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SNAPPE II AS A PREDICTOR OF NEONATAL MORBIDITY AND MORTALITY IN A NEONATAL INTENSIVE CARE UNIT AT A HOSPITAL IN SOWETO , SOUTH AFRICA

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Masters of Medicine in Paediatrics

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, in partial fulfillment of the requirements for the degree of Master of Medicine in Paediatrics

SNAPPE II AS A PREDICTOR OF NEONATAL MORBIDITY AND MORTALITY IN A NEONATAL INTENSIVE CARE UNIT AT A HOSPITAL IN SOWETO , SOUTH AFRICA

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DECLARATION

I, Nokukhanya Mabaso, hereby declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in Paediatrics in the University of the Witwatersrand. It has not been submitted before for any degree or examination at this or any other university.

Signed 

Nokukhanya Mabaso at Johannesburg, 6 November 2024

DEDICATION

This research project is dedicated to my parents who raised me and put me through medical school, allowing me to fulfil my dream to become a Paediatrician. Thank you for your love and support, as well as instilling in me the belief that I am taller than the task!

ACKNOWLEDGEMENTS

I would like to express my gratitude to my supervisors for their patience and unwavering support throughout this project. I would not have been able to complete this research without their guidance and wisdom at every step.

I am also grateful to my close family for the words of encouragement that kept me going, especially to my partner whose belief in me kept me was a motivation to complete my study.

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SNAPPE II AS A PREDICTOR OF NEONATAL MORBIDITY AND MORTALITY IN A NEONATAL INTENSIVE CARE UNIT AT A HOSPITAL IN SOWETO , SOUTH AFRICA

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Abstract

Objective:

To assess the use of the SNAPPE II score in predicting morbidity and mortality in a NICU in a resource limited setting.

Methods

This was a prospective, cohort study conducted in the NICU at Chris Hani Baragwanath Academic Hospital (CHBAH) from 1 November 2020 to 28 February 2021. A score > 30 was associated with severe illness. Data was analysed comparing the two groups (SNAPPE II < 30 and > 30).

Results

One hundred and twenty five neonates were included: 78 (62.4%) and 46 (36.8%) had a SNAPPE II score <30 and >30, respectively. Neonates with scores >30 had lower 5 minute Apgar scores (p<0.001), metabolic acidosis (p<0.001), higher lactate (p<0.001), and demised (p=0.005). High SNAPPE II score was associated with mortality (OR 1.04, p<0.001).

Conclusion

SNAPPE II is a predictor of neonatal mortality in NICU and may be a useful tool to prognosticate and rationalize resources.

Keywords: NICU, SNAPPE II, mortality, neonate

Introduction

The Sustainable development goals (SDG) were developed after 2015 by the United Nations members as a universal plea to end poverty and improve the lives and prospects of all human beings.(1) Similar to other countries in Sub-Saharan Africa child deaths are still a challenging issue in South Africa.(2) In 2015, the neonatal mortality rate (NMR) in South Africa accounted for 30% of the under 5 mortality rate.(3) In most African countries less than 25% of deaths are registered but South Africa is noted to be one of the few African countries that has rich sources of mortality data for children using the Perinatal Problem Identification Program (PIPP) which records still births and neonatal deaths.(4) According to UNICEF records, in 2020 NMR in SA was 10.6 deaths per 1000 live births which is a moderate decline from the 2016 rate of 12.6 per 1000 live births.(1) Over the years, illness severity scores have been adopted in order to predict mortality and morbidity among neonates admitted to neonatal intensive care units (NICUs). These scores can also be used to compare NMR between NICUs in different countries around the world.

The first illness severity score was developed by Richardson et al. in 1993 and was validated as a predictor of mortality and morbidity.(5,6) The score proved to be difficult to use due to the number of items included and Richardson then developed a second generation score known as SNAP II which was much simpler and more practical.(5) In 2001, an updated version of the SNAPPE called SNAPPE II was developed. SNAPPE II consisted of 9 parameters to be analyzed in the first 12 hours instead of the original 34 in the first 24 hours.(Appendix A) SNAPPE II is an accurate score used across all populations regardless of gestational age which makes it superior to other illness severity scores . The final score is based on the worst physiological derangements in the admission period. In the original study done by Richardson et al. SNAPPE II scores of 37 and above were associated with higher mortality.(5) In various other studies, scores between 30 and 40 showed increased risk of mortality.(6, 7)

Data validating the SNAPPE II score from a NICU in South Africa (SA) is to my knowledge lacking and although it has been used in other low middle-income countries (LMIC) countries similar to SA, the clinical profile of patients and outcomes may be different in this setting. The aim of this study was to apply the SNAPPE II score and assess its ability to predict mortality and

morbidity in a tertiary hospital in South Africa. This study will provide the basis of data on neonatal mortality scores in South Africa and in doing so, we may enable healthcare workers to prioritize treatment to the sickest newborns as well as counsel parents and prepare them for adverse outcomes.

Methods

Study design

This was a prospective study of neonates that were identified and included by the researcher. The data was collected from the patients' NICU charts and the score was calculated based on the relevant parameters in the first 24 hours of admission to NICU. The calculated score for each patient was then entered into a database.

Study Population

The study group consisted of all neonates, inborn and outborn, admitted to NICU at CHBAH between the period 1 November 2020 to 28 February 2021. Informed consent was taken from parents at admission to NICU. Those neonates whose guardians did not give consent or could not be contacted for consent were excluded from the study. Other exclusions were those neonates who were born at home or en-route to hospital and had unknown Apgar scores. Sample size calculated using 80% CI was 102 patients.

Data Collection

Data was collected prospectively within the first 24 hours of admission to NICU and used to calculate the SNAPPE II score. This data was entered anonymously, using a study number, into a data collection sheet and then transferred to a database using Microsoft Excel. The neonates were then followed up until either discharge or death from the NICU. Variables collected included maternal demographics such as age, gravity, parity and comorbidities. Neonatal demographics included gender, gestation, birth weight and diagnosis. Data was also extracted from the NICU charts to calculate the score, which included lowest mean blood pressure, lowest temperature, arterial partial pressure of oxygen (PaO_2), Fraction of Inspired Oxygen (FiO_2), lowest pH on the blood gas, urine output (by use of catherisation or number of wet nappies), birthweight and Apgar score at 1 and 5 minutes. It was also noted if the patient was small for gestational age (SGA) as determined using a Fenton Chart, or had seizures. The length of

intubation and length of stay in NICU and the relationship between this and the overall SNAPPE score was analysed. Morbidity outcomes were assessed by complications monitored such as sepsis, intraventricular haemorrhage (IVH), necrotising enterocolitis (NEC- all grades included) and bronchopulmonary dysplasia (BPD). Sepsis was defined as a positive blood culture and/or positive cerebrospinal fluid (CSF) culture. The study cohort included 165 neonates, 40 were excluded due to lack of consent or insufficient data thus 125 neonates were included for analysis. (Figure 1) The SNAPPE II score was calculated for each patient enrolled in the study. A score of greater than 30 was used in order to separate the study participants into 2 groups. These 2 groups were then analysed further to compare mortality and morbidity.

Statistical Analysis

Data was analyzed using Statistica (version 14.0.0.15, TIBCO software Inc) and Stata/IC 16.1 (StataCorp, USA). Categorical variables was represented as frequencies and proportions, continuous variables as means with standard deviations (SD) and medians with interquartile ranges (IQR) depending on the distribution of data. Comparisons between groups were done as Chi-Squared or Fishers exact test for categorical data and Mann-Whitney U test for continuous variables with skewed data. A p value of < 0.05 was regarded as significant.

Univariate logistic regression analyses were performed for determining the factors affecting the outcome of SNAPPE II score > 30 or < 30. Variables or factors with a p-value <0.01 was included in the adjusted odd ratios or logistic regression analyses to determine the factors favouring a higher SNAPPE II score > 30. A Kaplan Meier curve was generated to determine the percentage of survivors with a SNAPPE score < 30. The receiver operating characteristic curve (ROC curve) was performed to determine the sensitivity and specificity of the SNAPPE II score for mortality. The discriminatory performance of the curve was verified by calculating the area under the curve (AUC).

Ethics

Permission was requested and granted by the CEO of the hospital, Head of Department of Paediatrics at CHBAH and the Head of the Neonatal Unit. The Human Research Ethics Committee (HREC) at the University of the Witwatersrand approved the study (Ethics clearance no: M200453).

Results

During the 4 month study period, 165 neonates were admitted to the NICU. From this study group, 32 were excluded due to lack of consent with 11 refusing consent and 21 not being able to obtain consent. A further 8 patients were then excluded due to insufficient data available to calculate a score and included neonates born before arrival (BBA) whose Apgar scores were unknown. The study cohort included 125 neonates. (Figure 1)

Maternal Demographics (Table 1)

The mean maternal age was 27 years (± 6.9) with a median gravity and parity of 2 (1-3) and 1 (0-2), respectively. The majority of the mothers were HIV negative. Of the 39 (31%) HIV positive mothers, the mean viral load was 28 333 (±102185) with 10 mothers being virologically suppressed. There were no differences between maternal age, gravity and parity when comparing those with high and low SNAPPE II scores. (Table 1)

Neonatal Demographics (Table 2)

The mean gestational age and birthweight were 33 (±4) completed weeks and 2109 grams (±869), with no differences between the 2 groups. Lower Apgar scores at 1 minute and 5 minutes were reported in those with a higher SNAPPE II score. A higher SNAPPE II score did not predict a longer length of intubation [10 (±11) days] or length of stay [12 (±11) days] in NICU. Neonates with a higher SNAPPE II score were more acidotic (pH 7.1 vs pH 7.2; p=0.02, BD 11 vs 9; p=0.04), had higher lactates (6.4 vs 2.4; p<0.001) and had higher ventilator requirements (PIP: 24 vs 20; p=0.00 and PEEP: 9 vs 7; p=0.00). Oliguria (measured as 2 or less wet nappies in 24 hours) was reported in the group with a SNAPPE II > 30. Hypothermia was seen in the group with higher SNAPPE II score. (Table 2)

Outcomes

Morbidity Outcome

There were no differences in the groups with a SNAPPE II score < 30 and > 30 with regard to intraventricular haemorrhage (IVH) (p=0.17), necrotising enterocolitis (NEC) (p=0.83) and bronchopulmonary dysplasia (BPD), (p=0.06). None of the study participants were noted to have retinopathy of prematurity (ROP). There were 55 (44%) patients that had culture positive sepsis and 5 (4%) who had a positive CSF culture. Sepsis was not significantly associated with a higher SNAPPE II score and worse outcome compared to those without sepsis (p=0.80). (Table 2)

Mortality Outcomes

Of 125 neonates included in the study, 33 (26.8%) died. Fifty eight percent of these neonates had a SNAPPE II score > 30 (p=0.00). (Table 2)

There was a 3 times greater risk of mortality at a SNAPPE II score >30 (OR 3.0 (95% CI 1.3-6.80); p=0.009). In the adjusted multivariate analyses as shown in Table 3, a higher total SNAPPE II score had a 4% increase risk of mortality and NEC was associated with a higher mortality (OR 3.72 (95% CI 1.05-3.19); p=0.04).

At a SNAPPE II score of 30, a survival of 80% was observed and at a score of 55 or above, the chance of survival declined to 50%. (Figure 2)

The sensitivity and specificity at a score of 30 or above was 58% and 68% respectively with Stata. The positive predictive value (PPV) was 58% with negative predictive value (NPV) at 82%.

The ROC curve analysis for mortality with the SNAPPE II score revealed that the area under the curve was 0.7145 (95% CI 0.614-0.814). (Figure 3)

Discussion

This study aimed to determine whether a high SNAPPE II score (>30) would assist in predicting mortality and morbidity. Many studies have shown that the greater the score, above 30, the

greater the mortality.(5, 7-9) Fontenele M et al. who conducted a similar study in Brazil found that with each point added to the score, it increased the odds of mortality by 10% and a score of greater than 27 correlated with a 6 times greater chance of death.(7)

At a high SNAPPE II score, this study showed a 4% increase in mortality which is lower than that found in a similar study in Brazil(7).(9) But a 3 times greater risk of mortality if the score was >30. Our study computed the score within 24 hours of admission to NICU and not within 12 hours of birth.

The current study showed that patients with higher SNAPPE II score were critically ill with profound metabolic acidosis, higher ventilator requirements and more hypothermia. A study in Sao Paulo had similar findings, with more hypothermia and lower mean arterial pressures in their non-survivors.(10)

There are very few studies reporting on morbidity outcomes in relation to the SNAPPE II score. (11) The reason for this may be due to the difficulty in following up patients in the long term. Our study traced neonates until discharge from ICU and assessed those with IVH, ROP, BPD and NEC. We found that there was no correlation between a high SNAPPE II score and these comorbid conditions. One study followed up neonates to 1 year of corrected gestational age and found a significant relationship between higher SNAPPE II scores and poor neurodevelopmental outcome. Although this study had a significantly smaller cohort of 57 babies, born at < 32 weeks of gestation; it was the only study that followed patients for this length of time.(11)

Sepsis continues to be a major cause of morbidity and mortality in neonates and blood culture is the gold standard for identifying sepsis.(7) A study conducted in Brazil with a cohort of 247 neonates found that half the deaths were sepsis related and that blood culture positive sepsis was associated with higher mortality of 24%.(7) The presence of sepsis did not affect the overall SNAPPE II score. A study comparing culture negative and culture positive sepsis and their relation to the SNAPPE II score, concluded that there was no association between blood culture positive sepsis and a higher SNAPPE II score.(8)

In this study, we did not find a relationship between sepsis and a high SNAPPE II score. This correlates with findings done in other studies which showed that SNAPPE II score predicts

outcome independent of blood culture result and that there is a stronger association with sepsis and death than with sepsis and a high SNAPPE II score.(7, 8)

This study had a low positive predictive value (58%) for mortality. The SNAPPE II score was designed to compute scores within the first 12 hours after birth.(5)

Another finding to note in this study, was the poor sensitivity and specificity (58% and 68% respectively) in comparison to other studies which showed much higher results of sensitivity of 76.9 to 84% and specificity of 87 to 91%. (5-7). The same was seen regarding NPV and PPV, while other studies showed NPV of 94 and 96.5% with PPV of 66.7 to 95.3%, our results showed a NPV of 82% and PPV of 58%.(6, 7, 9) We can attribute these differences in results to the differences in study cohorts as the majority of these studies were conducted over a longer period of time and therefore had a greater number of study participants.(5, 7-9, 12)

The SNAPPE II score takes into account both physiologic and laboratory parameters and has performed almost as well as the CRIB score. It has been simplified from the original scoring systems but with this loses its predictive value. Laboratory indicators may differ in hospital and laboratory settings and procedures performed by NICU personal on or before admission to improve outcomes and these may not be taken into account by the score.(13) The score is calculated at one point in time and did not show promise when scores were collected longitudinally.

Illness severity scores are designed to assist clinicians to predict and monitor severity of the illness. However, they are to be less cumbersome and consider realistic circumstances. SNAPPE II score has limited value with sequential measurements.(14) In this population, the SNAPPE II score applied after birth and at varying postnatal age did not have a strong correlation with the prediction of mortality.

Limitations

The study was over a short time period of 4 months, in contrast to other studies between 6 to 18 months. There were larger cohorts in those studies, possibly explaining the difference found in some of their results. Neonates who were cooled and neonates born as BBA were not included as

some scores could not be computed due to data that could not be assigned. The definition of sepsis did not include other markers of sepsis, or culture negative sepsis and this may have affected the association of sepsis. There was no long-term follow-up of the study cohort.

Conclusion

A SNAPPE II score of greater than 30 was a predictor of mortality but a score > 55 was a stronger predictor in neonates admitted to NICU. NEC and a higher SNAPPE II score had a higher risk of mortality. Illness severity scores could help healthcare workers predict mortality during admission and interventions targeted appropriately in a resource limited setting which may help improve the survival rate in critically ill patients with more targeted interventions.

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Author contributions

NM, FN conceptualized the study. Data collection NM. Data management and analysis NM and KT. First draft written by NM. Editing of drafts NM, KS, KT, FN. All authors contributed to the final draft for submission.

Conflict of interests

None

Data availability

Dataset is available on request from the author.

Figure 1: Flow Diagram of Study Participants

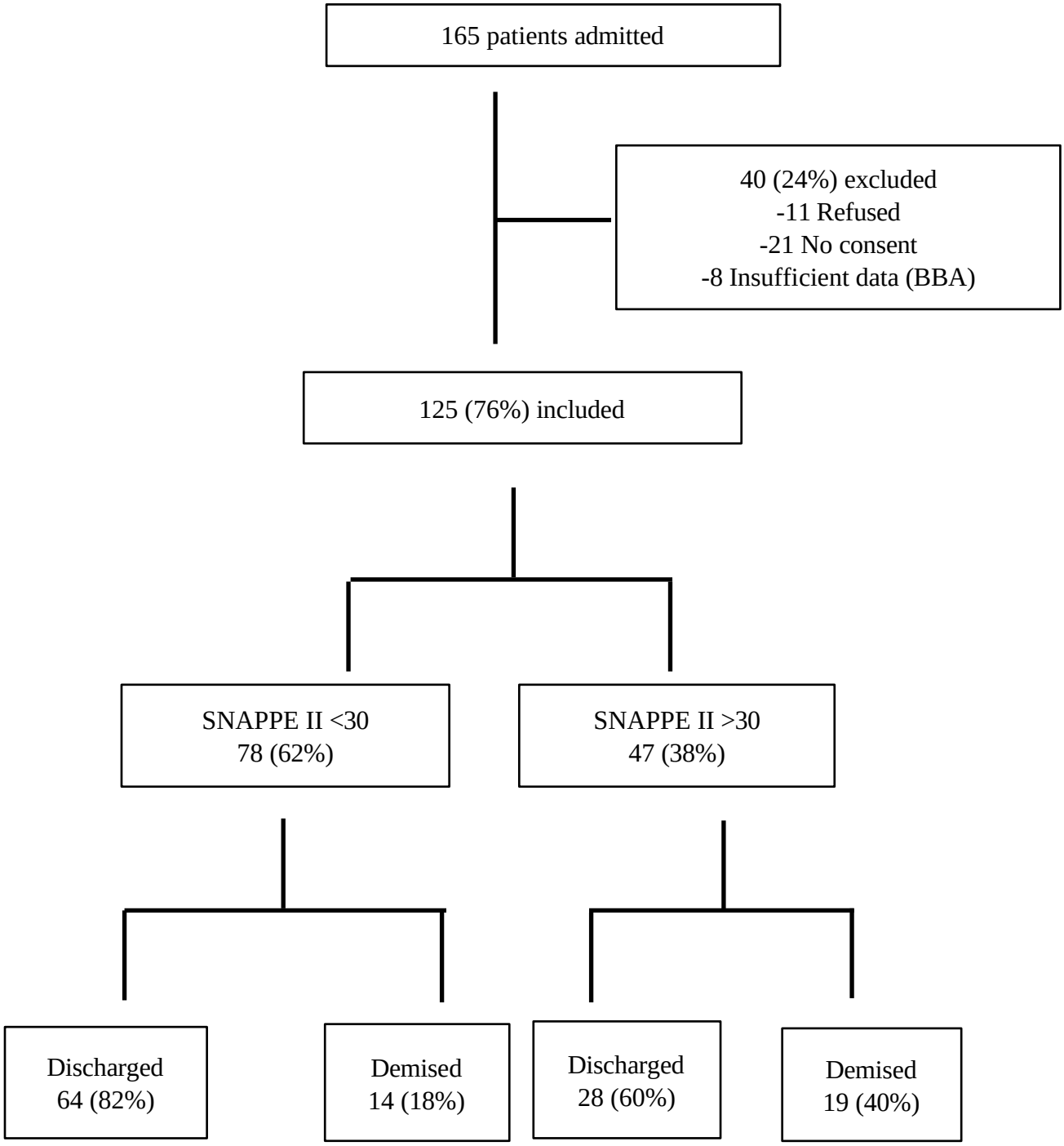


Table 1: Maternal characteristics

	Total	All	SNAPPE II <30	SNAPPE II >30	p-value
Age*	120	27.6 (±6.9)	27 (±7)	28 (±7)	0.57
Gravidity**	124	2 (1-3)	2 (1-3)	2 (2-3)	0.89
Parity**	125	1 (0-2)	1 (0-2)	1 (0-2)	0.71
HIV positive#	125	39 (31.2)	23 (29.5)	16 (34)	0.59

*Mean (SD)
**Median (IQR)
#N (%)

Table 2: Neonatal characteristics					
	N	**All** **Mean (SD)** **N=125**	**SNAPPE II <30** **Mean (SD)** **n=78**	**SNAPPE II >30** **Mean (SD)** **n=47**	**p-value**
Gestational Age	124	33 (±4)	33.6 (±4)	34.2 (±5)	0.44
Apgar 1 min*	124	7 (5-9)	8 (6-9)	5 (3-7)	**0.00**
Apgar 5 min*	124	9 (7-10)	9 (8-10)	7 (6-8)	**0.00**
Birth weight (grams)	125	2109 (±869)	2082 (±814)	2122 (±950)	0.80
Length of Intubation	124	10 (±11)	10 (±9)	11 (±13)	0.59
Length of stay (days)	124	12 (±11)	12 (±9)	12 (±13)	0.93
ABG pH	125	7.3 (±0.2)	7.3 (±0.1)	7.1 (±0.2)	**0.00**
pO2 mmHg	125	87 (±41)	90.9 (±40)	80.1 (±43)	0.15
pCO2 mmHg	125	45 (±21)	42 (±17)	51 (±27)	**0.03**
BD	124	8 (±6)	6 (±5)	11 (±7)	**0.00**
Lactate	125	4 (±4)	3 (±3)	6 (±5)	**0.00**
Urine output (nappies)*	125	2.3 (±1)	**2.5 (±1)**	**1.9 (±1)**	**0.00**
FiO2	125	0.7 (±0.2)	0.6 (±0.2)	0.8 (±0.2)	0.51
Peak Inspiratory Pressure	125	21 (±8)	20 (±11)	24 (±0)	**0.02**
PEEP	123	7 (±8)	6 (±4)	9 (±11)	**0.04**
Lowest Temperature	125	36.5 (±0.7)	36.6 (±0.3)	36.2 (±1.1)	0.72
Sepsis n (%) (Culture positive)	55	55 (44%)	35 (44.8%)	20 (42.5%)	0.80
Outcomes n (%) Discharged Demised	125	 92 (74%) 33 (26%)	 64 (82%) 14 (18%)	 28 (60%) 19 (40%)	0.04
Comorbidities n (%)					
IVH	125	23 (18.4%)	12 (15.4%)	11 (23.4%)	0.17
NEC	125	17 (13.6%)	11 (14.1%)	6 (12.8%)	0.83
BPD	125	20 (16%)	16 (20.5%)	4 (8.5%)	0.06

*Median (IQR)

ABG- arterial blood gas, PIP - Positive inspiratory pressure, MAP – mean arterial pressure, PEEP- peak end expiratory pressure, FiO2 – fractional inspired oxygen, pO2 - partial pressure of oxygen, pCO2 - partial pressure of

carbon dioxide, BD- base deficit, IVH- intraventricular haemorrhage , NEC -necrotising enterocolitis , BPD-bronchopulmonary dysplasia

Figure 2: Kaplan Meier curve for survival

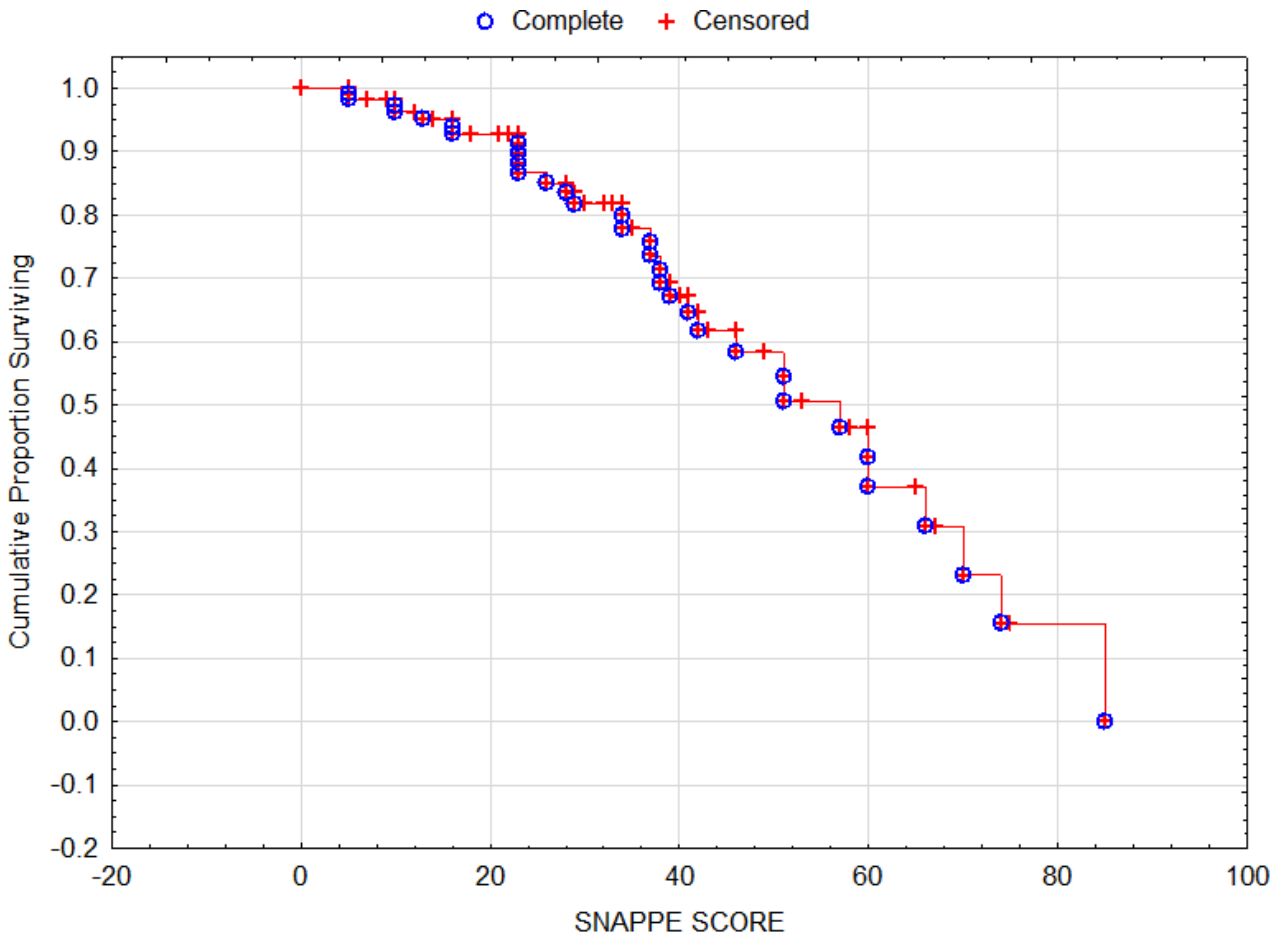


Table 3: Risk factors associated with mortality (n=123)

Risk factors	Adjusted Odds Ratio	95% Confidence interval	P-value
SNAPPE II score	1.04	1.02-1.07	0.00
NEC	3.72	1.05-13.19	0.04
IVH	1.96	0.60-6.31	0.26
Sepsis	1.79	0.63-5.13	0.27

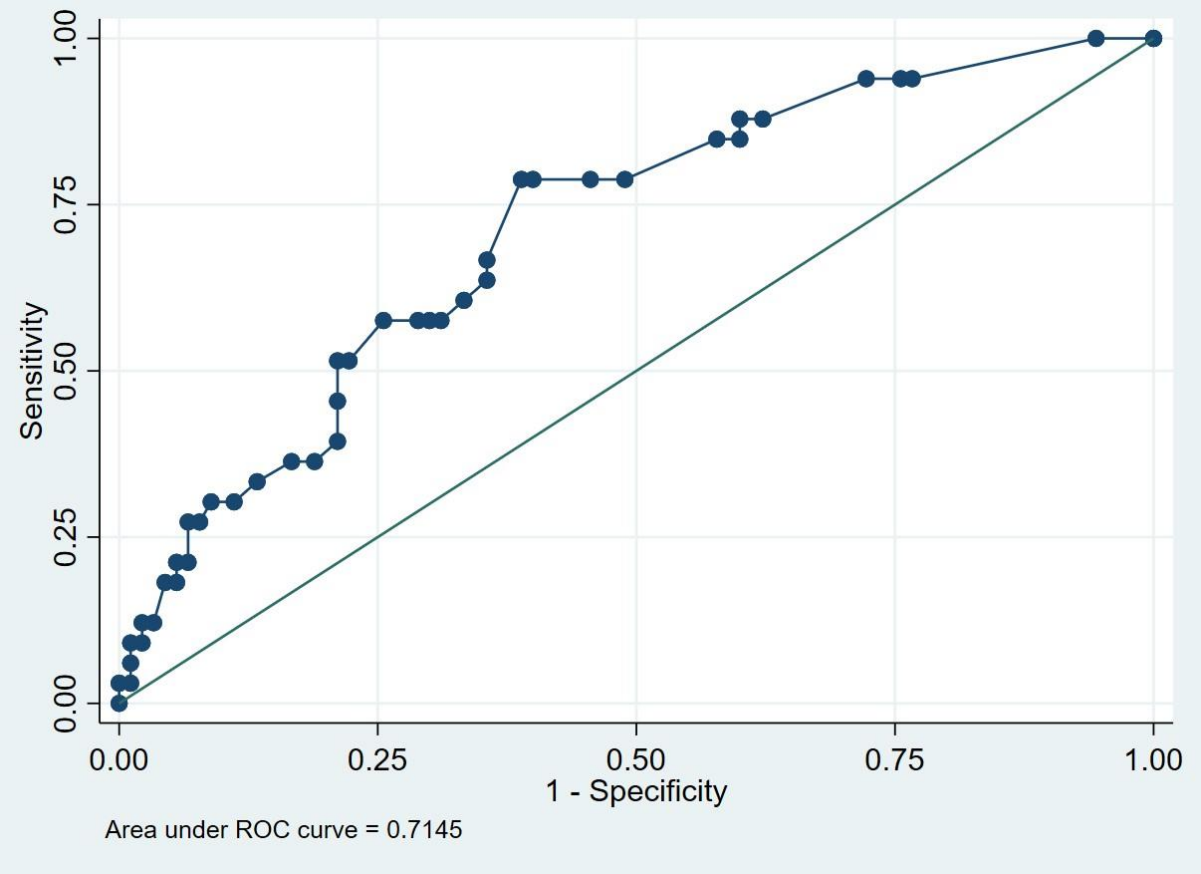


Figure 3: ROC curve analysis for mortality with SNAPPE II score

Appendix A: SNAPPE II Score

VARIABLE	MEASURE	SCORE	PATIENT SCORE
Lowest MAP	<20mmHg	19	
	20mmHg -29mmHg	9	
	>29 mmHg	0	
Lowest Temperature	< 35.0	15	
	35.0-35.6	8	
	> 35.6	0	
Po2/Fi02 ratio	<0.3	29	
	0.3-0.99	16	
	1.0-2.49	5	
	>2.49	0	
Lowest pH	<7.1	17	
	7.1-7.19	7	
	>7.19	0	
Seizure	None	0	
	Yes	5	
Urine Output	<0.1ml/kg/hr	18	
	0.1-0.9ml/kg/hr	5	
	>0.9ml/kg/hr	0	
Birth Weight	<750grams	17	
	750-999grams	10	
	>999grams	0	
Small for gestational Age	< 3rd percentile	12	
	> 3rd percentile	0	
Apgar score at 5minutes	<7	18	
	>7	0	
Total			

References

1. Chaudhuri RN. Millennium development goals to sustainable development goals: Journey continues for a better world. Indian J Public Health. 2015;59(4):255-8.
2. Mmusi-Phetoe RM. Social factors determining maternal and neonatal mortality in South Africa: A qualitative study. Curationis. 2016;39(1):1571.
3. Rhoda NR, Greenfield D, Muller M, Prinsloo R, Pattinson RC, Kauchali S, Kerber K. Experiences with perinatal death reviews in South Africa--the Perinatal Problem Identification Programme: scaling up from programme to province to country. BJOG. 2014;121 Suppl 4:160-6.
4. Damian DJ, Njau B, Lisasi E, Msuya SE, Boulle A. Trends in maternal and neonatal mortality in South Africa: a systematic review. Syst Rev. 2019;8(1):76.
5. Harsha SS, Archana BR. SNAPPE-II (Score for Neonatal Acute Physiology with Perinatal Extension-II) in Predicting Mortality and Morbidity in NICU. J Clin Diagn Res. 2015;9(10):SC10-2.
6. Muktan D, Singh RR, Bhatta NK, Shah D. Neonatal mortality risk assessment using SNAPPE- II score in a neonatal intensive care unit. BMC Pediatr. 2019;19(1):279.
7. Fontenele M, Silva CF, Leite AJM, Castro ECM, Carvalho FHC, Silva A. Snappe Ii: Analysis of Accuracy and Determination of the Cutoff Point as a Death Predictor in a Brazilian Neonatal Intensive Care Unit. Rev Paul Pediatr. 2020;38:e2019029.
8. Samanta M, Biswas C, Pal NK, Sarkar S, Goswami A, Hazra A, et al. Performance of SNAPPE-II score in neonatal sepsis: an experience from a tertiary care center. Turk J Pediatr. 2020;62(2):191-8.
9. Ali A, Ariff S, Rajani R, Khowaja WH, Leghari AL, Wali S, et al. SNAPPE II Score as a Predictor of Neonatal Mortality in NICU at a Tertiary Care Hospital in Pakistan. Cureus. 2021;13(12):e20427.
10. Lima RO, Ribeiro AP, Juliano Y, Franca CN, Souza PC. Survival prognosis of newborns from an intensive care unit through the SNAP-PE II risk score. Clinics (Sao Paulo). 2020;75:e1731.
11. Vardhelli V, Murki S, Tandur B, Saha B, Oleti TP, Deshabhotla S, et al. Comparison of CRIB-II with SNAPPE-II for predicting survival and morbidities before hospital discharge in neonates with gestation </= 32 weeks: a prospective multicentric observational study. Eur J Pediatr. 2022;181(7):2831-8.
12. Radfar M, Hashemieh M, Fallahi M, Masihi R. Utilization of SNAP II and SNAPPE II Scores for Predicting the Mortality Rate Among a Cohort of Iranian Newborns. Arch Iran Med. 2018;21(4):153-7.
13. Zeng Z, Shi Z, Li X. Comparing different scoring systems for predicting mortality risk in preterm infants: a systematic review and network meta-analysis. Front Pediatr. 2023;11:1287774.
14. Mesquita Ramirez MN, Godoy LE, Alvarez Barrientos E. SNAP II and SNAPPE II as Predictors of Neonatal Mortality in a Pediatric Intensive Care Unit: Does Postnatal Age Play a Role? Int J Pediatr. 2014;2014:298198.
15. Escobar GJ, Fischer A, Li DK, Kremers R, Armstrong MA. Score for neonatal acute physiology: validation in three Kaiser Permanente neonatal intensive care units. Pediatrics. 1995;96(5 Pt 1):918-22.
16. Richardson DK, Corcoran JD, Escobar GJ, Lee SK. SNAP-II and SNAPPE-II: Simplified newborn illness severity and mortality risk scores. J Pediatr. 2001;138(1):92-100.
17. Sutcuoglu S, Celik T, Alkan S, Ilhan O, Ozer EA. Comparison of neonatal transport scoring systems and transport-related mortality score for predicting neonatal mortality risk. Pediatr Emerg Care. 2015;31(2):113-6.

18. Rhoda N, Velaphi S, Gebhardt G, Kauchali S, Barron P. Reducing neonatal deaths in South Africa: Progress and challenges. South African Medical Journal. 2018;108(3):9-16.
19. Lloyd LG, de Witt TW. Neonatal mortality in South Africa: how are we doing and can we do better? S Afr Med J. 2013;103(8):518-9.
20. Samms-Vaughan M. Neonatal morbidity studies: their difficulties and their usefulness. 1993.
21. Stensvold HJ, Klingenberg C, Stoen R, Moster D, Braekke K, Guthe HJ, et al. Neonatal morbidity and 1-year survival of extremely preterm infants. Pediatrics. 2017:e20161821.
22. KARAARSLAN U, BAĞ Ö, ÖZER EA, HELVACI M. Comparison of CrIb-II and Snappe-II Scoring Systems in predicting the Mortality and Morbidity of Very Low birth Weight Infants.
23. Shrestha D, Dhoubhadel BG, Parry CM, Prajapati B, Ariyoshi K, Mahaseth C. Predicting deaths in a resource-limited neonatal intensive care unit in Nepal. Transactions of The Royal Society of Tropical Medicine and Hygiene. 2017;111(7):287-93.
24. Jain S, Bansal A. SNAPPE II score for predicting mortality in a level II neonatal intensive care unit İkinci basamak yenidoğan yoğun bakım ünitesinde mortaliteyi öngörmede SNAPPE II skorlaması. 2009.
25. Sundaram V, Dutta S, Ahluwalia J, Narang A. Score for neonatal acute physiology II predicts mortality and persistent organ dysfunction in neonates with severe septicemia. Indian pediatrics. 2009;46(9).
26. Silveira RC, Schlabendorff M, Procianoy RS. Predictive value of SNAP and SNAP-PE for neonatal mortality. Jornal de pediatria. 2001;77(6):447-54.
27. Sutton L, Bajuk B, Berry G, Sayer G, Richardson V, Henderson-Smart D. Score of neonatal acute physiology as a measure of illness severity in mechanically ventilated term babies. Acta Paediatrica. 2002;91(4):415-23.
28. Thimoty J, Hilmanto D, Yuniati T. Score for Neonatal Acute Physiology Perinatal Extension II (SNAPPE II) as the predictor of neonatal mortality hospitalized in neonatal intensive care unit. Paediatrica Indonesiana. 2009;49(3):155-9.
29. Tomulic KL, Mestrovic J, Zuvic M, Rubelj K, Peter B, Cace IB, Verbic A. Neonatal risk mortality scores as predictors for health-related quality of life of infants treated in NICU: a prospective cross-sectional study. Quality of life research. 2017;26(5):1361-9.

Protocol

SNAPPE II AS A PREDICTOR OF NEONATAL MORBIDITY AND MORTALITY IN A NEONATAL INTENSIVE CARE UNIT AT A HOSPITAL IN SOWETO , SOUTH AFRICA

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ABBREVIATIONS

Abbreviation	Explanation
BPD	**Bronchopulmonary Dysplasia**
CHBAH	**Chris Hani Baragwanath Academic Hospital**
CRIB	**Clinical Risk Index for Babies**
END	**Early Neonatal Death**
GDOH	**Gauteng Department of Health**
HREC	**Health research ethics comittee**
ICU	**Intensive Care Unit**
IVH	**Intraventricular haemorrhage**
LND	**Late Neonatal Death**
MAP	**Mean Arterial Pressure**
MDG	**Millenium Developmental Goals**
NEC	**Necrotising Enterocolitis**
NMR	**Neonatal Mortality Rate**
NTISS	**Neonatal Therapeutic Intervention Scoring System**
PPIP	**Perinatal Problem Identification Program**
ROP	**Retinopathy of Prematurity**
SDG	**Sustainable Development Goals**
SGA	**Small for Gestational Age**
SNAP	**Score for Neonatal Acute Physiology**
SNAPPE II	**Score for Neonatal Acute Physiology with Perinatal Extension**
VLBW	**Very Low Birth Weight**

SNAPPE II AS A PREDICTOR OF NEONATAL MORBIDITY AND MORTALITY IN A NEONATAL INTENSIVE CARE UNIT AT A HOSPITAL IN SOWETO, SOUTH AFRICA.

INTRODUCTION

The Millennium Development Goals (MDGs) are 8 international development goals established following the millennium summit of the United Nations in 2000. The fourth goal aimed at reducing childhood mortality rates, this included the under 5 mortality rate and the infant mortality rate. With this in mind more research is required that is relevant to specific causes of infant and under 5 mortality. The sustainable development goals were developed as we had not reached the MDG targets in 2015. Measurement of illness severity is a research area of growing importance in neonatal intensive care (NICU).(15) Although intensive care has improved over the decades and survival has increased, more advances are still needed in the critical care of neonates .(12) With this in mind, a number of scoring systems have been developed over the years to predict neonatal mortality. One such scoring system is the Score for Neonatal Acute Physiology (SNAP), initially developed in 1993 by Richardson et al, it is a validated illness severity and mortality risk score for the newborn period.(16) The SNAP is comprised of 34 routinely available vital signs and laboratory results but proved to be complicated and time consuming to use due to the large number and complexity of the items included. In 1998 Richardson et al., then developed a simpler, more reliable score known as SNAP II which had much fewer items, furthermore to this score 3 more variables were added, namely birth weight, Apgar score and small for gestational age and this final score is now known as Score for Neonatal Acute Physiology II with Perinatal extension (SNAPPE II). (5)

LITERATURE REVIEW

The first few hours of a newborns life are extremely critical in respect to mortality as well as neurodevelopment outcome.(17) The latest mortality rate of 21 per 1000 live births reported by SA Demographic Health Survey is quite concerning as it falls short of the Sustainable Development Goal (SDGs) target of 12 per 1000 live births. South Africa is one of the few sub-Saharan countries that has enough resources to collect more accurate data on neonatal

mortality rates (NMR). Most African countries capture fewer than 25% of deaths leading to insufficient data to comment on neonatal mortality. In 2015 the neonatal mortality rate in SA accounted for 44% of the infant mortality rate and 32% of the under-5 mortality rate. (18) Early neonatal deaths (ENDs), those occurring within the first 7 days of life, account for 75% of all neonatal deaths. Causes of these include mainly prematurity and complications of asphyxia. Late neonatal deaths (LNDs) are commonly due to infections and congenital anomalies.(19) The perinatal problem identification program (PPIP) collected from 2014-2015 shows that inadequate facilities / equipment in the neonatal unit as well as lack of neonatal ICU beds are 2 of the top 10 avoidable factors identifiable in neonatal deaths (18)

Neonatal morbidity data is very limited and as there is no clear definition of morbidity it has become a very difficult parameter to measure. The few studies that have been done on this topic outline 3 methods of collecting neonatal morbidity data, by clinical examination, parental recall and use of medical records. (20) Major neonatal morbidity has been defined as any of the following; severe bronchopulmonary dysplasia (BPD), necrotising enterocolitis (NEC) (Bells stage II or III), intraventricular hemorrhage (IVH) or retinopathy of prematurity (ROP). (21)

The timely recognition of babies at increased risk of mortality in the neonatal intensive care (NICU) setting is very important and plays a critical role in improving patient care. A number of scoring systems have been developed and adapted over the years focusing on this matter. These scoring systems have been used on different patient groups in NICUs all over the world. (22) Initially, birth weight and gestational age were the primary predictors of mortality but with further research these 2 parameters alone have been found to be insufficient in accurately predicting neonatal morbidity and mortality. (23) Different approaches have been used to measure severity of illness and predict outcomes for newborns in NICU, one of which focuses on physiological parameters. These parameters include temperature, blood pressure, arterial blood gas and urine output all measured at the time of admission to NICU. Three different scoring systems, namely the Neonatal Therapeutic Intervention Scoring System (NTISS), the Clinical Risk Index for Babies (CRIB) and the Score for Neonatal Acute Physiology (SNAP) all fall under physiology severity scores for neonates. (23)

The CRIB score was used on babies born at less than 1500 grams. It consists of 3 physiologic items as well as birth weight, gestational age and congenital anomalies. CRIB was then further improved and calculated using 5 items namely sex, birth weight, gestational age, worst base excess and temperature at admission.(24) This scoring system had an advantage over SNAPPE II in very low birth weight babies and preterm neonates. (23)

SNAPPE II is a simple and accurate score that has be used across all populations including NICUs in India, California, Iran, Brazil, Turkey and Canada.(12, 15, 16) (5) It can be applied to all newborns regardless of birth weight and gestational age. It includes 9 items, birth weight, SGA, Apgar score at 5 minutes, urine output, lowest mean blood pressure, worst PaO2/FiO2 ratio, lowest pH, presence of seizures and lowest temperature. This information would be collected within 12 hours of NICU admission and takes about 4 to 5 minutes to complete. CRIB II and SNAPPE II are the 2 scores that have been commonly used and whose performance has been recognized. The CRIB score is more accurate as a mortality predictor in VLBW babies less than 32 weeks gestation in NICU and the SNAPPE as a mortality and end organ dysfunction predictor. (23)(24) SNAPPE II has also been noted to be a more reliable overall predictor of mortality as its accuracy has been tested in a very large group of cohort of neonates than the other systems. (23)

Neonatal septicemia is an important and preventable cause of neonatal mortality. Applying severity scores in this condition can also assist in identifying critically ill neonates and can be useful in prognostication.(25) Infection is the third most common cause of late neonatal death in South Africa. (18) Regarding neonatal severity scores, most research has been focused on applying these scores to neonates within the first 48 hours of life, there have been very few studies that apply the score to neonates beyond that age group. A study done in Northern India validated the use of SNAPPE II specifically to neonates after onset of severe septicemia. (25)This study was quite relevant as neonatal sepsis contributes largely to NICU admissions in our setting. It found that neonates with severe septicemia have a higher chance of demise if they have a higher SNAPPE II score, that being a score greater than 40. Furthermore, additional analysis was done on the individual parameters of the SNAPPE II score and what was found is that only those items relating to circulatory stability or perfusion (Mean Arterial Pressure (MAP), acidosis and oliguria) were significantly associated with

higher risk of death. (26). Therefore, the individual parameters of the SNAPPE II score would not contribute equally to predicting the risk of demise, shock was found to be a better predictor of death than hypoxia.

The importance of measuring illness severity in the ICU setting has been acknowledged for many years now. (27) The ideal severity illness score should be easy to use, be able to predict mortality and morbidity, be beneficial in optimizing neonatal hospitalization costs and be accurate when applied to all neonatal groups. (28) All of the neonatal mortality risk scores mentioned in this paper have a reasonable ability to predict death but SNAPPE II showed the best discrimination ability in previous studies. SNAPPE II had an advantage over the other scores due to its good sensitivity, specificity and was the scoring system that was used the most. (29) For this reason it was the obvious choice of scoring system to be applied in our setting.

RELEVANCE/ JUSTIFICATION OF STUDY

Chris Hani Baragwanath Academic Hospital (CHBAH), is a tertiary institution run by the Gauteng Department of Health (GDoH) located in Soweto, Johannesburg, South Africa. It services the entire population of Soweto and also operates as a referral centre for MOUs, district and regional hospitals. The neonatal unit is comprised of 120 authorized beds and 185 usable beds of which 18 are neonatal ICU beds. Due to the overwhelming patient load it is often difficult to obtain NICU beds as frequently as they are needed. In many instances some patients can demise prior to obtaining a bed or getting the level of care that they need. It then becomes quite important to be able to identify those patients that would most likely have more morbidity in NICU care. The current study will not be used to limit admissions to NICU.

STUDY AIMS AND OBJECTIVES

The purpose of this study is to apply SNAPPE II in our local NICU setting thereby assessing its validity as a predictor of mortality and morbidity in neonatal intensive care (NICU).
Inclusion Criteria: Neonates within 48 hours of birth/admission

Exclusion Criteria: Neonates with congenital malformations incompatible with life

: Born Before Arrival deliveries where Apgar scores are not known

: Infants admitted for observational purposes

METHODS

This will be a **prospective cohort study** that will include all neonates admitted to Chris Hani Baragwanath Academic Hospital NICU **over a 4month period**. It will include approximately 60 to 70 patients per month over the outlined period. All neonates with congenital anomalies incompatible with life will be excluded as well as those discharged within 24 hours of admission. The remainder of the neonates admitted will be allocated a SNAPPE II score within 12 hours of admission to NICU. The parameters analyzed will be birth weight, Apgar score at 5 minutes, urine output, presence or absence of seizures, pH, PO2/FiO2 ratio, temperature, mean blood pressure (BP) and small for gestational age (SGA) . SGA will be defined as a birthweight below the 10th centile plotted on a Fenton chart or foot length measurement. Urine output may also be measured as number of wet nappies per day if catheter measurement not possible. The final SNAPPE II will be based on the worst physiologic derangements in the admission period outlined at 12 hours of age. **The neonates will be followed up until death or discharge from NICU.** An analysis will then be made of the scores of the survived group and that will be compared to the scores of the non-survivors. In addition to that we will need to determine the risk of morbidity of those patients in the survived group. The survivors will be further stratified according to SNAPPE II score. In order to assess morbidity we will be looking at presence of NEC (stage II and III), Severe Bronchopulmonary dysplasia (BPD), Intraventricular hemorrhage (IVH) and Retinopathy of prematurity (ROP) [see Appendix C].

DATA ANALYSIS

Data will be collected and entered into a Microsoft Excel spreadsheet, statistical analysis will be performed using Statistica Software (Statsoft USA, version 13). Patient identifiers will be kept separately from the other variables and will be linked by a study number. Continuous variables will be reported as means or medians depending on the distribution of the data.

Categorical variables will be reported as proportions. A score of 30 will be used as significant. Neonates will be divided into 2 groups, those with scores above 30 and those with scores below 30. Comparison between categorical variables will be done using the Chi-squared or Fishers' exact test where appropriate. The Students t-test will be used to compare means whereas the Mann-Whitney U test will be used to compare medians. Logistic regression analysis will be undertaken to analyze variables associated with outcomes and complications in the two groups with a SNAPPE score < 30 and > 30. A p-value of <0.05 will be considered statistically significant.

ETHICS

Consent will be obtained from the parents or guardians of each neonate prior to scores being calculated (Appendix H). Ethics approval will be sought from the Human Research Ethics committee (HREC) from the University of Witwatersrand prior to the study being conducted. The hospital CEO and Head of Department and Head of Division will be approached for approval to conduct the study.

RISK AND BENEFITS

This study will assist clinicians to identify critically neonates upon admission to NICU. It will also assist them in predicting the prognosis of these neonates not just in terms of risk of demise but also in terms of morbidity. There will be no risk to the study participants as the score will be calculated using standard vital signs and routine tests done on all neonates admitted to the NICU at CHBAH.

TIMELINE

	June 2019 - September 2019	February 2020 - March 2020	Pending Ethics Approval	

Literature review				
Protocol preparation				
P r o t o c o l assessment				
Ethics				
Data collection				
Data analysis				
Write dissertation				

FUNDING

The costs involved in completing this study will be carried by the researcher.

LIMITATIONS

Data for the study will be collected by medical doctors working in NICU at the time. As this will be a prospective study, consent will need to be obtained from the parent or caregiver prior to getting the data , therefore a limitation of the study would be in instances where consent cannot be obtained within the 12 hour admission period.

REFERENCES

1. Escobar, G.J., et al., Score for neonatal acute physiology: validation in three Kaiser Permanente neonatal intensive care units. Pediatrics, 1995. **96**(5 Pt 1): p. 918-22.
2. Radfar, M., et al., Utilization of SNAP II and SNAPPE II Scores for Predicting the Mortality Rate Among a Cohort of Iranian Newborns. Arch Iran Med, 2018. **21**(4): p. 153-157.
3. Richardson, D.K., et al., SNAP-II and SNAPPE-II: Simplified newborn illness severity and mortality risk scores. J Pediatr, 2001. **138**(1): p. 92-100.
4. Harsha, S.S. and B.R. Archana, SNAPPE-II (Score for Neonatal Acute Physiology with Perinatal Extension-II) in Predicting Mortality and Morbidity in NICU. J Clin Diagn Res, 2015. **9**(10): p. SC10-2.
5. Sutcuoglu, S., et al., Comparison of neonatal transport scoring systems and transport-related mortality score for predicting neonatal mortality risk. Pediatr Emerg Care, 2015. **31**(2): p. 113-6.
6. Rhoda, N., et al., Reducing neonatal deaths in South Africa: Progress and challenges. South African Medical Journal, 2018. **108**(3): p. 9-16.
7. Lloyd, L.G. and T.W. de Witt, Neonatal mortality in South Africa: how are we doing and can we do better? S Afr Med J, 2013. **103**(8): p. 518-9.
8. Samms-Vaughan, M., Neonatal morbidity studies: their difficulties and their usefulness. 1993.
9. Stensvold, H.J., et al., Neonatal morbidity and 1-year survival of extremely preterm infants. Pediatrics, 2017: p. e20161821.
10. KARAARSLAN, U., et al., Comparison of CrIb-II and Snap-pe-II Scoring Systems in predicting the Mortality and Morbidity of Very Low birth Weight Infants.
11. Shrestha, D., et al., Predicting deaths in a resource-limited neonatal intensive care unit in Nepal. Transactions of The Royal Society of Tropical Medicine and Hygiene, 2017. **111**(7): p. 287-293.
12. Jain, S. and A. Bansal, SNAPPE II score for predicting mortality in a level II neonatal intensive care unit İkinci basamak yenidoğan yoğun bakım ünitesinde mortaliteyi öngörmede SNAPPE II skorlaması. 2009.
13. Sundaram, V., et al., Score for neonatal acute physiology II predicts mortality and persistent organ dysfunction in neonates with severe septicemia. Indian pediatrics, 2009. **46**(9).
14. Silveira, R.C., M. Schlabendorff, and R.S. Procianoy, Predictive value of SNAP and SNAP-PE for neonatal mortality. Jornal de pediatria, 2001. **77**(6): p. 447-454.
15. Sutton, L., et al., Score of neonatal acute physiology as a measure of illness severity in mechanically ventilated term babies. Acta Paediatrica, 2002. **91**(4): p. 415-423.
16. Thimoty, J., D. Hilmanto, and T. Yuniati, Score for Neonatal Acute Physiology Perinatal Extension II (SNAPPE II) as the predictor of neonatal mortality hospitalized in neonatal intensive care unit. Paediatrica Indonesiana, 2009. **49**(3): p. 155-9.
17. Tomulic, K.L., et al., Neonatal risk mortality scores as predictors for health-related quality of life of infants treated in NICU: a prospective cross-sectional study. Quality of life research, 2017. **26**(5): p. 1361-1369.

APPENDICES

Appendix A: Scoring Systems

1. Clinical Risk Index for Babies CRIB SCORE

• Birth Weight	>1350g	0
	851-1350g	1
	701-850g	4
	<700g	7
• Gestational Age	>24 weeks	0
	<24weeks	1
• Congenital Malformation	None	0
	Not life threatening	1
	Life threatening	3
• Maximum base excess	-7	0
	-7 to -9	1
	-10 to -14.9	2
	<-15	4
• Minimum appropriate FiO2	<0.4	0
	0.41-0.8	2
	0.81-0.9	3
	0.9-1.0	4
• Maximum appropriate FiO2	<0.4	0
	0.41-0.8	1
	0.81-0.9	3
	0.9-1.0	5

2. Neonatal Therapeutic Intervention Scoring System (NTISS)

Respiratory	Subs core			**Cardiovascular**	Subs core		
Supplemental oxygen[a]	1	☐ **yes**		Indomethacin administration	1	☐ **yes**	☐ **no**
C.P.A.P.[a]	2	☐ **yes**	☐ **no**	Volume expansion (<=15 mL/kg)[c]	1	☐ **yes**	☐ **no**
Mechanical ventilation[a]	3	☐ **yes**		Volume expansion (>15 mL/kg)[c]	3	☐ **yes**	
Mechanical ventilation with muscle relaxation[a]	4	☐ **yes**		Vasopressor administration (1 agent)[d]	2	☐ **yes**	☐ **no**

Hight-frequency ventilation[a]	4	☐ yes		Vasopressor administration (>1 agent)[d]	3	☐ yes	
Surfactant administration	1	☐ yes	☐ no	Cardiopulmonary resuscitation	4	☐ yes	☐ no
Endotracheal intubation	2	☐ yes	☐ no	Pacemaker on standby[e]	3	☐ yes	☐ no
Tracheostomy care[b]	1	☐ yes		Pacemaker used[e]	4	☐ yes	
			☐ no				
Tracheostomy placement[b]	1	☐ yes					
Extracorporeal membrane oxygenation	4	☐ yes	☐ no				
Drug therapy				**Monitoring**			
Antibiotic administration (<= 2 agents)[f]	1	☐ yes		Frequent vital signs	1	☐ yes	☐ no
			☐ no				
Antibiotic administration (> 2 agents[f]	2	☐ yes		Phlebotomy (5-10 blood draws)[h]	1	☐ yes	
Diuretic administration (enteral)[g]	1	☐ yes		Extensive phlebotomy (> 10 blood draws)[h]	2	☐ yes	☐ no
			☐ no				
Diuretic administration (parenteral)[g]	2	☐ yes		Cardiorespiratory monitoring	1	☐ yes	☐ no
Anticonvulsant therapy	1	☐ yes	☐ no	Thermoregulated environment	1	☐ yes	☐ no
Aminophylinne administration	1	☐ yes	☐ no	Noninvasive oxygen monitoring	1	☐ yes	☐ no
Other unscheduled medication	1	☐ yes	☐ no	Arterial pressure monitoring	1	☐ yes	☐ no
Steroid administration (postnatal)	1	☐ yes	☐ no	Central venous pressure monitoring	1	☐ yes	☐ no
Potassium binding resin administration	3	☐ yes	☐ no	Urinary catheter	1	☐ yes	☐ no
Treatment of metabolic acidosis	3	☐ yes	☐ no	Quantitative intake and output	1	☐ yes	☐ no
Metabolic / nutrition				**Transfusion**			
Gavage feeding	1	☐ yes	☐ no	Intravenous gamma globulin	1	☐ yes	☐ no

Phototherapy	1	☐ yes	☐ no	Double volume exchange transfusion	3	☐ yes	☐ no
Intravenous fat emulsion	1	☐ yes	☐ no	Partial volume exchange transfusion	2	☐ yes	☐ no
Intravenous amino acid solution	1	☐ yes	☐ no	Red blood cell transfusion (<=15 ml/kg[i]	2	☐ yes	☐ no
Insulin administration	2	☐ yes	☐ no	Red blood cell transfusion (>15 ml/kg)[i]	3	☐ yes	
Potassium infusion	3	☐ yes	☐ no	Platelet transfusion	3	☐ yes	☐ no
				White blood cell transfusion	3	☐ yes	☐ no
Procedural				**Vascular access**			
Transport of patient	2	☐ yes	☐ no	Peripheral intravenous line	1	☐ yes	☐ no
Dialysis	4	☐ yes	☐ no	Arterial line	2	☐ yes	☐ no
Single chest tube in place[j]	2	☐ yes		Central venous line	2	☐ yes	☐ no
Multiple chest tubes in place[j]	3	☐ yes	☐ no				
Thoracentesis	3	☐ yes	☐ no				
Pericardial tube in place[l]	4	☐ yes					
Pericardiocentesis[l]	4	☐ yes	☐ no				
Minor operation [k]	2	☐ yes					
Major operation [k]	4	☐ yes	☐ no				

NTISS = SUM (points for activities performed) = 0 Abstraction guidelines

3. Score for Neonatal Acute Physiology with Perinatal Extension (SNAPPE)

VARIABLE	MEASURE	SCORE	PATIENT SCORE
Lowest MAP	<20mmHg	19	
	20mmHg -29mmHg	9	
	>29 mmHg	0	

Lowest Temperature	< 35.0	15	
	35.0-35.6	8	
	> 35.6	0	
Po2/FiO2 ra;o	<0.3	29	
	0.3-0.99	16	
	1.0-2.49	5	
	>2.49	0	
Lowest pH	<7.1	17	
	7.1-7.19	7	
	>7.19	0	
Seizure	None	0	
	Yes	5	
Urine Output	<0.1ml/kg/hr OR <3 nappies	18	
	0.1-0.9ml/kg/hr OR 3-5 nappies	5	
	>0.9ml/kg/hr OR >5 nappies	0	
Birth Weight	<750grams	17	
	750-999grams	10	
	>999grams	0	
Small for gesta;onal Age	< 3rd percenNle	12	
	> 3rd percenNle	0	
Apgar score at 5minutes	<7	18	
	>7	0	
Total			

Appendix C: Definitions of Comorbidities

1. **NECROTISING ENTEROCOLITIS (NEC)**

Will be defined according to the Modified Bells' Staging

Stage	Systemic signs	Intestinal signs	Radiological signs
I A (Suspected)	Temperature instability, apnea, bradycardia, lethargy	Poor feeding, emesis, ↑ pre-gavage residuals, mild abdominal distension	Normal or intestinal dilation, mild ileus
I B (Suspected)	Same as above	Above and blood from rectum	Same as above
II A (Proven)	Same as above	Above + absent bowel sounds + mild abdominal tenderness	Intestinal dilation, ileus, pneumatosis intestinalis
II B (Proven)	Above + metabolic acidosis + thrombocytopenia	Above + definite abdominal tenderness	Above + portal vein gas + possible ascites
III A (Advanced)	Above + hypotension, respiratory acidosis, neutropenia	Above + peritonitis, marked distension of abdomen	Above + definite ascites
III B (Advanced)	Same as above	Same as above	Above + pneumoperitoneum

2**. BRONCHOPULMONARY DYSPLASIA (BPD)**

	<32 weeks GA	>32 weeks GA
Treatment with oxygen	>21% for at least 28 days	>21% for at least 28 days
Time point of assessment	36 weeks PMA or discharge*	>28 days but <56 days postnatal age or discharge*
Grade :		
Mild	Breathing room air at 36 weeks PMA or discharge*	Breathing room air at 56 days Postnatal age or discharge*
Moderate	Need for <30% oxygen at 36 weeks PMA or discharge*	Need for <30% oxygen at 56 days Postnatal age or discharge*
Severe	Need for ≥30% oxygen and/or positive pressure (IMV/CPAP) at 36 weeks PMA or discharge*	Need for ≥30% oxygen and/or positive pressure (IMV/CPAP) at 56 days Postnatal age or discharge*

Jobe AH, Bancalari E. Bronchopulmonary dysplasia. Am J Respir Crit Care Med 2001;163:1723-9 Definition of Bronchopulmonary Dysplasia: Diagnostic Criteria. Reprinted with permission of the American Thoracic Society. Copyright © 2016 American Thoracic Society. Jobe, A.H.; Bancalari, E.Bronchopulmonary Dysplasia. Am. J. Respir. Crit. Care Med. 2001, 163.

3. **INTRAVENTRICULAR HAEMORRHAGE (IVH)**

Defined according to the Papile Criteria

Papile Criteria	Description	Volpe Criteria	Description
Grade I	Hemorrhage limited to the germinal matrix area; may be unilateral or bilateral	Grade I	Blood in the germinal matrix area with or without minimal intraventricular hemorrhage (less than 10% of the ventricular space with blood)
Grade II	Blood noted within the ventricular system but not distending it	Grade II	Intraventricular hemorrhage with blood occupying 10–50% of the ventricular space (sagittal view)
Grade III	Blood in ventricles with distension or dilation of the ventricles	Grade III	Intraventricular hemorrhage with blood occupying greater than 50% of the ventricles with or without periventricular echodensities
Grade IV	Intraventricular hemorrhage with parenchymal extension	Separate notation of other findings	Periventricular hemorrhagic infarction Cystic periventricular leukomalacia

4. Retinopathy of prematurity (ROP)

Will be defined according to the ERTROP criteria

1. No ROP (immature or mature vascularization)
2. Mild ROP (stage 1 or 2 ROP in zone II or III, without plus disease)
3. Severe ROP (any prethreshold, any stage 3, or threshold ROP).

APPENDIX D

Data Collection Sheet

Patient Study Number :

1. Maternal Demographics

Age	
Parity, Gravidity	
Comorbidities	
HIV status	Pos/Neg
Residence	

2. Infant details

Date of birth	
Sex	Male/Female/Ambiguous
Gestation	
Place of Birth	BBA/MOU/Clinic/Hospital
Apgars	1min 5 min 10 min
Birthweight (g)	
Resuscitation Measures	BMV/CPR/Intubation/Adrenaline/
Diagnosis	
Mode of delivery	NVD/Breech/Vacuum/Caesar/Forceps
Diagnosis at admission to NICU	
Reason for admission to the NICU	
Date of intubation	
Date of extubation	
Date of Discharge/Death from NICU	
Presence of sepsis	Yes/No
	Early Neonatal Sepsis/Late Neonatal Sepsis
If Yes	Blood Organism
If Yes	Cerebrospinal Fluid Organism
Complications in NICU	Pneumothorax/Pulmonary Haemorrhage/Cardiac Arrest

3. Haemodynamic and Ventilation Status

Lowest Mean Blood pressure	
Inotropes	Dopamine/Dobutamine/Adrenaline/ Hydrocortisone
Urine Output (mls/kg/d) OR wet nappies	
ABG	pH PO2 PCO2 BD Lactate
Mode of Ventilation	nCPAP/IPPV/HFOV
Ventilation Settings : FiO2	
PIP	
MAP/ Amplitude	
Lowest Temperature (°C)	
Seizure	Yes/No
Time of SNAPPE II Score	
Date of SNAPPE II Score	

4. Comorbidities

BPD: Grade	Yes/No	Grade
NEC: Stage	Yes/No	Stage
IVH: Grade	Yes/No	Grade
ROP Stage	Yes/No	Stage

5. Outcomes

Death/Discharge Date of discharge/demise:

SNAPPE II Score

VARIABLE	MEASURE	SCORE	PATIENT SCORE
Lowest MAP	<20mmHg	19	
	20mmHg -29mmHg	9	
	>29 mmHg	0	
Lowest Temperature	< 35.0	15	
	35.0-35.6	8	
	> 35.6	0	
Po2/FiO2 ratio	<0.3	29	
	0.3-0.99	16	
	1.0-2.49	5	
	>2.49	0	
Lowest pH	<7.1	17	
	7.1-7.19	7	
	>7.19	0	
Seizure	None	0	
	Yes	5	
Urine Output	<0.1ml/kg/hr OR <3 nappies	18	
	0.1-0.9ml/kg/hr OR 3-5	5	
	>0.9ml/kg/hr OR >5 nappies	0	
Birth Weight	<750grams	17	
	750-999grams	10	
	>999grams	0	
Small for gestational Age	< 3rd percentile	12	
	> 3rd percentile	0	
Apgar score at 5minutes	<7	18	
	>7	0	

Total			

Ethics

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R14/49 Dr Nokukhanya Mbalenhle Maibaso

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M200453 MED19-10 096

NAME: (Principal Investigator)	*Dr* Nokukhanya Mbalenhle Mabaso
DEPARTMENT:	School of Medicine Chris Hatnl Baragwanath Academic Hospital
PROJECT TITLE:	The score for neonatal acute physiology with perinatal extensilon (SNAPPE II) as a predictor of neonatal morbidity and mortality in a neonatal Jntensive care unit at a hospita in Soweto, South Afr1ca
DATE CONSIDERED	24/04/2020
DECISION:	Approved unoon itrona fly
CONDITIONS:	
SUPERVISOR:	Phindile Nakwa
APPROVED BY:	r C Penny, Chairperson DrCIP _rson, HREC {Medical)
DATE OF APPROVAL:	14/09/2020

This cleairanoe certificate is valid for :5 yearg from data of approval. Extension may be lliPPlied for.

DECLARATION OF INVESTIGATORS

To be completed in uplicate and ONE COPY returnee! to the Research Office Secretary in Room 301, Third or, Facumtyof Heal Sciences, Phillip TobroJS Bt1ildi g, 29 Prine ss of Wales Terrace, F'arktown, 2 00, ll.Iniversity of !he WitWaters,.rand. I/we M[y understand the co.ndjtio.ns under which I am/w .i .aulhorizoo 10 carry out lhe above-rne11lionsd re,search alld lfwe undena e to ensure compliance will, the.se conditions. Should airry dep.arture b9 contemplated, from fhe research protocol as approved, I/we und,e e to or rest1bmit he application to lfle CommlUee I agree to submit ai yearly progrMS rep.on The dal.e annual re-oel'tilieaHoo, I be orie year afler the date of coll\lened mee'ting where the s.tudy was I ltia ly reviewed, In t-s case-, t e study was rn:ilrally rnvlewed Ap!i and wi I Inerefare be due In !he onlh of April each year U r.po ctiang.es la d'le application ay invalidale lhe ctearanoe given by the HREC {Medical)-

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