing SNAPPE-II score and found that overall institutional predictive value to be >30 to estimate NICU mortality. Samanta M et al (2020)[11] researched performance related to culture positive sepsis. The focus of objective was to test SNAPPE-II score in the presence of sepsis both culture positive and negative sepsis. The cut –off value >20 proved to be higher sensitivity of 74.5 % with specificity 48.3%, positive predictive value(PPV) 27.6% and negative predictive value (NPV) 87.7%.

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SNAPPE-II score was a useful tool that predicted neonatal mortality in NICU in the study by Muktan D et al (2019)[24]. The area under curve in ROC curve was 0.197 (95%)CI 0.854 to 0.980.The validated the use SNAPPE-II score for the prediction neonatal mortality setting a cut-off of 38. The sensitivity, specificity, PPV, NPV that could estimate score >38 for mortality were 84.4,91, 66.7 an d96.5 % respectively.

Harsha S et al(2015)[25] have done a prospective observational study concluded that SNAPPE II score is a good predictor of mortality but does not accurately predict the length of the stay with PPV of 95.3%, sensitivity of 76.9% and specificity of 87.1%. Compared to present study (specificity 47%), this study had high specificity (87.1%) and a good PPV which highly signifies the association between the score and the mortality rate.

A validation study done by Richardson et al (1993)[3]with the primary outcome being the in-hospital mortality rate concluded that SNAPPE-2 score had excellent association with the mortality rate with AUC of 0.91. Compared to their study, present study also showed significant association between the score and the mortality rate (p value <0.0001) but the ROC showed a moderate association with AUC 0.62

A prospective cohort study conducted by Aryana GK et al (2016)[14] concluded that SNAPPE II score is a good predictor of mortality in NICU babies with ROC of 0.92 which highly signifies the association between the score and the mortality rate, but in present study the ROC was 0.622 which indicates a moderate association between the severity of the score and the mortality rate.

In the study by Rachuri S et al (2019) [15], the mean SNAPPE 2 score associated with mortality was 34 with sensitivity of 78.8% and specificity of 47% (ROC 0.622) compared to a prospective observational study done by RA M et al(2005)[8] where a score of 30 was associated with higher mortality (ROC 0.863) with sensitivity 81.8%, specificity 76.9%.

Gagliardi L et al (2004)[17] collected data from 720 very low birth weight infants compared different neonatal illness scores. A result showed CRIB and CRIB-II has a greater discriminatory ability than SNAPPE II.

Contrary to present study, a prospective observational study done by Ramirez et al (2014)[7] concluded that results were not strong enough to establish the correlation between the score and the risk of mortality.

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Brattli S et al (2004)[18] done a prospective cohort study on 189 very low birth weight infants concluded that both CRIB-II and SNAPPE-II were found to predict mortality of very low birth weight babies whereas their value was poor in predicting morbidity.

Variation in the cut-off score and discrimination might be due to the factors affecting the score such as diseases, severity of illness, quality of care in NICU etc.

Thimoty J et al (2009)[10] determine the cut-off point to validate the SNAPPE-II score to predict neonatal mortality was 51. The study offered excellent discrimination and caliberation,AUC 0.933 (95% CI0.843-1). The current study discriminated AUC as 0.94 comparable with similar finding by Richardson et al (1993)[3]of AUC as 0.91 andZupancic JA et al (2007)[29] revalidated ROC scores at AUC of0.9.

A lower cut-off value given by Ashrafzadeh M et al (2019)[13]was associated withSNAPPE-II score of27.5. The sensitivity and specificity at the cut-off point of 27.5 were 79% and 89% respectively. They noted PPV and NPV of SNAPPE-II system were 58.9% and 93.45 respectively, however the chances of deaths predicted by the positive likelihood ratio was 4.01 and the likelihood of survival (false positive 0.197) in that study. A significant correlation was reported between overall neonatal mortality and SNAPPE-II score.

The variability in the ROC scores to predict the outcome might be due to disease spectrum, severity of illness, the level ofNICU care. The underline disease pathology may act as independent mortality risk factor altering the outcome of neonates. In spite of all possibilities, the overall strength of SNAPPE-IIscore was excellent.

Conclusion:

In this prospective study, the conclusion includes that the mortality in newborns is inversely proportional to gestational age. The low mean arterial pressure is found to be related with high mortality howeverthe gender distribution, lower temperatures, pO_2/FiO_2 ratio and presence of acidosis are statistically insignificant whereas the association of decreased urine output is significantly associated with increased mortality. Low APGAR (<7) indicates poor outcome in very low birth weight neonates. The less weight of neonates, specifically extremely low birth weights have significant association with higher mortality. This study found no association between SGA and non-SGA neonates with ventilator mortality, the sepsis rate and the mortality of neonates on inotropic support and of very low birth weight neonates. A short duration of stay has highest mortality with RDS as the most common cause of death. Hence, the overall performance of SNAPPE II score was good with AUC 0.94

(good discrimination) giving a reasonable agreement between observed and expected mortality.

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