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“EVALUATION OF SCORE FOR NEONATAL ACUTE PHYSIOLOGY II (SNAP II) AS A PREDICTOR OF MORTALITY IN NEONATES HOSPITALISED WITH SEPTICEMIA.”

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INTRODUCTION

INTRODUCTION

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteraemia in the first month of life. It encompasses various systemic infections of the newborn such as septicaemia, meningitis, pneumonia, arthritis, osteomyelitis, and urinary tract infections.

The risk factors include lack of antenatal care, unsupervised or poorly supervised home deliveries, unhygienic and unsafe delivery practices and cord care, prematurity, low birth weight, lack of exclusive breast-feeding, and delays in recognition of danger signs in both mother and baby.

Neonatal morbidity and mortality are major global public health challenges representing an increasing proportion of overall under-5 child mortality, with the vast majority of neonatal deaths occurring in resource-limited settings.(1)

According to World Health Organization (WHO) estimates, there are about 5 million neonatal deaths a year, 98% occurring in developing countries. Infection, prematurity, and birth asphyxia are the main causes.

Early diagnosis is difficult due to its nonspecific clinical presentation. The ideal approach should be identifying high-risk neonates and targeting them for intensive therapy.

Illness severity score help in tracking and quantifying the morbidity of a neonate and thereby in estimating the probability of a specific outcome in a particular infant that is of interest. They help in identifying high risk infants or neonates at high risk of death.

Scoring systems involve using appropriately weighted demographic, physiological, and clinical data to calculate a score that quantifies morbidity in the given neonate. The principle for such an approach has been long established in many branches of medicine.

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 and specific morbidities

4. Usefulness for all groups of neonates to be described.

Although the mortality risk of admitted infants usually varies with gestational age and birth weight, other perinatal factors along with physiological conditions and disease severity in the first hours of life may also contribute to mortality. Neonatal septicemia may lead to a systemic inflammatory response syndrome (SIRS) and if untreated, may progress to severe septicemia and organ dysfunction (OD).

Therefore, several illness severity scores and neonatal disease scoring systems such as the Clinical Risk Index for Babies (CRIB), CRIB-II Score for Neonatal Acute Physiology (SNAP), SNAP–Perinatal Extension (SNAPPE), and SNAPPE-II have been developed with the aim of determining initial illness severity and predicting mortality and developmental outcome in infants. Application of these severity scores may also be useful for prognostication

and evaluation of the effectiveness of therapeutic protocols in the Neonatal Intensive Care Unit (NICU).

The SNAP, SNAP-PE and their next generation variants SNAP II and SNAP-PE II have been primarily used in NICUs.
In 2001, Richardson et al. (4) developed and validated SNAP II score reducing the number of evaluated items to six, in order to facilitate utilization of the system and the period of data collection to 12 hours. This score consists of 6 physiological parameters, namely

- lowest mean arterial pressure (MAP),
- worst ratio of partial pressure of oxygen (PaO2) to fraction of inspired oxygen (FiO2),
- lowest temperature (in ºF),
- lowest serum pH,
- occurrence of multiple seizures,
- urine output (<1mL/kg/hr)

Previous studies have applied SNAP II as a measure of illness severity in mechanically ventilated term babies and to predict short term adverse respiratory outcomes in newborns 34 weeks gestation admitted to the NICU (5,6). SNAP-II has also been used in predicting mortality among infants with congenital diaphragmatic hernia.(7)

Many babies may not be very sick at admission to NICU and may develop severe sickness later in the course of NICU stay. Hence, SNAP II will be applied to neonates with septicemia admitted in the NICU.

This study has been aimed to investigate whether SNAP II score applied in the 1st 12 hours of onset of sepsis/hospitalisation can predict mortality in neonates with septicemia and to determine the contribution of the individual parameters of SNAP II score to the death.

AIM

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OBJECTIVES

AIM AND OBJECTIVES

Aim of the study:

Evaluation of Sore for Neonatal Acute Physiology II (SNAP II) as a predictor of mortality in neonates hospitalised with septicaemia.

Objectives of the study:

1) To study the relationship between score for neonatal acute physiology II (SNAP II) and Death.
2) To determine the contribution of the individual parameters of SNAP II score to the risk of Death.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

SEPSIS IN THE NEWBORN

Neonatal sepsis is a common life threatening disease and continues to be a major cause of neonatal mortality in India.

Some population-based studies have reported clinical sepsis rates ranging from 49 to 170/1000 live births in rural India. Incidence has not changed much over the past decade, and the fatality due to sepsis is between 30% and 65%. The risk factors include lack of antenatal care, unsupervised or poorly supervised home deliveries, unhygienic and unsafe delivery practices and cord care, prematurity, low birth weight, lack of exclusive breast-feeding, and delay in recognition of danger signs in both mother and baby.

Early diagnosis is difficult due to its nonspecific clinical presentation. The ideal approach should be identifying high-risk neonates and targeting them for intensive therapy.

Neonatal morbidity and mortality are major global public health challenges representing an increasing proportion of overall under-5 child mortality, with the vast majority of neonatal deaths occurring in resource-limited settings.(9)

A study conducted by **S Vergnano, M Sharland, P Kazembe, C Mwansambo, P T Heath**, in the year 2004, quotes that the incidence of neonatal sepsis varies from

7.113 to 3817 per 1000 live births in Asia, from 6.519 to 2315 per 1000 live births in Africa, and from 3.59 to 8.910 per 1000 live births in South America and the Caribbean. By comparison, rates reported in the United States and Australasia range from 1.5 to 3.5 per 1000 for EOS sepsis and up to 6 per

1000 live births for LOS sepsis, a total of 6–9 per 1000 for neonatal sepsis.[10]

BadriThapa, Anurag Thapa, Dhan Raj Aryal, KusumThapa, Asha Pun, SudhirKhanal, KishoriMahatl(2013) in their study quoted that most of the 4 million neonatal deaths every year are in low-income and middle-income countries. Infections account for an estimated 1.44 million (36%) deaths, and about half of the deaths in regions are associated with high neonatal mortality rates. Among infections, neonatal sepsis is one of the leading causes of neonatal morbidity and mortality in developing countries. In this study, the prevalence rate of neonatal sepsis in NICU was 37.12%. The prevalence was higher than the prevalence in developed countries and consistent with developing countries.[11]

In another study conducted by **McIntire, Donald D. PhD; Leveno, Kenneth J. MD** (2008), Neonatal death rates were analyzed from 34 to 40 weeks of gestation to compare mortality rates for late preterm births to births at term and to derive a reference standard. In this analysis, the neonatal mortality rates at 38 and 39 weeks of gestation reached a nadir of 0.2 per 1,000 live births, and 39 weeks was then chosen as the referent for comparison to weeks 34 through 37. The neonatal death rates at 39 weeks were significantly lower when compared with those at 34, 35, 36, or 37 weeks, with P values ranging from .005 to <.001 for each biweeklycomparison.[12]

Definition

National Neonatal Forum of India has defined neonatal sepsis as follows:

Probable (clinical) sepsis

It is found in an infant having a clinical picture suggestive of septicemia if anyone of the following criteria are present:

- Existence of predisposing factors:

  Maternal fever, foul smelling liquor, prolonged rupture of membranes (>24 hrs), or gastric polymorphs (>5 per high-power field).

- Radiological evidence of pneumonia

Culture Positive Sepsis

In an infant having a clinical picture suggestive of septicemia, pneumonia or meningitis, if either of the following criteria are found:

- Isolation of pathogens from blood or CSF or urine or abscess(es)
- Pathological evidence of sepsis.

CLASSIFICATION

Neonatal sepsis can be classified into two major categories depending up on the onset of symptoms

EARLY-ONSET SEPSIS

Early onset (< 72 hrs) infections are caused by organisms prevalent in the maternal genital tract or in the delivery area. The risk factors for early-onset sepsis include

• Low birth weight .

• Prolonged rupture of membranes >24 hrs;

• Foul smelling liquor,

• Multiple per vaginal examinations,

• Intrapatum maternal fever,

• Difficult or prolonged labour

Early onset sepsis manifests frequently as pneumonia and less commonly as septicemia or meningitis.

LATE-ONSET SEPSIS

It is caused by the organisms thriving in the external environment of the home or the hospital. The infection is often transmitted through the hands of the care providers.

The onset of symptoms is usually delayed beyond 72 hours after birth and the presentation is that of septicemia, pneumonia or meningitis. The associated factors of late-onset sepsis include:

• Low birth weight,

• Lack of breastfeeding,

• Superficial infections (pyoderma, umbilical sepsis),

• Disruption of skin integrity with needle pricks and use of intravenous fluids.

CLINICAL FEATURES

The most common characteristics and manifestations are depicted in following. Clinical manifestations of neonatal sepsis

Lethargy	Cyanosis*	Hypothermia	Abdomina l distension
Refusal to suckle	Tachypnea*	Poor perfusion	Diarrhea
Poor cry	Chest retractions*	Bleeding	Vomiting
Not arousable / comatose	Grunt*	Shock	
Fever#	Apnea/gasping*	Renal failure	
Seizures#			Sclerema
High pitched cry#			Poor weight gain
Blank look#			
Bulging fontanel#			
Excessive crying/irritability#			

*Particularly suggestive of pneumonia, # Particularly suggestive of meningitis

Meningitis is often silent, the clinical picture being dominated by manifestations of associated septicemia. However, the appearance of

excessive or high-pitched crying, fever, seizures, blank look, neck retraction or bulging anterior fontanel are highly suggestive of meningitis.

In sick neonates, the skin may become tight giving a hide-bound feel (sclerema) and the perfusion becomes poor (capillary refill time of over 3 seconds). Cyanosis may appear. A critical neonate may develop shock, bleeding and renal failure.

The clinical criteria considered (NNF criteria) are – poor feeding, irritability / excessive cry, lethargy poor cry and reflexes, fever, hypothermia, jaundice, vomiting, abdominal distension, tachypnea and grunting, convulsions, diarrhea, pustules, sclerema, cyanosis, bulged fontanale, DIC/bleeding, poor perfusion / shock, apnea.

Also significant predisposing factors for presumed early onset sepsis will be taken into consideration (according to NNF guidelines) during inclusion of cases.

Neonates (<28 days), will be diagnosed to have septicemia that shall be defined as a suspected or confirmed infection in the presence of Systemic Inflammatory Response Syndrome (SIRS) .

DIAGNOSIS OF SEPSIS (As per NNF)

In presence of risk factors, the baby's gestation is assessed along with the presence of symptoms.

If the baby's gestation is > 35 weeks and the neonate is asymptomatic, a sepsis screen is to be done.

Direct method

Isolation of microorganisms from blood, CSF, urine, pleural fluid or pus is

diagnostic. In clinically suspected cases of sepsis, a blood culture prior to starting antibiotics is to done.

Indirect method

There are a variety of tests which are helpful for screening of neonates with sepsis TLC : A total leucocyte count below 5000/mm3

- An absolute neutrophil count of < 1800 per cu mm is an indicator of infection.
- Neutropenia is more predictive of neonatal sepsis than neutrophilia.
- Immature neutrophils (Band cells + myelocytes + metamyelocytes) to total neutrophils ratio (I/T) > 0.20 means that immature neutrophils are over 20 percent of the total neutrophils because bone marrow pushes even the premature cells into circulation, to fight infection.
- The micro-ESR may be elevated with sepsis and a fall of > 15 mm during first hour indicates infection.
- C-reactive protein (CRP): A CRP value of > 10mg/L is taken as positive.
- A negative CRP is reassuring.

There are a variety of other tests which can be used to predict sepsis but it may be difficult to perform them at all places and hence the clinical acumen remains crucial. A practical positive "sepsis screen" takes into account two or more positive tests out of the five given below:

1. Leukopenia (TLC <5000/cmm)
2. Neutropenia (ANC <1800/cmm)
3. Immature neutrophil to total neutrophil (I/T) ratio (>0.2)
4. Micro ESR (> 15mm 1st hour)
5. CRP+ve

All neonates with late onset sepsis are to be evaluated by doing a lumbar puncture to rule out meningitis. The CSF cytology and the biochemistry values need to be interpreted in the light of the normal range of the values for CSF in the term and preterm neonates.

Neonatal Scoring Systems

Illness severity score help in tracking and quantifying the

- morbidity of a neonate,
- the estimated probability of a specific outcome in a particular infant that is of interest
- need to identify high risk infants suitable for a particular intervention

Scoring systems involve using appropriately weighted demographic, physiological, and clinical data collected on the infant to calculate a score that quantifies its morbidity.

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mortality. Neonatal septicemia may lead to a systemic inflammatory response syndrome (SIRS) and if untreated, may progress to severe septicemia and organ dysfunction (OD). Therefore, several illness severity scores and neonatal disease scoring systems such as the Clinical Risk Index for Babies (CRIB), CRIB-II Score for Neonatal Acute Physiology (SNAP), SNAP–Perinatal Extension (SNAPPE), and SNAPPE-II have been developed with the aim of determining initial illness severity and predicting mortality and developmental outcome in infants. Application of these severity scores may also be useful for prognostication and evaluation of the effectiveness of therapeutic protocols in the Neonatal Intensive Care Unit (NICU).

Previous scoring systems

SEQUENTIAL (SEPSIS-RELATED) ORGAN FAILURE ASSESSMENT (SOFA):

The Sequential Organ Failure Assessment (SOFA) score is a scoring system that assesses the performance of several organ systems in the body (neurologic, blood, liver, kidney, and blood pressure/ hemodynamics) and assigns a score based on the data obtained in each category. The higher the SOFA score, the higher the likely mortality. The SOFA score was designed as a research tool so that groups of patients (e.g., those with sepsis, and infection in the bloodstream which can lead to shock and death) could be categorized based on their risk of death. SOFA creates a standardized, numeric score that is familiar to critical care physicians. Physicians can use it to compare patient status and the score has been shown to have a significant correlation with outcome. This makes it helpful for triage teams. Of the scoring systems available, SOFA achieves a good balance between easily available data and good prediction. When calculated

daily it can also be used to establish trends in the individual patient's course. SOFA was developed to be used with populations and though it was good at determining overall mortality, the score cannot predict individual mortality well. SOFA score cannot be used in isolation to exclude a patient from receiving interventions. The predictive value of the score also depends on the disease state.

SOFA was well-validated in adults, but not in children.

In the year 1996, J.-L. **Vincent ,R. Moreno, J. Takala, S. Willatts, DeMendonga, H. Bruining, C.K. Reinhart RM. Suter , L.G. Thijs** , in the Erasme University Hospital, Belgium conducted a study using the SOFA (Sepsis. related Organ Failure Assessment) score in describing organ dysfunction/failure.(13)

In the year 2013 , **Charan Bale, Arjun L. Kakrani, Varsha S. Dabadghao, Zubin**

D. Sharma ,Pimpri, Pune, Maharashtra, India , conducted a study to assess the severity of sepsis and multi-organ failure at presentation and after 48 h and its correlation with SOFA. They concluded that Sequential assessment of organ dysfunction in ICU at presentation and at 48 h was a good indicator of prognosis. Both mean and highest SOFA scores are particularly useful predictors of outcome, independent of the initial score. A high SOFA score at 48 h of presentation predicts an increased mortality rate.(14)

In the year 2016, **Jared A. Greenberg, MD, MSc, Michael Z. David, MD, PhD, Matthew M. Churpek, MD, MPH, PhD, David L. Pitrak, MD, Jesse B.**

Hall, MD, and John P. Kress, MD conducted a study in patients with hematologic malignant tumors and severe sepsis. They concluded that Modifying the SOFA score to account for infections before admission to the intensive care unit improved the prognostic usefulness of the scores for patients with hematologic malignant tumors and severe sepsis.(15)

QUICK (Q) SEQUENTIAL (SEPSIS-RELATED) ORGAN FAILURE ASSESSMENT (QSOFA):

The Quick (q) Sequential (Sepsis-related) Organ Failure Assessment (SOFA) score is proposed as a surrogate for organ dysfunction and may act as a risk predictor for patients with known or suspected infection, as well as being a prompt for clinicians to consider the diagnosis of sepsis. The Quick SOFA (qSOFA) was developed to provide an abbreviated version that can easily be performed at the bedside by the non- specialist. It was developed using a parsimonious model to achieve a simple scoring system with the fewest number of variables associated with the greatest predictive ability. The main utility of qSOFA appears to be for the characterization of patients with suspected or known infection, in whom sepsis should be considered, who are at a higher risk of developing a poor outcome, and who may benefit from more frequent observations and targeted interventions (i.e., sepsis bundle and or Critical Care admission). In this context it is acting as a risk predictor although it is not specifically part of the diagnosis of sepsis. At the same time qSOFA may act as a surveillance tool and it is suggested that in patients not yet recognized to have infection, a positive qSOFA could also be of value to prompt the consideration of infection. qSOFA had the lowest sensitivity but the second highest specificity.

In 2016, **Raith et al** evaluated the predictive validity of qSOFA in a retrospective analysis of the large, internationally respected, Australian and New Zealand Intensive Care Society (ANZICS) Adult Patient Database of admissions to adult general ICUs. The authors confirmed that the predictive validity of qSOFA in the ICU setting was inferior to the full SOFA score (16)

In the year 2017, **François Lamontagne, David A. Harrison, Kathryn M. Rowan** qSOFA for Identifying Sepsis Among Patients With Infection. It was foundthat qSOFA had similar or better predictive validity for the selected outcomes expected to be more common following sepsis than the more complex measures tested—SOFA and the Logistic Organ Dysfunction System —that require a greater number of clinical and laboratory variables. However, among patients with infection in the ICU, qSOFA had statistically worse predictivevalidity.(17) In the year 2017, Freund et al evaluated the predictive validity of qSOFAin a prospective study of patients presenting to EDs in France, Switzerland, Spain, and Belgium. Among 879 patients (median age 67 years, 379 with respiratory tract infection, in-hospital mortality of 8%) presenting with suspected infection to 30 EDs over a 4-week period, the investigators confirmed that the predictive validity of qSOFAin the ED setting was similar to that of the full SOFA score and that the addition of lactate did not improve predictive validity. qSOFA performed better than systemic inflammatory response syndrome (SIRS) criteria and severe sepsis to predict in-hospital mortality(18)

Eli J. Finkelsztein1 , Daniel S. Jones1 , Kevin C. Ma1 , Maria A. Pabón1 , Tatiana Delgado1 , Kiichi Nakahira1 , John E. Arbo2 , David A. Berlin1 , Edward J. Schenck1 , Augustine M. K. Choi1 and Ilias I. Siempos1,(2017)

conducted a study comparing qSOFA and SIRS for predicting adverse outcomes of patients with suspicion of sepsis outside the intensive care unit. They concluded that in patients with suspected infection who eventually required admission to the ICU, qSOFA calculated before their ICU admission had greater accuracy than SIRS for predicting mortality and ICU-free days. These findings may help clinicians gain further insight into the usefulness of qSOFA.(19)

MORTALITY IN EMERGENCY DEPARTMENT SEPSIS (MEDS):

Mortality in Emergency Department Sepsis (MEDS) scores use clinical and laboratory variables to grade the severity of organ failure and have been demonstrated to correlate with mortality among those admitted from the ED with sepsis [8]. The MEDS score requires a subjective assessment of likelihood of short-term mortality and may perform less accurately at higher illness severity.

THE RAPID EMERGENCY MEDICINE SCORE (REMS):

The Rapid Emergency Medicine Score (REMS), an abbreviated version of APACHE II, has previously been specifically evaluated as a predictor of in hospital mortality for nonsurgical patients presenting to the emergency department (ED). It was concluded that REMS had predictive accuracy similar to the established but more complicated APACHE II. The investigators suggested that a severity-of-disease classification in the ED combined with an accurate description of the disease could prognosticative stratify acutely ill patients and assist investigators when comparing the success rates of new forms of therapy. This scoring index could be used to evaluate the use of

hospital resources and compare the efficacies of different EDs. The investigators also suggested that REMS could be suitable as a triage instrument for nurses in the ED. However, it would be of great value to examine the predictive accuracy of REMS regarding long-term mortality. The use and interest would be to allow patients, families, physicians, and nurses to have an idea of predicted mortality and prognosis[20].

CLINICAL RISK INDEX FOR BABIES (CRIB):

The CRIB score was created to predict mortality for infants born at less than 32 weeks gestation at birth and was derived using data from infants Birth weight, Gestation, Congenital malformation, Maximum base deficit in first 12 hours , Minimum appropriate FIO2 in first 12 hours and Maximum appropriate FIO2 in first. A further advantage is that CRIB is assessed over the first 12 hours of life, making it less susceptible to treatment effects than some other scores.

In the year 2004, **L Gagliardi, A Cavazza, A Brunelli, M Battaglioli, D Merazzi, F Tandoi, D Cella, G F Perotti, M Pelti, I Stucchi, F Frisone, A Avanzini, R Bellu`** compared CRIB, CRIB II and SNAPPE II in assessing the mortality risk in very low birth weight infants. It was concluded that CRIB and CRIB-II had greater discriminatory ability than SNAPPE-II. Risk adjustment using all scores is imperfect, and other perinatal factors significantly influence VLBW survival. CRIB-II seems to be less confounded by these factors. (21)

I. K. MARETE, A. O. WASUNNA And P. A. OTIENO (2011, KENYA,AFRICA) conducted a study to evaluate the use of CRIB II score as a tool to predict the risk for neonatal mortality among the LBW babies and concluded that CRIB II score of > 4 was found to have better prediction for mortality among the LBW babies compared to the traditionally used predictors and can be used to prioritize care for such neonates for better outcome.(22)

SCORE FOR NEONATAL ACUTE PHYSIOLOGY (SNAP)

SNAP, the principal alternative to CRIB, was developed using data from three units in Boston, USA in 1990 [23]. This score is applicable to any infant admitted to a neonatal unit, but, because of the small number of VLBW infants in the population from which it was derived, it has reduced sensitivity to differences between the most premature infants.25 SNAP scores are based on 28 items collected over the first 24 hours of life from a variety of sources including every body system and selected blood test results. Unlike the CRIB score, where parameters are weighted according to their statistical relation to death, the variables were weighted according to expert opinion, with a score of 0, 1, 3, or 5 assigned to each variable. The original cohort was also used to extend SNAP to form the SNAP-PE score (score for neonatal acute physiology— perinatal extension) by adding birth weight, small for gestational age (weight,5th centile for gestation), and low Apgar score at five minutes. Although the SNAP score assesses many body systems, and is able to predict death well, it is much more difficult to collect than the CRIB score. In Richardson's comparison, SNAP predicted death better than birth weight alone (Az 0.87 v 0.77), and SNAP-PE was even better (Az0.93)[24].

The SNAP score (developed and mainly used in the United States and Canada) is used for describing populations, stratifying risk in epidemiologic and clinical trials and projecting resource utilization. It is based on 28 variables obtained during the first 24 hours after admission with each parameter weighted according to expert opinion, with a score of 0, 1, 3 or 5 assigned to each variable (6)

SCORE FOR NEONATAL ACUTE PHYSIOLOGY II (SNAP II)

In 2001, Richardson et al. [25] developed and validated SNAP II score reducing the number of evaluated items to six (mean blood pressure, lowest temperature, PO2/FiO2 ratio, serum pH, multiple seizures, and urine output), in order to facilitate utilization of the system and the period of data collection to 12hours.

Previous studies have applied SNAP II as a measure of illness severity in mechanically ventilated term babies and to predict short term adverse respiratory outcomes in newborns 34 weeks gestation admitted to the neonatal intensive care unit (NICU) [65,27,28]. Many babies may not be very sick at admission to NICU and may develop severe sickness later in the course of NICUstay.

Hence, SNAPII will be applied to the diagnosis of septicemia in babies already admitted in the NICU. This study is aimed to investigate whether SNAP II score applied in the 1st 12 hours of onset of sepsis can predict mortality in neonates with septicemia and to determine the contribution of the individual parameters of SNAP II score to the death.

In 2001, Richardson et al. (23, 35) developed and validated SNAP II score reducing the number of evaluated items to six (mean blood pressure, lowest temperature, PO2/FiO2 ratio, serum pH, multiple seizures, and urine output), in order to facilitate utilization of the system and the period of data collection to 12 hours.

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neonatal intensive care unit (NICU) [24]. Many babies may not be very sick at admission to NICU and may develop severe sickness later in the course of NICU stay.

P.P. Maiya, S. Nagashree and MehaboobShariff Shaik [2013] [29] found that SNAP correlated well with mortality ;the sensitivity and specificity of SNAP score

>15 in predicting mortality were 63% and 95% respectively. The positive and negative predictive values were 72% and 92.5% respectively. Very low birth weight babies and ventilated preterm neonates had higher mortality and the best cut-off SNAP score for predicting mortality in these groups was 10. In all the other groups, SNAP score > 15 correlated well with higher mortality. By using multiple regression analysis on three variables including birth weight, gestational age and SNAP, SNAP was found to show the best correlation with mortality. On correlating SNAP with duration of hospital stay ,76.8% of the surviving neonates with SNAP <16 stayed for

<15 days, whereas the rest stayed longer despite low SNAP. All the 9 babies with SNAP >15 who survived stayed for >15 days. SNAP is a measure of illness severity and correlates well with neonatal mortality. SNAP may assist the clinician in explaining the probable outcome and therapeutic intervention needed and the cost of treatment to the parents, SNAP scores >10 in VLBW babies and >15 in others are associated with higher mortality**.**

VenkataseshanSundaram, Sourabh Dutta, Jasmina Ahluwalia and Anil Narang [2009] [30] studied Forty neonates completed the study. Twenty-five died within 14 days. The median SNAP II was significantly higher in babies who died versus those who survived [median (IQR): 43 (36 – 53.5) vs 18 (16 - 37), P<0.001]. A SNAP II greater than 40 had 88% positive predictive value for death and persistent OD each, and 86.6% and 86% specificity for death and persistent OD, respectively. On day 14 from enrolment, more organs normalized/improved in the subjects with SNAP II of ≤40. Perfusion related SNAP II parameters were significantly associated with death and organ dysfunction. Severely septic neonates with high SNAP II scores (>40) have higher risk of dying and persistent organ dysfunction. Individual SNAP II parameters do not contribute equally in prediction of mortality.

YanhongLi, Jie Yan, Mengxia Li, Zhihui Xiao, Xueping Zhu, Jian Pan, Xiaozhong Li and Xing Feng [2013] [30]: In their study, high SNAP scores were significantly associated with increased risk for Bronchopulmonary Dysplasia (BPD) or death in critically ill preterm infants with less than 33 gestational weeks. SNAP is predictive of BPD or death, with additional prognostic value when used in conjunction with other perinatal risk factors. The combination of SNAP score with gestational age, apnea of prematurity, PDA, and surfactant use appears to be the best predictive model for BPD or death during the early postnatal period in this population. Large studies are needed to further explore the role of the SNAP score for prediction of BPD or death in neonates.

Olaf Dammann, Mary Naples, Francis Bednarek, Bhavesh Shah et al [2008], [32] studied total of 1,399 inborn infants born before the 28th week of gestation were given Scores for Neonatal Acute Physiology (SNAP-II and SNAPPE-II) based on data collected within the first 12 h of admission to the intensive care unit and had a protocol brain ultrasound scan read independently by 2 sonologists. After adjustment for gestational

age, high SNAP-II and SNAPPE-II scores predicted intraventricular hemorrhage, moderate/severe ventriculomegaly and echo dense lesions in cerebral white matter. Only 2 SNAP-II extremes, the highest decile for gestational age and a Z score 1 1, also predicted echo lucent lesions in the white matter. Neither SNAP-II nor SNAPPE-II predicted any statistically significant diagnosis of cerebral palsy. MDI and PDI scores, 55 were consistently predicted by both high SNAP-II and SNAPPE- II, whereas scores in the 55–69 range were inconsistently predicted. High SNAP-II and SNAPPE-II inconsistently predicted a positive screen for autism spectrum disorder and small head circumference at 24 months. The physiologic instability in the first 12 post-natal hours identified by illness severity scores conveys information about the risks of brain damage and neuro developmental dysfunctions. This risk information might reflect postnatal characteristics in the causal chain. On the other hand, high SNAP scores might be indicators of immaturity andvulnerability.

NahedFahmyHelal, Nashwa MamdouhSamra, Eman Abdel Ghany Abdel Ghany and Ebtehal Adel Said[2013][33] studied Eighty Egyptian newborns hospitalized for neonatal sepsis were investigated through a multicenter observational prospective study to determine whether SNAP II applied in the 1st 12 hours of admission would predict mortality and or Organ Dysfunction(OD). The median SNAP II was significantly higher in babies who died or developed OD versus those who survived and improved (P=0.003 and P=0.001 respectively). Individual parameters of the SNAP II didn't contribute equally to the risk of death, low mean arterial blood pressure and lowest blood pH were significantly associated with OD and death (P=0.002). ROC curves for the SNAP II score ≥ 40 showed moderate predictive accuracy and 90.4% and 88.9% sensitivity for OD and death, respectively. SNAP II ≥ 40 can predict OD and death with moderate predictive accuracy when applied on

admission to neonates with sepsis. Parameters related to perfusion (mean arterial pressure and acidosis) were significantly associated with death as well as organ dysfunction at day14.

MalihehKadivar ;SetarehSagheb ; FaribaBavafa, RN; LidaMoghadam&BabakEshrati [2007] [34] studied 198 newborn infants , The mean and standard deviation (SD) of the variables including postnatal age, birth weight, SNAP, and finally Apgar scores at 1 minute and 5 minutes of neonates under this study were 7.6 (0.5) days, 2479.8 (29.4) grams, 21.6 (1.1), 7.47(0.08), and 7.71 (0.06), respectively.

Twenty five of the 198 patients died (12.6%). Gestational age (P=0.03), birth weight (P=0.02), Apgar score at 5 minutes (0.001), and SNAP-PE II (P=0.04) were significantly related to the mortality rate. By Analyzing through logistic regression to evaluate the predictive value of these variables in relation to the risk of mortality, it was shown that only SNAPPE II and Apgar score at 5 minutes could significantly predict the neonatal mortality.

According to this study SNAP-PE II and Apgar score at 5 minutes can be used to predict mortality among the NICU patients. SNAP-PE II score had the best performance in predicting mortality in this study. More studies with larger samples are suggested to evaluate all of the abovementioned parameters among neonates who are admitted to NICUs countrywide.

MATERIALS

&

METHODS

MATERIALS AND METHODS

Research methodology organizes all the components of the study in a way that is more likely to lead valid answers. It has crucial implications for validity and credibility of the study findings. This chapter gives a brief description of the materials and methods adopted to study the Evaluation of Score for Neonatal Acute Physiology II (SNAP II) as a Predictor of Mortality in Neonates Hospitalized with Septicemia" of tertiary care centre Latur (MS) India.

RESEARCH QUESTION

Evaluation of Score for Neonatal Acute Physiology II (SNAP II) as a Predictor of Mortality in Neonates Hospitalized with Neonatal Sepsis.

RESEARCH APPROACH

In view of the problem selected for the study and the objectives to be accomplished, combine observation and interview approaches were considered to be appropriate.

RESEARCH DESIGN

The research design selected for this study is a Prospective cohort study.

Target population

Neonates Hospitalised with

Septicemia of tertiary care hospital of

↓

Latur City.

Sampling Method

Simple Random Sampling

↓

Instrument

Individual Interview, Clinical &laboratorical Examination

↓

Data analysis

Descriptive Statistics

↓

Outcome

Outcome of Evaluation of Score for Neonatal Acute Physiology II (SNAP II) as a Predictor of Mortality of Neonatal Sepsis

Schematic diagram showing research design

SETTINGS OF THE STUDY

It is the Physical location where study was conducted. This study was conducted in tertiary care hospital of Latur City.

PERIOD OF STUDY

Our study included 60 patients presenting with neonatal septicemia admitted to MIMSR Medical College, Latur 1st Oct 2018 to 1st Oct. 2020.

SAMPLING TECHNIQUE

Neonates were selected using simple random sampling.

STUDY GROUP

All suspected and confirmed cases of sepsis in the presence of Systemic Inflammatory Response syndrome (SIRS) were enrolled.

SAMPLE SIZE

Sample size has been calculated using:

$$n = \frac{z^2 p\,(1-p)}{d^2}$$

p=prevalence /Incidence

z=1.96 (Constant for 5% of all error)

d=0.05 (Allowable error of 5%)

APPROVAL FOR STUDY

Approval for the study was obtained from the Institutional Ethical Committee of MIMSR Medical College, Latur [MS].

METHOD OF DEVELOPING THE STUDY TOOL

The following steps were carried out in developing the instrument.

- Review of related literature.
- Discussion with guide and experts.

TOOL USED

Description of Tool

<u>Section I</u> – Demographic Profile

To ascertain demographic details, relevant maternal history and to note the findings of clinical examinations of neonates, a well-designed structural Performa was used where all requisite details pertaining to the study were noted.

<u>Section II</u> – Laboratory Findings Investigations:

i. Sepsis screen (according to NNF criteria) (6)

a. Total leukocyte count

b. I/T ratio (band cell ratio)

c. Absolute neutrophil count

d. m-ESR

e. C reactive protein

ii. Blood culture

iii. Biochemistry investigations

METHODOLOGY

1) All patients who had clinical features of sepsis (as per NNF guidelines) such as lethargy, refusal to feed, seizures , high pitched cry, excessive irritability, tachypnea, were screened after thorough clinical examination and history taking.
2) Also all patients having a background of predisposing factors for septicemia making it presume to be early onset sepsis (according to NNF criteria) such as maternal fever, foul smelling liquor, prolonged rupture of membranes (>24 hrs) were considered while inclusion of cases.
3) Sepsis screen was applied to all these patients. . A positive "sepsis screen" took into account two or more positive tests out of the five given below:
   - Leukopenia (TLC <5000/cmm)
   - Neutropenia (ANC <1800/cmm)
   - Immature neutrophil to total neutrophil (I/T) ratio (> 0.2)
   - Micro ESR (> 15mm 1st hour)
   - CRP +ve
4) Consent of parents was taken and all patients with positive sepsis screen were enrolled into the study. Simultaneously Blood cultures were sent.
5) BLOOD CULTURE Depending on the blood culture patients were divided into 3 groups
   a) Blood culture positive cases
   b) Blood culture negative but sepsis screen positive cases

c) Blood culture negative and sepsis screen negative cases, but with a clinical course compatible with sepsis

6) All the enrolled neonates had their severity assessed using SNAP II. This score consisted of 6 physiological parameters, namely

- lowest mean arterial pressure (MAP),
- worst ratio of partial pressure of oxygen (PaO2) to fraction of inspired oxygen (FiO2),
- lowest temperature (in ºF),
- lowest serum pH, occurrence of multiple seizures, and
- Urine output (<1mL/kg/hr).

7) The data collection window was the first 12 hours from the onset of septicaemia / hospitalization, during which period the above parameters were recorded prospectively.

8) Weighted scores were given based on the presence or absence of each parameter.

9) TOOLS for SNAP II SCORING

VARIABLES	VALUES	POINTS
Mean blood pressure	≥ 30 mmHg	0
	20-29 mmHg	9
	<20 mmHg	19
Temperature	>35.6°C	0
	35 - 35.6°C	8
	<35°C	15
PO_2 (mmHg) / FiO_2 (%)	>2.49	0
	1.0-2.49	5
	0.3-0.99	16
	<0.3	28
Lowest serum pH	≥ 7.2	0
	7.1-7.19	7
	<7.1	16
Multiple seizures	No	0
	Yes	19
Urine output(ml/kg/h)	≥ 1	0
	0.1-0.9	5
	<0.1	18

10) Traditional axillary glass mercury thermometer (AGMT) was used with a dwell time of 3 minutes to access the temperature of neonates.

11) Multichannel monitor was used to determine systolic BP (SBP), diastolic BP (DBP), and mean arterial pressure (MAP) by oscillometric method. Infant BP cuffs (sizes 6-11 cm, 4-6 cm) were used. The smallest cuff size that covered at least two- thirds of the right upper arm length and encompassed the entire arm circumference was selected. The appropriate-sized cuff was applied to the right upper arm with baby in supine position. Three successive BP recordings were taken at 2-minute intervals. The average of these three readings, rounded off to the nearest mmHg, was calculated and recorded for further analysis.

12) Serum pH of all patients was estimated by doing an ABG within first 12 hours of onset of sepsis/hospitalization.

13) Urine Output was systematically measured by diaper weight every 3 h even at night time. As variations in bladder retention could lead to erroneous oliguria classification using shorter time intervals, we measured total diuresis in a 24-h interval and calculated Urine Output in mL/kg/h.

14) Severity of the illness was graded according to the SNAP II score as follows: Mild: 1-20

Moderate: 21-40

Severe: >40.

15) All subjects were followed up until death or recovery & discharge

Statistical Analysis

Data was entered in Microsoft Excel and analyzed using SPSS version 24.0th. Mean and Standard deviation were calculated for quantitative variables, and proportion was calculated for categorical variables. Also represented in form of visual impression like pie-diagram, bar-diagram.

To assess the association of SNAP II with different parameters, Chi square test for categorical variables was used. Karl person correlation coefficient was used to calculate relationship between two variables. P-value of <0.05 was considered statistically significant. Also Sensitivity and specificity was calculated for SNAP II Score with the final diagnosis.

OBSERVATIONS

&

RESULTS

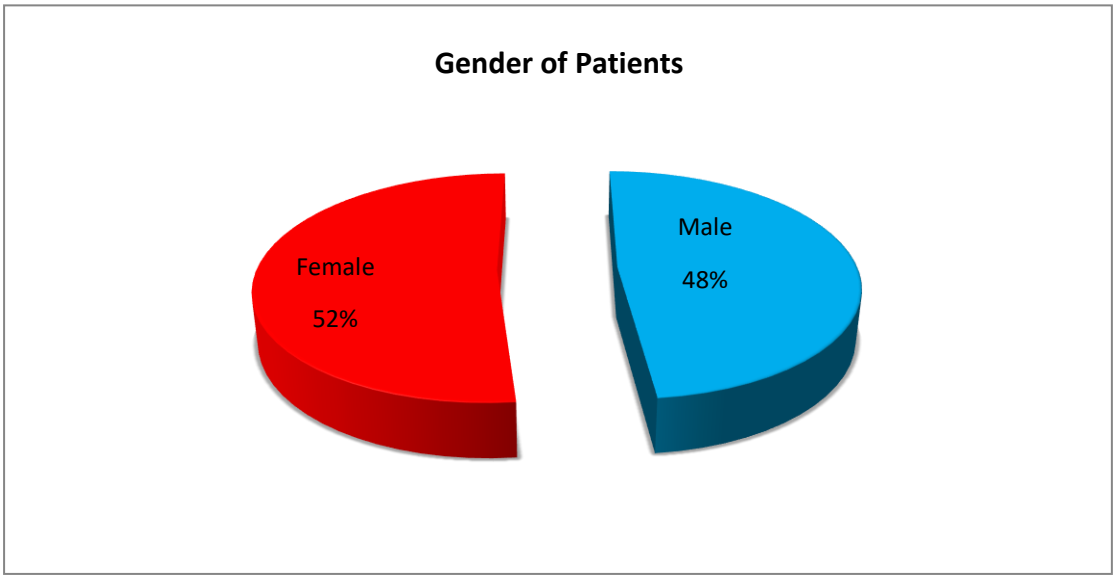
OBSERVATIONS & RESULTS

Table 1: Demographic profile of Neonates

		No. of patients [N=60]	Percentage
Gender	Male	29	48.3%
	Female	31	51.7%
Age-Group [in days]	Up to 1 Day	19	31.7%
	2—15 Day	31	51.7%
	16--30 Day	10	16.7%

In the present study, 60 neonate have been studied, out of these 29(48.3%) were male and 31(51.7%) were female.

Maximum 31(51.7%) patients were from age of 2-15 Days, 19(31.7%) were up to 1 Day [up to 24 Hours] and 10(16.7%) were 16-30 Days at the time of admission.


Gender of Patients
Female
52%
Male
48%

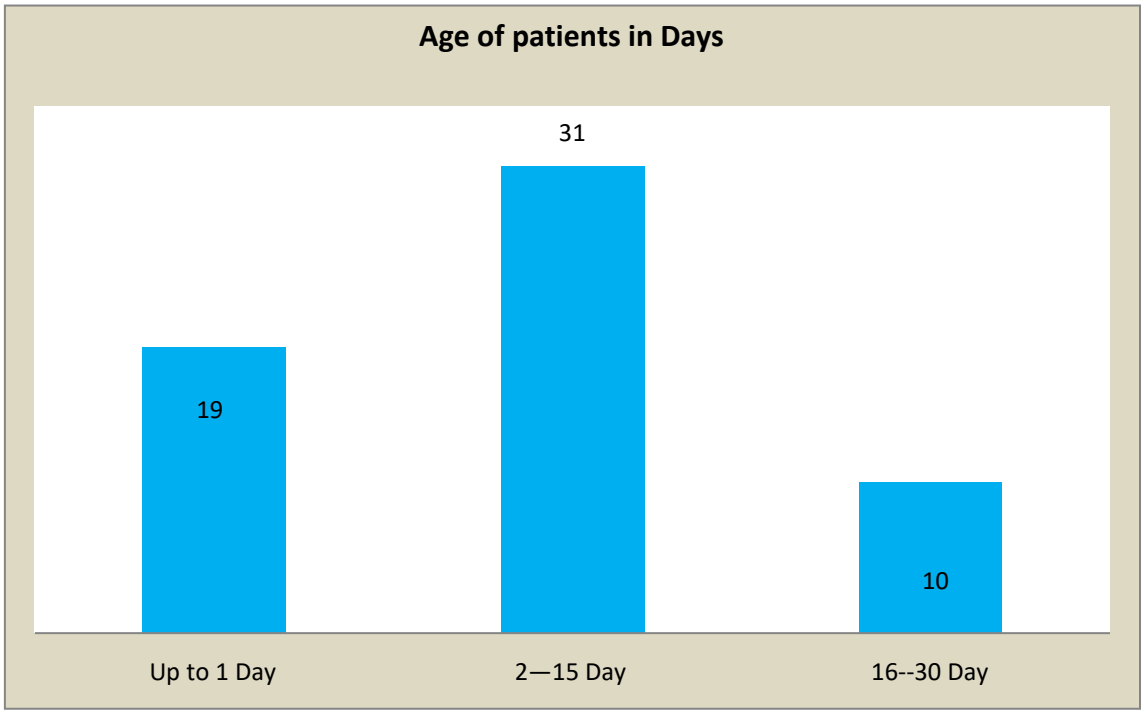

Age of patients in Days
19
31
10
Up to 1 Day
2—15 Day
16--30 Day

Table 2: Distribution of Neonates according to Gestation

Gestation	No. of patients	Percentage
Preterm	31	51.7%
Term	29	48.3%

Table 2 shows that, more than half [i.e. 31(51.7%)]of the study subjects were preterm and rest [i.e. 29(48.3%)] were term

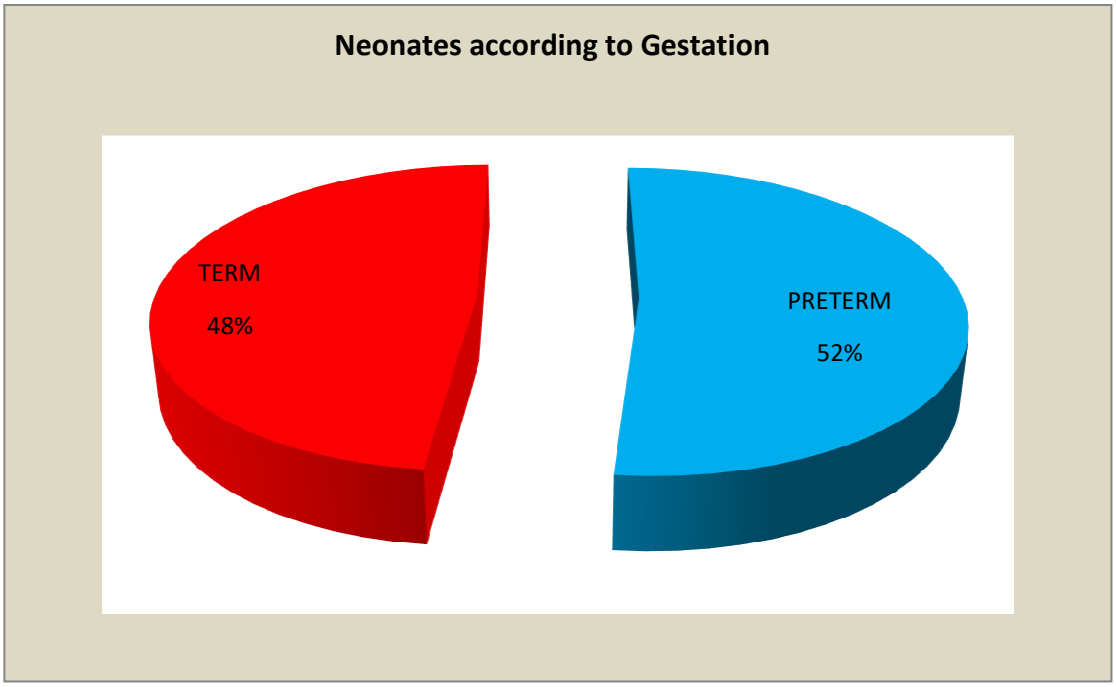


Table 3: Distribution of Neonates according to Gestation

Particular		No. of patients	Percentage
Preterm	SGA	10	32.3%
[n=31]	AGA	21	67.7%
Term	SGA	03	10.3%
[n=29]	AGA	26	89.7%

SGA –Small for gestational age AGA – Appropriate for gestational age.

As per Table 3, out of 31 preterm neonates, 10(32.3%) neonates were SGA and 21(67.7%) were AGA neonates. Out of 29 term neonates, 03(10.3%) were SGA and 26(89.7%) were AGA.

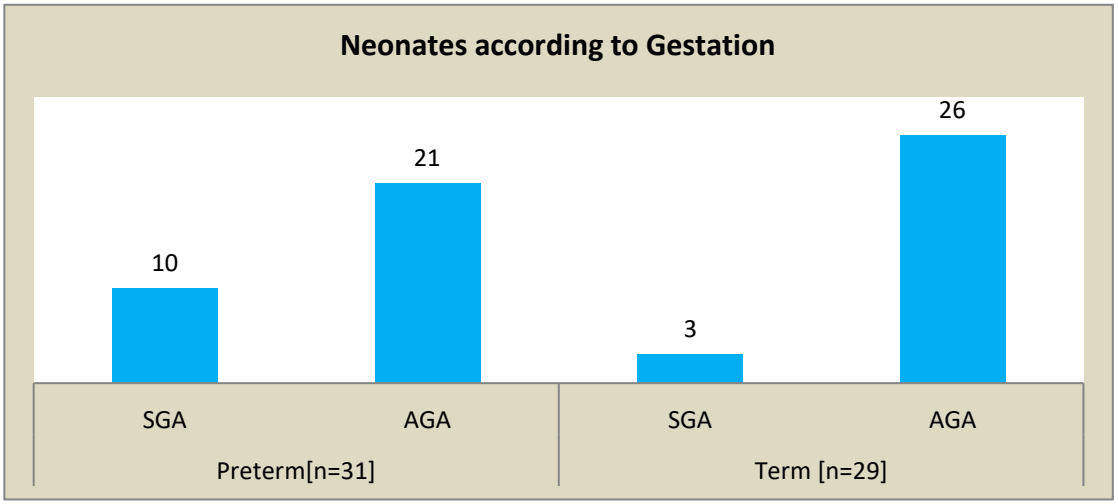


Table 4: Distribution of outcome of blood culture and organisms in positive blood culture

ORGANISMS		NO.OF PATIENTS	PERCENTAGE
Blood culture	Positive	09	15.0%
	Negative	51	85.0%
Positive Blood culture [n=09]	Staph aureus	03	5.00%
	Klebsiellapneumonea	03	5.00%
	Acinatobacterbaumani	01	1.7%
	Enterococcus fecalis	01	1.7%
	E.Coli	01	1.7%

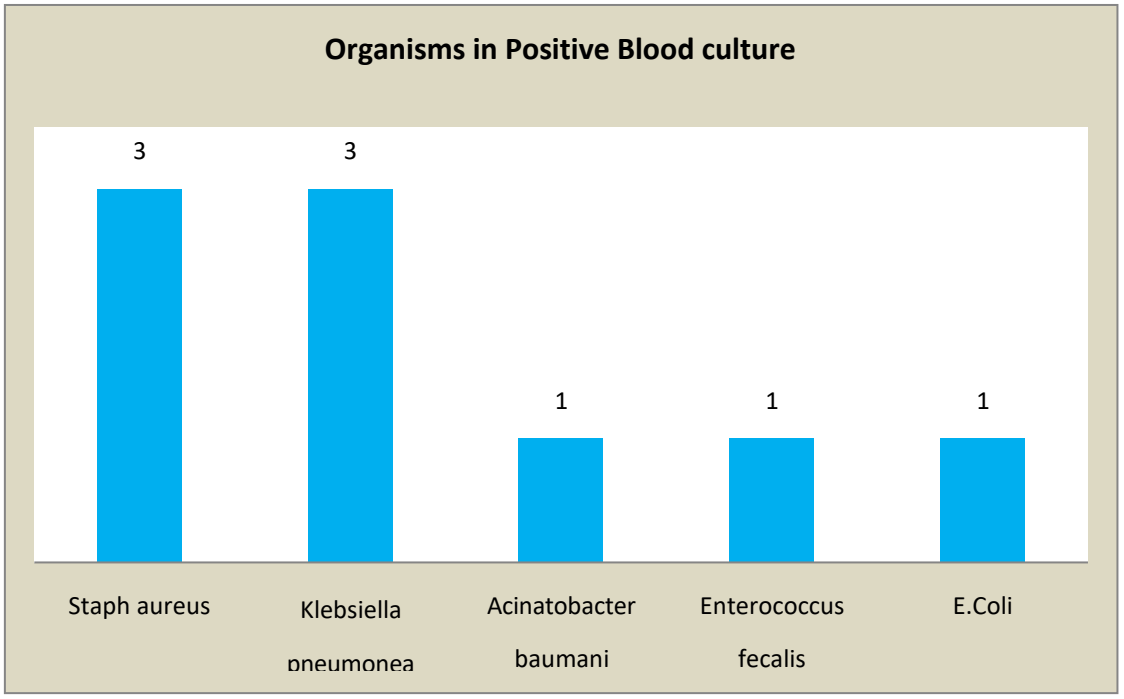
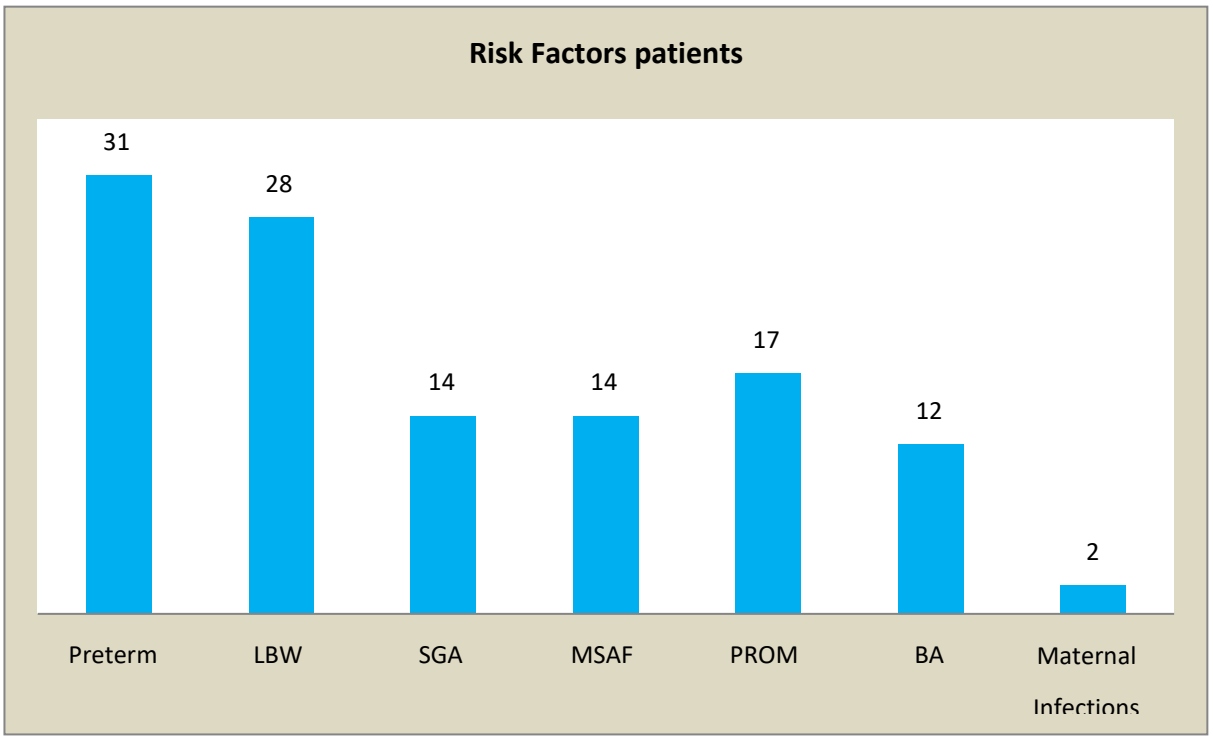


Table 3 shows that, blood culture was positive in 09 (15.0%) neonates.

All culture negative subjects had a positive sepsis screen. The most common causative organisms were Staph aureus 03(5.0%) and Klebsiellapneumonea 03(5.0%).

Table 5: Risk Factor in Neonates enrolled in study

Risk Factor	No. of patients	Percentage
Preterm	31	51.7%
LBW	28	46.7%
SGA	14	23.3%
MSAF	14	23.3%
PROM	17	28.3%
BA	12	20.0%
Maternal Infections	02	3.33%

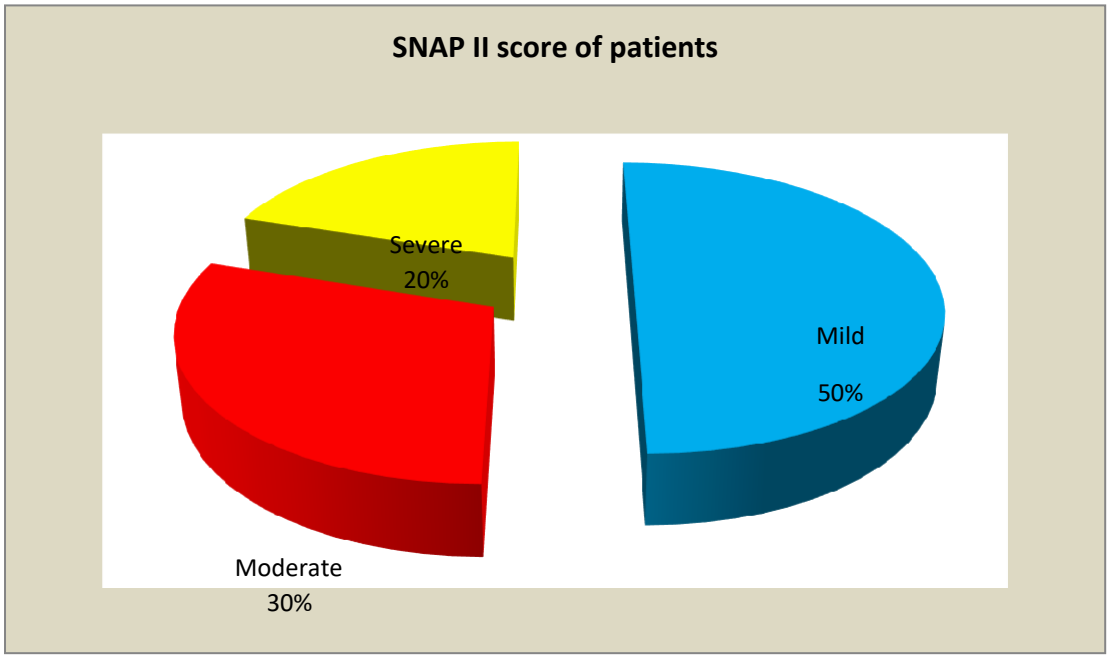


LBW- low birth weight, SGA- Small for gestational age , MSAF- Meconium stained amniotic fluid, PROM- premature rupture of memebrane , BA- Birth asphyxia

The risk factors in neonates were : 31 (51.7%) neonates presented as preterm births, 28(46.7%) neonates with Low birth weight, 17(28.3%) with PROM , and 02(3.33%) with confirmed maternal infections .

Table 6: Distribution of Neonates according to SNAP II Score

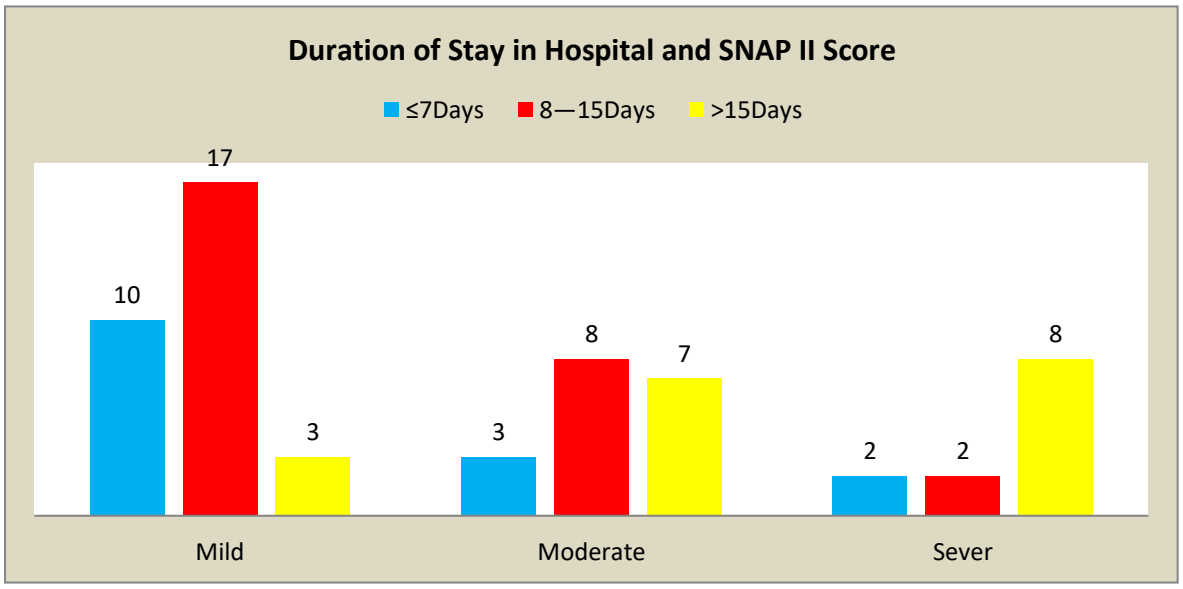
SNAP Score	No. of patients [N=60]	Percentage
Mild	30	50.0%
Moderate	18	30.0%
Severe	12	20.0%
Total	60	100%



As above it is shown that, out of 60 neonates, Majority of them, 30(50.0%) had Mild SNAP Score, 18(30.0%) neonates had moderate score and 12(20.0%) neonates were having Severe SNAP Score.

Table 7: Association between Duration of Stay in Hospital and SNAP II Score

Duration of Stay in Hospital	SNAP II Score						Total		Chi-square value& p-value
	Mild		Moderate		Severe				
	No.	%	No.	%	No.	%	No.	%	
≤7 Days	10	33.33%	03	16.7%	02	16.7%	15	25.0%	
8—15 Days	17	56.67%	08	44.4%	02	16.7%	27	45.0%	X^2=8.83
>15 Days	03	10.0%	07	38.9%	08	66.7%	18	30.0%	**P=0.043**
Total	30	100%	18	100%	12	100%	60	100%	

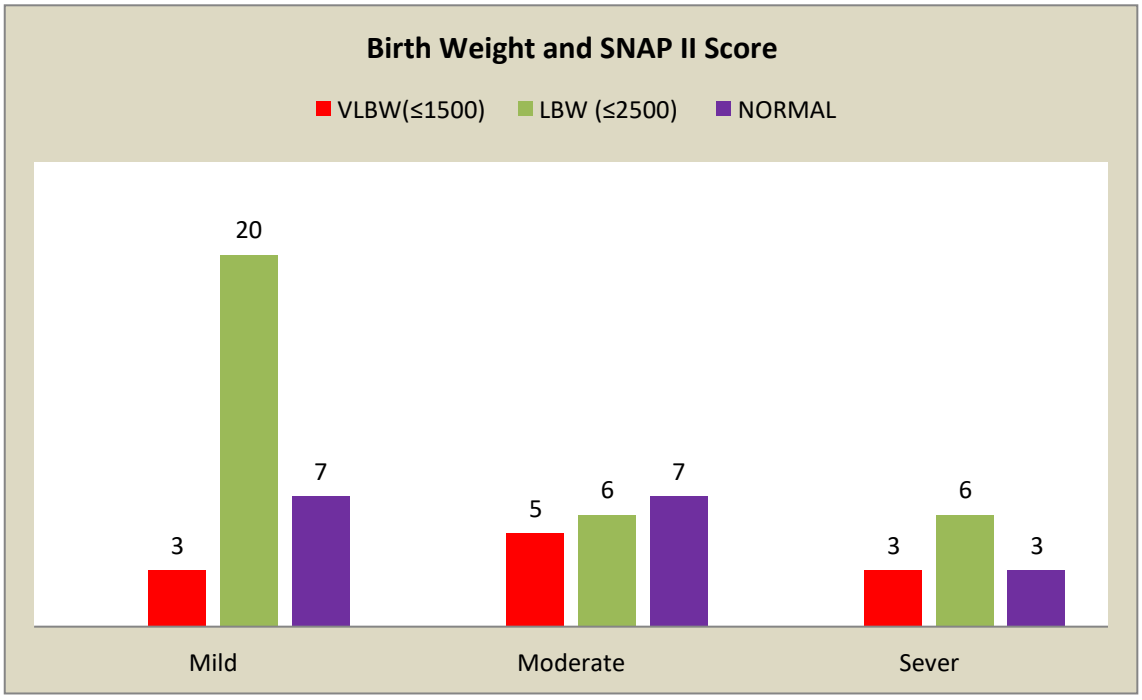


Out of 30 mild SNAP II Score neonates, maximum 17(56.67%) neonates were admitted for 8-15 days in Hospitals. Of the 12 severe SNAP Score neonates, majority of them 08(66.7%) were admitted for more than 15 days in the Hospital. There was statistically significant association between Duration of Stay in Hospital and SNAP Score [p=0.043].

Table 8: Association between Birth Weight and SNAP II Score

Birth Weight	SNAP II Score						Total		Chi- square value&p-value
	Mild		Moderate		Sever				
	No.	%	No.	%	No.	%	No.	%	
VLBW(≤1500)	03	10.0%	05	27.8%	03	25.0%	11	18.3%	X^2=2.36
LBW (≤ 2500)	20	67.7%	06	33.3%	06	50.0%	32	53.3%	p-value=
NORMAL	07	23.3%	07	38.9%	03	25.0%	17	28.3%	0.223
Total	30	100%	18	100%	12	100%	60	100%	

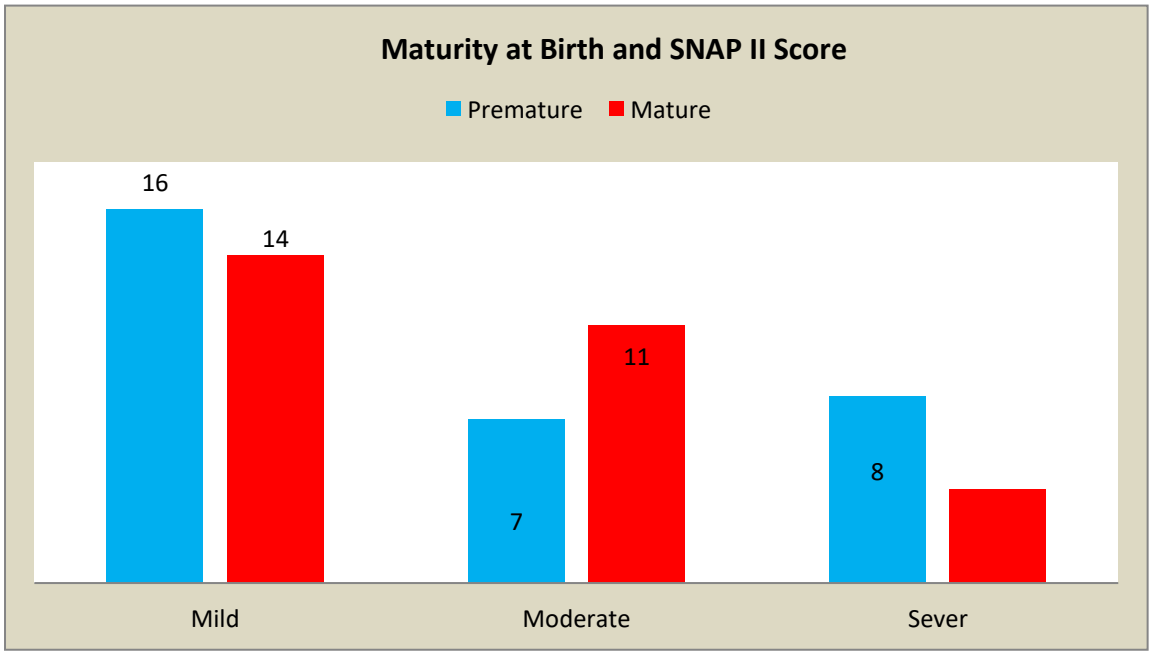
VLBW - Very low birth weight, LBW- Low birth weigth



As Table 8 shows that, no statistically significant association was found between birth Weight and SNAP Score [p=0.223].

Table 9: Association between Gestation Age at Birth and SNAP II Score

Gestation Age	SNAP II Score						Total		Chi-square value& p-value
	Mild		Moderate		Sever				
	No.	%	No.	%	No.	%	No.	%	
Preterm	16	53.3%	07	38.9%	08	66.7%	31	51.7%	X^2 = 2.29 P=0.381
Term	14	46.7%	11	61.1%	04	33.3%	29	48.3%	
Total	30	100%	18	100%	12	100%	60	100%	

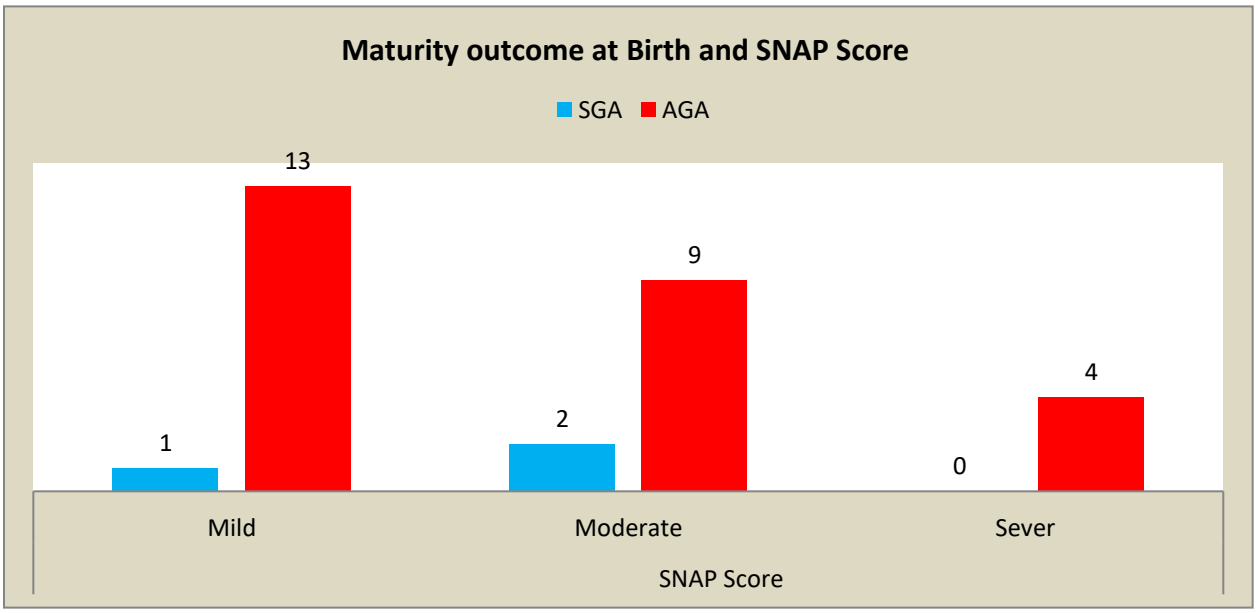


As per Table 9, there was no statistically significant association between Maturity at Birth and SNAP II Score of patients[p=0.381].

Table 10: Association between Term babies and SNAP II Score

Term babies	SNAP II Score						Total		Chi-square value& p-value
	Mild		Moderate		Sever				
	No.	%	No.	%	No.	%	No.	%	
SGA	01	7.1%	02	18.2%	00	00	03	10.3%	
AGA	13	92.8%	09	81.8%	04	100%	26	89.7%	X^2 = 1.34 P=0.510
Total	14	100%	11	100%	04	100%	29	100%	

SGA –Small for gestational age **AGA – Appropriate for gestational age**.

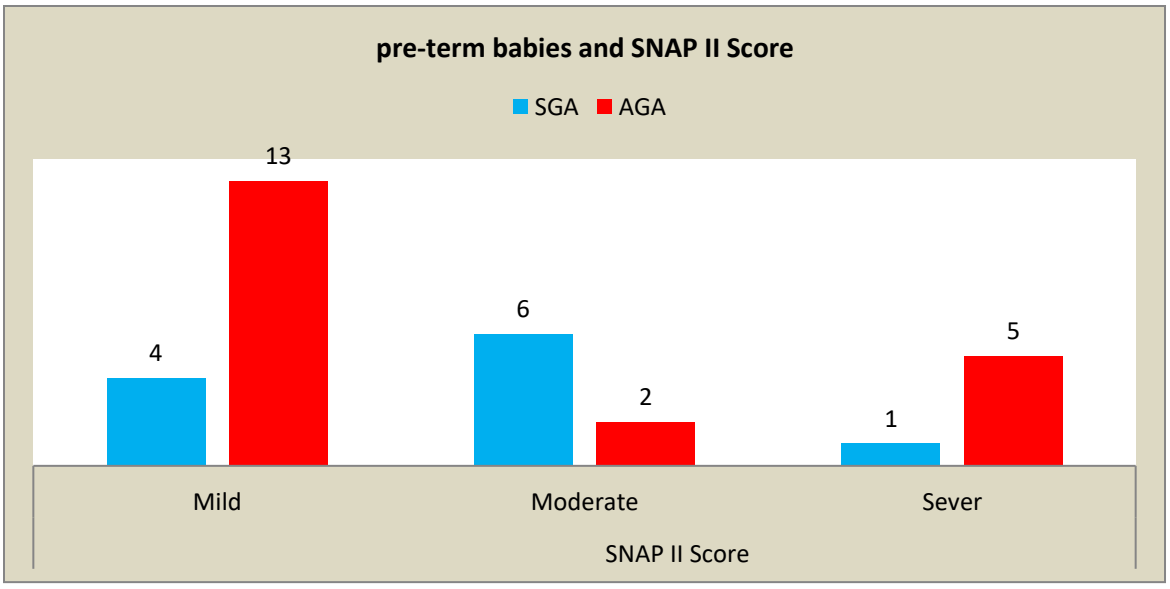


There was no statistically significant association between Maturity at Birth and SNAP Score of patients [p=0.510].

Table 11: Association between pre-term babies and SNAP II Score

Preterm babies	SNAP II Score						Total		Chi-square value& p-value
	Mild		Moderate		Sever				
	No.	%	No.	%	No.	%	No.	%	
SGA	04	23.5%	06	75.0%	01	16.7%	11	35.5%	X^2 = 7.45 **P=0.024**
AGA	13	76.5%	02	25.0%	05	83.3%	20	64.5%	
Total	17	100%	08	100%	06	100	31	100%	

SGA –Small for gestational age **AGA – Appropriate for gestational age**.



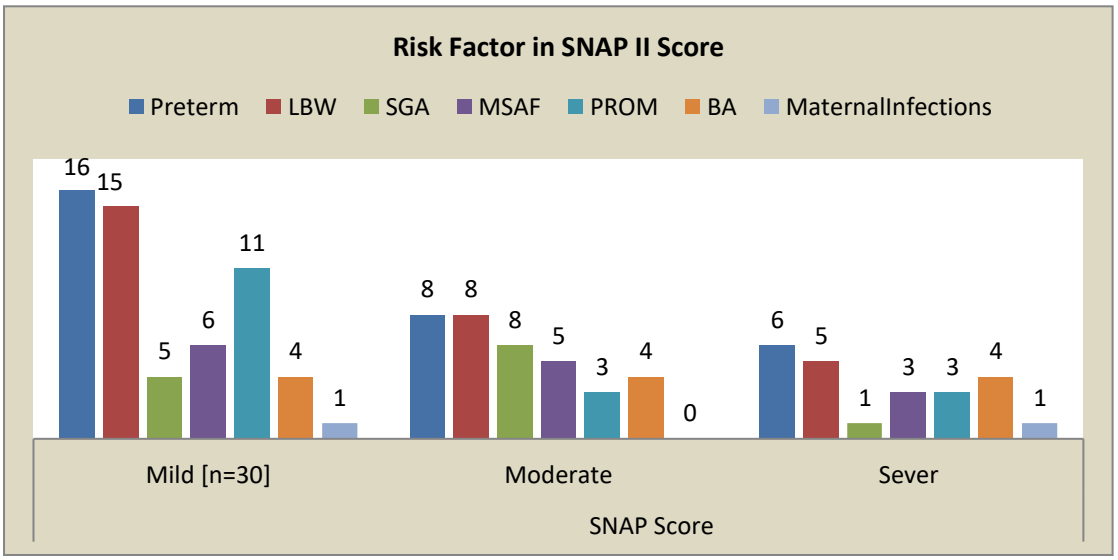
The above Table 11 and figure says that, there was statistically significant association between pre-maturity at birth and SNAP Score of patients[p=0.024].

Table 12: Association between Risk Factor and SNAP II Score

Risk Factor	**SNAP II Score**						**Total**		**Chi- square value&p-value**
	Mild [n=30]		Moderate [n=18]		Severe [n=12]				
	No.	%	No.	%	No.	%	No	%	
Preterm	17	56.7%	08	44.4 %	06	50.0%	31	51.7 %	X^2 = 0.356 P=0.837
LBW	15	50.0%	08	44.4 %	05	41.7%	28	46.7 %	X^2 = 0.290 P=0.865
SGA	05	16.7%	08	44.4 %	01	8.3%	14	23.3 %	X^2 = 6.74 **P=0.034**
MSAF	06	20.0%	05	27.8 %	03	25.5%	14	23.3 %	X^2= 0.917 P=0.632
PROM	11	36.7 %	03	19.5 %	03	25.5%	17	28.3 %	X^2 = 2.30 P=0.317
BA	04	13.3	04	22.2	04	33.3%	12	20.0	X^2 = 2.22 P=0.329

		%		%				%	
Maternal Infections	01	3.3%	00	00	01	8.3%	02	3.33 %	$X^2 = 1.55$ P=0.460

LBW- low birth weight, SGA- Small for gestational age , MSAF- Meconium stained amniotic fluid, PROM- premature rupture of memebrane , BA- Birth asphyxia



There was no statistically significant association between different risk factors and SNAP II Score of neonates.

Table 13: Correlation between SNAP II Score with Mean Blood Pressure, Temperature, PO2/FIO2, Lowest Serum pH

Correlation	r-value	P-value
SNAP Score vs Mean Blood Pressure	-0.297	P=0.021 S
SNAP Score vs Temperature	-0.586	P<0.0001 S
SNAP Score vs PO2/FIO2	-0.451	P<0.0001 S
SNAP Score vs Lowest Serum pH	-0.576	P<0.0001 S

There was negative correlation between SNAP II score and Mean Blood Pressure and this relationship were found to be statistically significant [p=0.021].

Also There were negative correlation between SNAP score and Temperature, **PO2/FIO2 & Lowest Serum pH**, these relationship were found to be statistically significant [p<0.0001].

Table 14: Association between Seizures and SNAP II Score

		SNAP II Score						Total		Chi-square value & p-value
		Mild		Moderate		Severe				
		No.	%	No.	%	No.	%	No.	%	
SEIZURES	Absent	30	100%	12	66.7%	05	41.7%	47	78.3%	X^2 = 19.2 P<0.0001 S
	Present	00	00	06	33.3%	07	58.3%	13	21.7%	
	Total	30	100%	18	100%	12	100%	60	100%	
Urine Output	Normal	30	100%	18	100%	11	91.7%	59	98.3%	X^2 = 3.98 P=0.142 NS
	Low	00	00	00	00	01	8.3%	01	1.7%	
	Total	30	100%	18	100%	12	100%	60	100%	

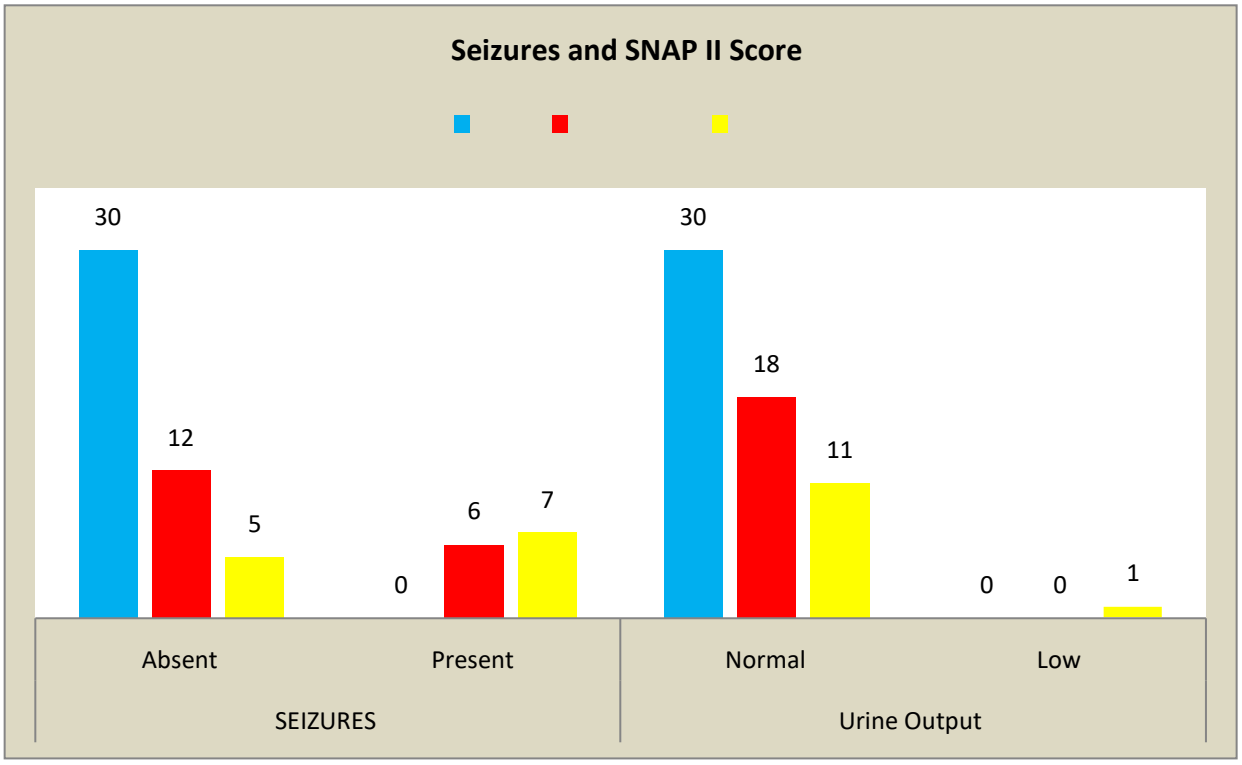
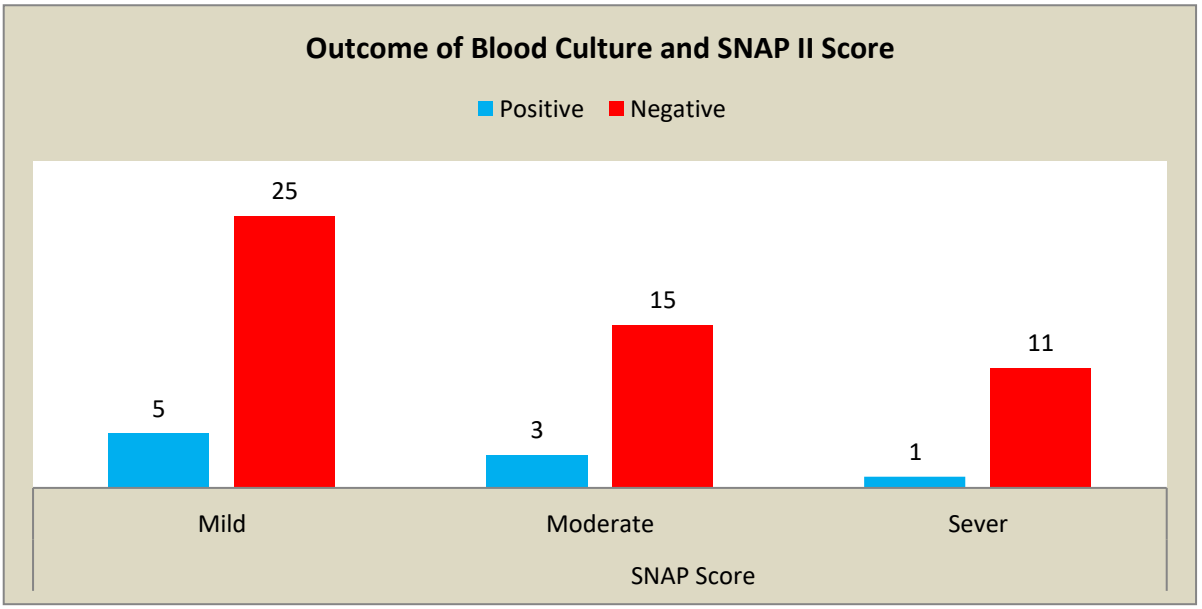


Table 14 shows that, out of 60 neonates, **Seizures** were present in 13(21.7%) neonates and all neonates were from Moderate 06(33.3%) and severe category 07(58.3%). There was statistically significant association between Seizures and SNAP II Score [p<0.0001]. Only one neonates, had a low urine output, there was no statistically significant association between Urine outcome and SNAP II Score[p=0.142].

Table 15: Association between outcome of Blood Culture and SNAP II Score

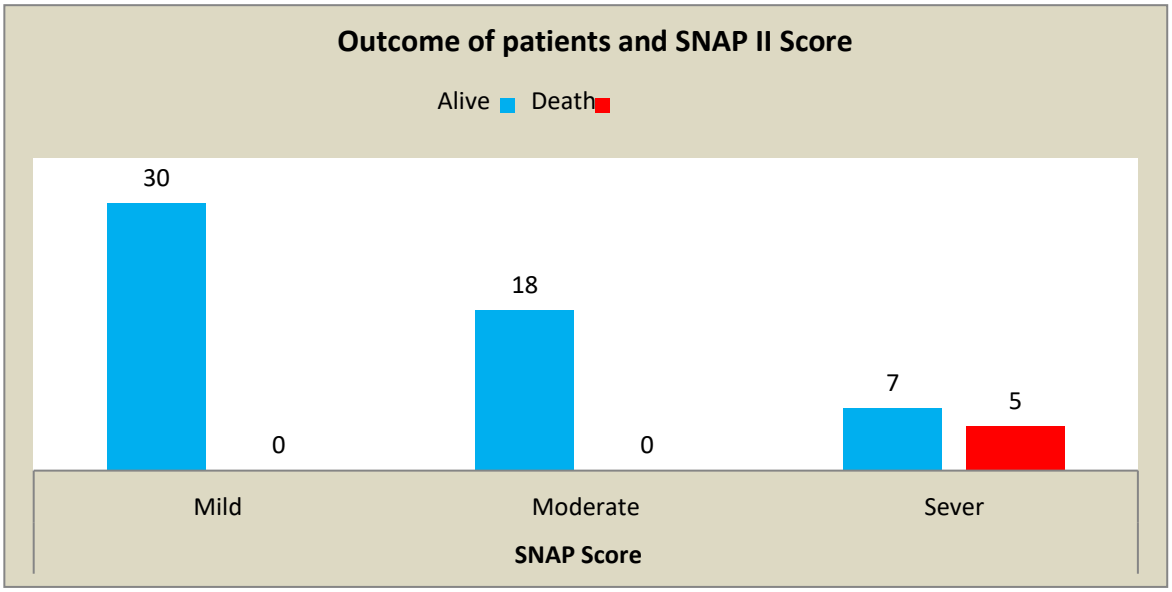
Blood Culture	SNAP II Score						Total		Chi-square value &p-value
	Mild		Moderate		Severe				
	No.	%	No.	%	No.	%	No.	%	
Positive	05	16.7%	03	20.0%	01	8.3%	09	17.6%	$X^2 = 0.523$ P=0.770
Negative	25	83.3%	15	80.0%	11	91.7%	51	82.4%	
Total	30	100%	18	100%	12	100%	60	100%	



As per above Table 15, out of 60 neonates, 09(17.6%) neonates had blood culture positive and there was no statistically significant association between outcome of Blood Culture and SNAP II Score [p=0.770].

Table 16: Association between outcome of patients and SNAP II Score

OUTCOME OF PATIENTS	SNAP II Score						Total		Chi-square value&p-value
	Mild		Moderate		Severe				
	No.	%	No.	%	No.	%	No.	%	
Alive	30	100%	18	100%	07	58.3%	55	91.7%	$X^2 = 48.3$ P<0.0001
Death	00	00	00	00	05	41.7%	05	8.3%	
Total	30	100%	18	100%	12	100%	60	100%	



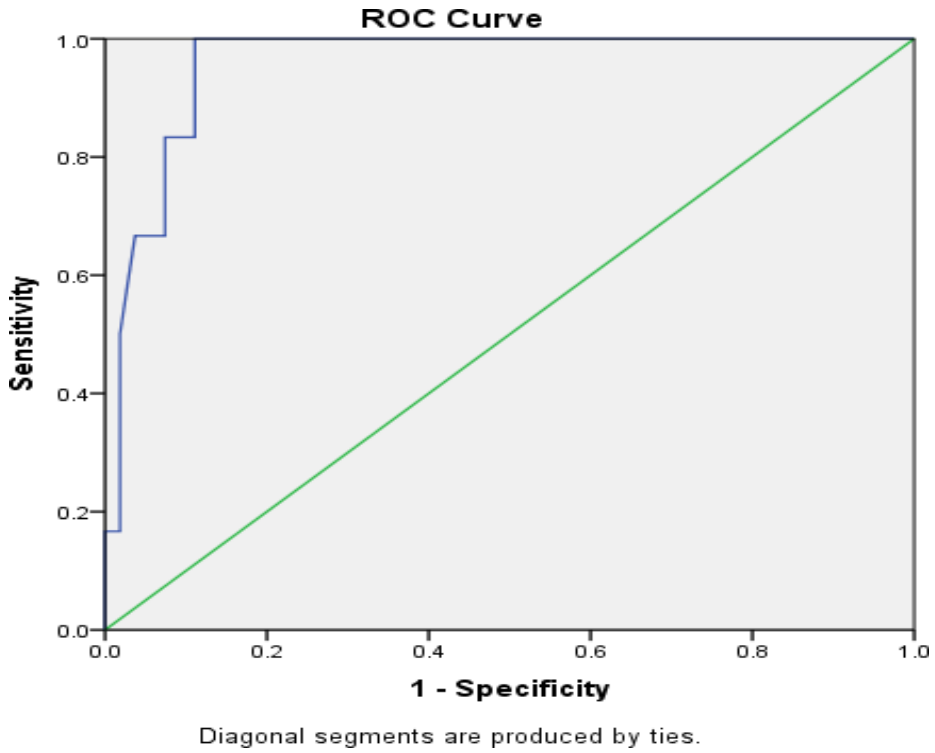
All the 05 death of neonates were having SNAP II score in sever category [i.e.>40 score] so there was statistically significant association between final outcome of neonates and SNAP II Score.

Table 17: Sensitivity & Specificity of SNAP II with the outcome of patients

SNAP Score	Outcome		Total
	Death	Alive	
>40 Score	05	07	12
≤40 score	00	48	48
Total	05	55	60

Statistic	Formula	Value	95% CI
Sensitivity	$\frac{a}{a+b}$	100.00%	47.82% to 100.00%
Specificity	$\frac{d}{c+d}$	87.27 %	75.52% to 94.73%
Positive Predictive Value	$\frac{a}{a+c}$	41.67% (*)	26.34% to 58.80%
Negative Predictive Value	$\frac{d}{b+d}$	100.00 % (*)	
Accuracy	$\frac{a+d}{a+b+c+d}$	88.33% (*)	77.43% to 95.18%

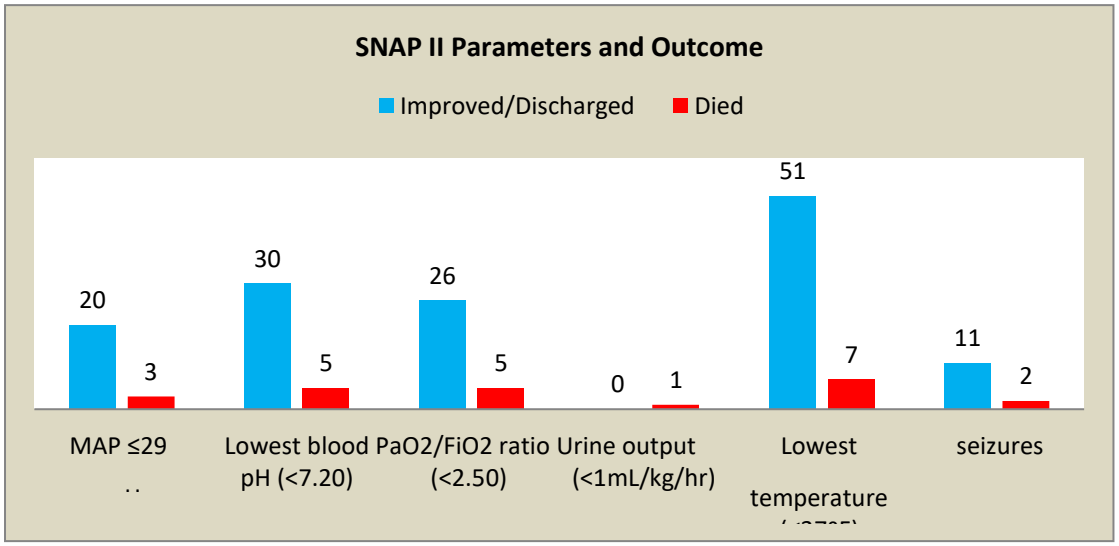
ROC curve for SNAP as a predictor of death in neonates with sepsis



The area under the (ROC) curve for SNAP II and death was 0.926 (95% CI 0.781- 0.962), as shown in above figure.

Table 18: SNAP II Parameters andOutcome

Parameters	Improved /Discharged [n=55]	Died [n=05]	Total	X2value	p-value
MAP ≤29 mmHg	20	03	23	1.08	P=0.298
Lowest blood pH (<7.20)	30	05	35	3.14	**P=0.042**
PaO2/FiO2 ratio (<2.50)	26	05	31	4.26	**P=0.029**
Urine output(<1mL/kg/hr)	00	01	01	11.2	**P=0.001**
Lowest temperature (≤37^{0}C)	53	05	58	1.88	P=0.665
seizures	11	02	13	1.08	P=0.299



When the individual SNAP-II parameters were analyzed, it was found that

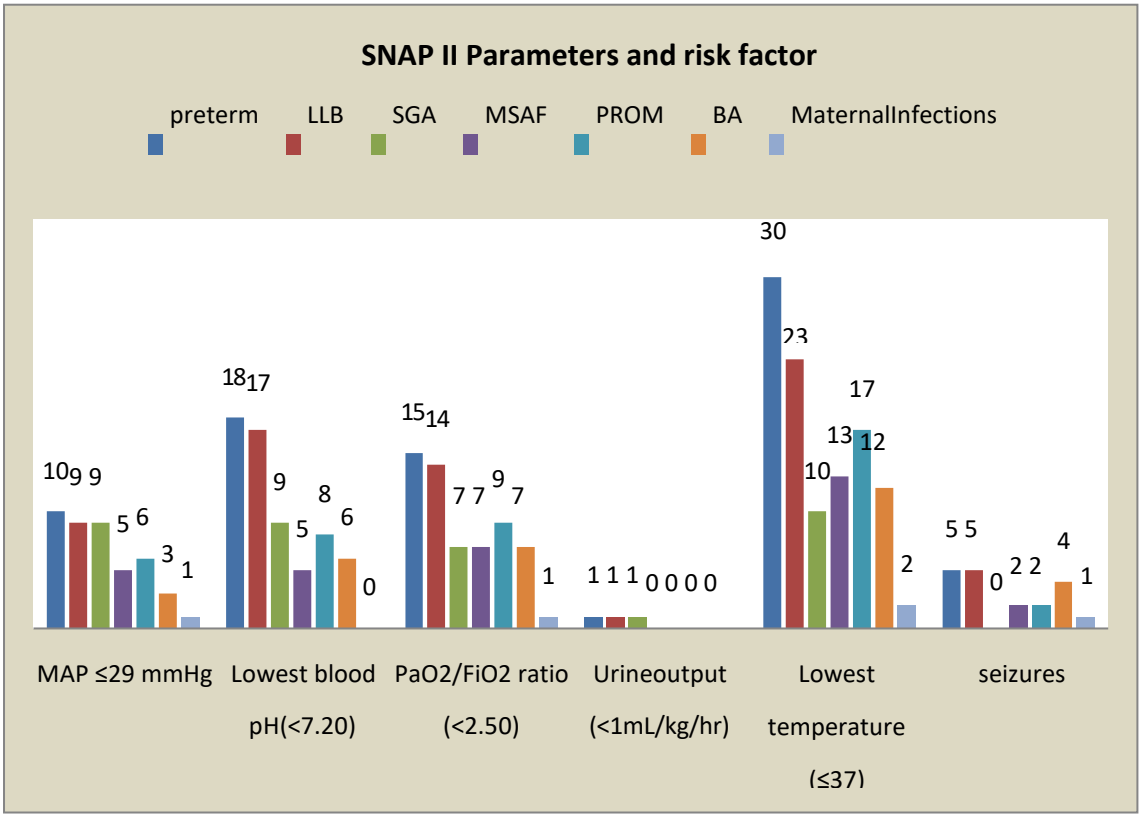
parameters related to lowest blood pH, PaO2/FiO2 ratio (<2.50) & Urine output (<1mL/kg/hr) were significantly associated with final outcome.

Table 19: SNAP II Parameters and risk factor

Parameters	Preterm [n=31]	LLB [n=28]	SGA [n=11]	MSAF [n=14]	PROM[n=17]	BA [12]	Maternal Infections [n=2]
MAP ≤29 mmHg	10 (32.2%)	09 (32.1%)	09 (81.8%)	05 (35.7%)	06 (35.3%)	03 (25.0%)	01 (50.0%)
Lowest blood pH(<7.20)	18 (58.1%)	17 (60.7%)	09 (81.8%)	05 (35.7%)	08 (47.1%)	06 (50.0%)	00
PaO2/FiO2 ratio (<2.50)	15 (48.4%)	14 (50.0%)	07 (63.6%)	07 (50.0%)	09 (52.9%)	07 (58.3%)	01 (50.0%)
Urine output (<1mL/kg/hr)	01 (3.2%)	01 (3.6%)	01 (9.1%)	00	00	00	00
Lowest temperature (≤37)	30 (96.7%)	23 (82.1%)	10 (90.9%)	13 (92.8%)	17 (100%)	12 (100%)	02 (100%)
Seizures	05 (16.1%)	05 (17.9%)	00	02 (14.3%)	02 (11.8%)	04 (33.3%)	01 (50.0%)

In all risk factors, majority of neonates were having lowest temperature (≤37). In pre- term neonates 18 (58.1%) were having lowest blood pH (<7.20). In

LLB 17(60.7%) neonates were having lowest blood pH (<7.20). In maximum SGA neonates were having MAP≤29mmHg, lowest blood PH, PaO2/FiO2 ratio (<2.50) SNAP II Parameter.


SNAP II Parameters and risk factor
preterm
LLB
SGA
MSAF
PROM
BA
MaternalInfections
10 9 9 5 6 3 1
18 17 9 5 8 6 0
15 14 7 7 9 7 1
1 1 1 0 0 0 0
30 23 10 13 17 12 2
5 5 0 2 2 4 1
MAP ≤29 mmHg
Lowest blood pH(<7.20)
PaO2/FiO2 ratio (<2.50)
Urineoutput (<1mL/kg/hr)
Lowest temperature (≤37)
seizures

DISCUSSION

DISCUSSION

This present study was carried out on neonates where SNAP-II had been applied to neonates with septicemia to predict mortality. Like other illness severity scores, SNAP II was originally developed to predict the risk of dying [25] at admission to NICU. Most previous studies have applied SNAP II to assess the illness severity within the first 12 hours after admission in the NICU[36,37].

In the present study, 60 neonate have been studied, out of these 29(48.3%) were male and 31(51.7%) were female. Whereas study conducted by **VenkataseshanSundaram et al [30]** found maximum were males. **NahedFahmyHelal et** al [38] conducted on 80 neonates of septicemia out of which 43(53.8%) neonates were male and 37 (46.3%) were females.

In 31 preterm neonates, 11 (35.5%) neonates were SGA and 20 (64.5%) were AGA and Out of 29 term neonates, 03(10.3%) neonates were SGA and 26(89.7%) were AGA. Similar observations were noted by **VenkataseshanSundaram et al [30]** i. e. out of 40 neonates, 28(70.0%) were AGA and 12(30.0%) wereSGA.

The incidence and microbiology of neonatal sepsis varies worldwide. Blood culture has been regarded as the gold standard for the confirmation of sepsis. Reports from all over world show the isolation rates on blood culture to vary from 6.7% to 55.4% **[41,42].** In present study Blood culture was positive in 09 (15.0%) neonates. Whereas **VenkataseshanSundaram et al [30]** observed comparatively more Blood culture positive neonates i.e. 33 (82.5%) and Blood culture was positive in 23 (28.75%) neonates reported by **NahedFahmyHelal**

et al [38] also **Shashi Gandhi et al [39]** reported 32% of blood culture positive cases. The discrepancy in percentage of culture positive neonates in this study as compared to those done previously is mostly because most of the neonates admitted in our tertiary health care had been referred from outside hospitals after having received antibiotics.

All culture negative subjects had a positive sepsis screen. The most common causative organisms were Staph aureus 03(5.0%) and Klebsiella pneumonea 03(5.0%). Whereas **NahedFahmyHelal et** al [38] reported most common causative organism as coagulase negative Staphylococci(10%).

The risk factors in neonates were: 31 (51.7%) neonates presented with preterm, 28(46.7%) neonates with Low birth weight, 17(28.3%) with PROM, and 02(3.33%) with confirmed maternal infections.

In present study, Out of 60 neonates, Majority of the neonates, 30(50.0%) had Mild SNAP II Score, 18(30.0%) neonates were moderate and 12(20.0%) of the neonates had severe SNAP II. Similar findings was noted by **NahedFahmyHelal et** al [38] i.e. Forty six (57.7%) neonates had mild illness [SNAP II=1-20], 22 (27.5%) had moderate illness [SNAP II=21-40] and 12(14.8%) had severe illness [SNAP II>40] and study conducted by **VenkataseshanSundaram et al [30]** found 35% of the study subjects had moderate illness (SNAP II=21-40) and 40% had severe illness (SNAP II>40).

All the 05 deaths in neonates had SNAP II score in severe category [i.e.>40 score], so there was statistically significant association between final outcome of neonates and SNAP II Score. The present study also noted that the median SNAP II was significantly higher in the babies who died versus those who survived. **Maiya, etal.**

[40]have reported the mean SNAP-II inbabieswhosurvivedversuswhodiedas4.88

vs 17.38 (P<0.001).

Out of 30 mild SNAP Score patients, maximum 17(56.67%) patients were admitted for 8-15 days in Hospitals. Of the 12 severe SNAP-II Score patients ,majority of the patients 08(66.7%) were admitted for more than 15 days in the Hospital. There was statistically significant association between Duration of Stay in Hospital and SNAP-II Score [p=0.043].

There was no statistically significant association between different risk factors [i.e. pre-term, LBW etc] and SNAP-II Score of neonates.

There was statistically significant association between pre-maturity at birth and SNAP-II Score of patients [p=0.024].

There was negative correlation between SNAP II score and Mean Blood Pressure and this relationship were found to be statistically significant [p=0.021]. Also There were negative correlation between SNAP-II score and Temperature,**PO2/FIO2 & Lowest Serum pH**, these relationship were found to be statistically significant [p<0.0001].

There was statistically significant association between Seizures and SNAP II Score [p<0.0001] and there was no statistically significant association between Urine outcome and SNAP II Score [p=0.142].

Present study reported there was no statistically significant association between outcome of Blood Culture and SNAP-II Score [p=0.770].

In present study, When the individual SNAP-II parameters were analyzed, it was found that parameters related to lowest blood pH, PaO2/FiO2 ratio (<2.50) & Urine output (<1mL/kg/hr) were significantly associated with final

outcome. 35 neonates had a lowest blood pH (<7.20) of which 30 survived and 5 died during the study (p= 0.042). 31 neonates had PaO2/FiO2 ratio (<2.50) of which 26 neonates survived while 5 died during the study (0.029). One neonate who had a urine output of <1ml/kg/hr died during the study(p=0.001).

MAP ≤ 29 mmHg, lowest temperature (≤37ºF) & seizures were not significantly associated with final outcome. 23 neonates had a MAP ≤ 29 mmHg of which 20 were discharged and 3 died during the study. 58 neonates had a low core temperature of which 53 survived while 5 died during the study. Multiple seizures were observed more commonly in babies who died but did not attain statistical significance. These results indicate that individual parameters of the SNAP II did not contribute equally to the risk of death.

In the study conducted by, **NahedFahmyHelal et** al [38] found that respiratory system was the most frequently system involved at enrollment followed by the hematologic system then the cardiovascular system and when the individual SNAP II parameters were analyzed, it was found that parameters related to circulatory instability like low mean arterial pressure and lowest blood pH were significantly associated with death as well as organ dysfunction at day 14, P= 0.002. Also hypoxemia was significantly observed in babies with persistent OD and who died vs. those who survived, P<0.001. These results indicate that individual parameters of the SNAP II did not contribute equally to the risk of death.

Each parameter of SNAP II was derived by assigning weighted points based on the relative risk of mortality conferred by the presence of that parameter **[4].** Evaluated the individual parameters of the score as they may not

contribute equally to the risk prediction **[40].**

When we constructed ROC curves for the SNAP II, they showed moderate predictive accuracy. The area under the (ROC) curve was 0.926 (95% CI 0.781-0.962) with sensitivity (100%) and specificity was 87.27% for death. Similar results was found by **Sundaram et al. study [30]** the area under the (ROC) curve for SNAP II curve for death was 0.82 (95% CI 0.68-0.95, P<0.001) and **NahedFahmyHelal et** al [38] found that ROC curves for the SNAP II score ≥ 40, they showed moderate predictive accuracy. The area under the (ROC) curve was 0.829 with sensitivity (90.4%) for OD and was 0.699 with sensitivity (88.9%) for death.

SUMMARY
&
CONCLUSION

SUMMARY

The overriding aim of the present study was **Evaluation of Score for Neonatal Acute Physiology II (SNAP II) as a Predictor of Mortality in Neonates Hospitalised with Septicaemia"**

Objectives:

1) To study the relationship between score for neonatal acute physiology II (SNAP II) (applied within 12 hours from the onset of sepsis) and death.
2) To determine the contribution of the individual parameters of SNAP II score to the risk of Death.

In view of the above objectives, descriptive and inferential statistic was used. The study was conducted during 1st Oct 2018 to 1st Oct. 2020 in Department of pediatrics MIMSR Medical College, Latur [MS]. The population for this study includes proven neonates of Septicemia, who satisfied inclusion and exclusion criteria of the study. Approval for the study was obtained from the Institutional Ethical Committee of MIMSR Medical College, Latur [MS].

Signs and symptoms of clinical sepsis (as per NNF guidelines) were screened after thorough clinical examination and history taking. Also any predisposing factors for septicemia making it presume to be early onset sepsis (according to NNF criteria) was considered while inclusion of cases.

All neonates diagnosed to have septicemia (defined as clinical signs and either blood culture or sepsis screen positive or radiological evidence of pneumonia) with evidence of SIRS were eligible for enrollment.

Sepsis screen consists of C reactive protein (CRP), Micro erythrocyte sedimentation rate (m ESR), Total leukocyte count (TLC), Absolute neutrophil count (ANC) and Immature to total ratio (ITR). It was considered positive if any two or more out of these five are abnormal.

SNAP II was applied on all the enrolled neonates. This score consists of 6 physiological parameters, namely lowest mean arterial pressure (MAP), worst ratio of partial pressure of oxygen (PaO2) to fraction of inspired oxygen (FiO2), lowest temperature (in ºF), lowest serum pH, occurrence of multiple seizures, and urine output(<1mL/kg/hr).

The data collection window was the first 12 hours from the onset of septicemia, during which period the above parameters were recorded prospectively.

Weighted scores were given based on the presence or absence of each parameter. Severity of the illness was arbitrarily graded according to the SNAP II score as follows: Mild: 1-20, Moderate: 21-40, and Severe: >40. All subjects had followed up until death or recovery, up to a maximum of 14 days.

In the present study, 60 neonate have been studied, out of these 29(48.3%) were male and 31(51.7%) were female. In 31 preterm patients, 14 (35.5%) patients were SGA and 20(64.5%) were AGA patients and Out of 29 term patients, 03(10.3%) patients were SGA and 26(89.7%) were AGA patients.

Blood culture was positive in 09 (15.0%) neonates. All culture negative subjects had a positive sepsis screen. The most common causative organisms were Staph aureus 03(5.0%) and Klebsiella pneumonea 03(5.0%).

The risk factors in neonatal were as: 31 (51.7%) neonates presented with preterm, 28(46.7%) neonates with Low birth weight, 17(28.3%) with PROM, and 02(3.33%) were confirmed maternal infections.

Out of 60 patients, Majority of the patients, 30(50.0%) had Mild SNAP II Score, 18(30.0%) patients were moderate and 12(20.0%) of patients were having severe SNAP Score.

Out of 30 mild SNAP-II Score patients, maximum 17(56.67%) patients were admitted for 8-15 days in Hospitals. Of the 12 severe SNAP II Score patients, majority of the patients 08(66.7%) were admitted for more than 15 days in the Hospital. There was statistically significant association between Duration of Stay in Hospital and SNAP-II Score [p=0.043].

There was not statistical significant association between different risk factors of sepsis [i.e. Preterm, LBW etc.] and SNAP-II Score of neonates.

There was negative correlation between SNAP II score and Mean Blood Pressure and this relationship were found to be statistically significant [p=0.021]. Also There were negative correlation between SNAP-II score and Temperature,**PO2/FIO2 & Lowest Serum pH**, these relationship were found to be statistically significant [p<0.0001].

There was statistically significant association between Seizures and SNAP II Score [p<0.0001]. Only one neonates, had a low urine output, there was no statistically significant association between Urine outcome and SNAP II Score [p=0.142].

Out of 60 neonates, 09(17.6%) neonates had blood culture positive and there was no statistically significant association between outcome of Blood Culture and SNAP Score [p=0.770].

In present study, When the individual SNAP-II parameters were analyzed, it was found that parameters related to lowest blood pH, PaO2/FiO2 ratio (<2.50) & Urine output (<1mL/kg/hr) were significantly associated with final outcome. Lowest temperature (≤37ºF), seizures were not significantly

associated with final outcome. Multiple seizures were observed more commonly in babies who died but did not attain statistical significance. These results indicate that individual parameters of the SNAP II did not contribute equally to the risk of death.

The Sensitivity of SNAP II score with the outcome of patients was 100% & Specificity was 87.27%. The positive predictive value of SNAPII score was 41.67% and negative predictive value was 100%. Whereas accuracy of SNAP II score was 88.33%. The area under the (ROC) curve for SNAP II and death was 0.926 (95% CI 0.781-0.962).

Forms this study we conclude that neonates with septicemia, with high SNAP II scores, have significantly higher risk of dying. SNAP II ≥ 40 can predict death with moderate predictive accuracy when applied on admission to neonates with sepsis. These results indicate that individual parameters of the SNAP II did not contribute equally to the risk of death. So it is recommended that SNAP II is applied to all neonates with septicemia and monitoring of the serial scores should be done so as to evaluate the progress of illness.

CONCLUSION

This study concludes that neonates with septicemia having high SNAP II scores had significantly higher risk of dying. SNAP II ≥ 40 can predict death with moderate predictive accuracy when applied to neonates with sepsis. SNAP II score had 100% sensitivity over outcome of neonates. There was no statistically significant association between different risk factors of sepsis and SNAP II Score of neonates. The neonates with higher SNAP II scores were observed to have prolonged duration of stay in hospital. When the individual SNAP-II parameters were analyzed, it was found that parameters related to lowest blood pH, PaO2/FiO2 ratio (<2.50) & Urine output (<1mL/kg/hr) were significantly associated with final outcome. But the lowest temperature (≤37ºF) & seizures were not significantly associated with final outcome. Multiple seizures were observed more commonly in babies who died but did not attain statistical significance. These results indicate that individual parameters do not equally contribute to the risk of death. But when used in combination as SNAP II, they contribute to the risk of fatal outcome thereby improving the predictive accuracy of the score in assessment of risk of death. SNAP II score is cost effective and a simple test that does not require any special investigation. A limitation of this study is the small sample size with limited number of neonates. The score was applied to only 60 patients with neonatal sepsis associated with different primary diagnoses and different severity stages of sepsis. We suggest further studies in this direction in Indian setup with larger sample size so as to further explore the role of SNAP II in predicting risk of mortality in neonates with neonatal sepsis. We conclude that it can be used as a screening tool in identifying high risk neonates / neonates at risk of dying within 12 hours of onset of neonatal

sepsis/hospitalizationso that more aggressive therapy can be initiated in the management of sick neonates and thereby improve the outcome.

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ANNEXURES

Consent form

:- **संमतीपत्र**

संमतीपत्रदेणाऱ्याचेनाव:

मीखालीलसहीकरणार, संमतीपत्रललखखतदेतो/देतेकी, मी_____

_____

“EVALUATION OF SCORE FOR NEONATAL ACUTE PHYSIOLOGY II (SNAP II) AS A PREDICTOR OF MORTALITY IN NEONATES HOSPITALISED WITH SEPTICEMIA

.”**यावैद्यकीयशोधप्रबंधातमीस्वतःच्यामर्जीनेकोणत्याहीदबावाखालीनयेतासहभागी होतआहे**.

सदरीलवैद्यकीयपरीक्षणाचेउलिष्टवस्वरूपतसेचत्यामुळे माझ्याआरोग्यावरहोणाऱ्या सववपररणामबिलमलाकल्पनादेण्यातआलीआहे.

मलासदरीलवैद्यकीयपरीक्षणातूनकोणत्याहीक्षणीबाहेरपडण्याचीपरवानगीदेण्यात आलेलीआहे.

परीक्षकाचीसही:संमतीपत्रदेणाऱ्याचीसही

: **लिकाण**: **लिकाण**

: **तारीख**: **तारीख**

ANNEXURE I

PROFORMA
(CASE RECORD FORM)

CLINICAL PROFILE OF PATIENTS WITH NEONATAL SEPSIS
Case No._____

Name		OPD No.	
Age		IPD No.	
Address		DoA	
		Time of Adm	
		DoD / DoE	
Sex			
Maturity			
Birth weight			

RISK FACTORS FOR SEPSIS:

Premature rupture of membrane (PROM)	YES	NO
Meconium stained amniotic fluid (MSAF)	YES	NO
Foul smelling liquor	YES	NO
Low birth weight	YES	NO
Prematurity	YES	NO
Low Apgar score at birth	YES	NO

CLINICAL FEATURES :

CENTRAL NERVOUS SYSYTEM

CONVULSIONS	YES	NO	NOT ABLE TO FEED	YES	NO
BULGING FONTENALLE	YES	NO	NOT ABLE TO SUCK AT ALL	YES	NO
PUS DISCHARGE FROM EAR	YES	NO	ABNORMAL MOROS	YES	NO
LETHARGY OR UNCONCIOUSNESS	YES	NO	REDUCED MOVEMENTS	YES	NO

RESPIRATORY SYSSTEM:

INCREASED RATE OF BREATHING	YES	NO	GRUNTING	YES	NO
CHEST INDRAWING	YES	NO	CREPITATIONS	YES	NO
NASAL FLARING	YES	NO	CYANOSIS	YES	NO

CARDIOVASCULAR SYSTEM

REDUCED CAPILLARY REFILL	YES	NO		YES	NO

GASTROINTESRINAL SYSTEM:

Neoanatal Hyperbilirubinemia	YES	NO		YES	NO
Diarrhoea	YES	NO		YES	NO
Abdominal distension	YES	NO		YES	NO
Feed Intolerance	YES	NO		YES	NO
Vomiting	YES	NO		YES	NO

HEMATOLOGICAL SYSTEM:

Bleeding:	YES	NO	Petechiae :	YES	NO	Purpura	YES	NO

SKIN SIGNS :					
REDNESS AROUND THE UMBILICUS	YES	NO	MOTTLING	YES	NO
DISCHARGE FROM UMBBLICCUS	YES	NO			
PUSTULES :	YES	NO	(IF YES)Numb Of Pustules:		
TEMP> 37.7 OR LESS THAN 35.5	YES	NO			

OTHER CLINICAL FINDINGS:

EXAMINATION FINDINGS

ANTHROPOMETRY:

Weight		Head Circumference	
Length		Chest Circumference	
Pondral Index		Anterior Fontanel	

VITALS:			
Pulse Rate		CRT	
PP			
Resp Rate			
BP			

MARKERS OF SEPSIS			
Total leukocyte count		m-ESR	
I/T ratio (band cell ratio)		C reactive protein	
Absolute neutrophil count			
Blood culture			
Urine Culture			
CSF Culture			
OTHER INVESTIGATIONS			
DIAGNOSIS			
STAY			
Treated with Antibioitics : i) ii) iii) iv)		Blood Transfusions given: Yes/No	
On O2 support	Yes	No	
OUTCOME			

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	
BLOOD PRESSURE								
TEMPERATURE								
PO2								
FiO2								
Serum Ph								
Seizures								
Urine Output								

VARIABLES	VALUES	POINTS
Mean blood pressure	≥ 30 mmHg	0
	20-29 mmHg	9
	<20 mmHg	19
Temperature	>35.6°C	0
	35 - 35.6°C	8
	<35°C	15
PO_2 (mmHg) / FiO_2 (%)	>2.49	0
	1.0-2.49	5
	0.3-0.99	16
	<0.3	28
Lowest serum pH	≥ 7.2	0
	7.1-7.19	7
	<7.1	16
Multiple seizures	No	0
	Yes	19
Urine output(ml/kg/h)	≥ 1	0
	0.1-0.9	5
	<0.1	18

SNAP
Mild 1-20
Moderate 21-40
Severe: >40

Thank You