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Paediatrics

STUDY OF RISK FACTORS IN EARLY ONSET NEONATAL SEPSIS

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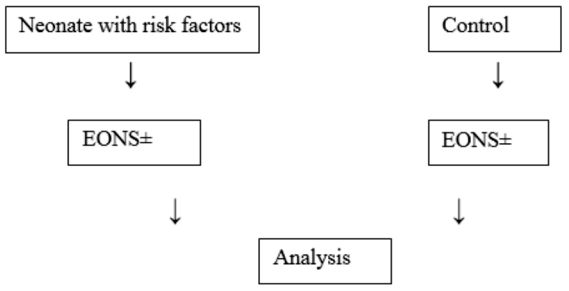
ABSTRACT **Introduction:** Neonatal sepsis is one of the major causes of morbidity and mortality in newborn. Early onset neonatal sepsis (EONS) is a severe disease and has high mortality rate. The clinical signs of EONS are nonspecific and the confirmation of diagnosis may consume time. Therefore, the diagnostic approach is necessary by considering the risk factors. **Objective:** The aims of this study are to identify the risk factors of newborn infants for early onset sepsis Methods: This is a cohort retrospective study, conducted over year from July 2016 to June 2017 at neonatology department SDM college of Medical sciences and Hospital Dharwad. The sample population included newborn infants whose mother had risk factors of sepsis. The information of the risk factors from neonate and diagnoses of EONS was obtained from their medical record. There were 262 samples: 232 cases of EONS and 30 of control. Results: The results of analysis revealed 3 risk factors from mother maternal fever, foul smelling liquor, PROM >18hour and 3 risk factors from infant which were associated to EONS: APGAR score <7 at one minute Gestational <37 weeks and birth weight <1500 grams **Conclusion:** Based on this study, we concluded that the risk factors of EOS maternal fever foul smelling liquor, PROM >18 hours, low APGAR score, gestational age <37 weeks and very low birth weight and were helpful in the early management of sepsis.

KEYWORDS : Early Onset Neonatal Sepsis, Risk Factors, neonate

Introduction

Neonatal mortality (NM) until nowadays is still the highest mortality in human life. It has a close relation to infant mortality rate (IMR), which used as the indicator of health development in countries.1 In 2009, WHO reported that there is 3.3 million of neonatal mortality from 6 million of infant mortality.2 Neonatal sepsis accounts for 33% of neonatal mortality in developing countries.3 Neonatal sepsis is a clinical syndrome occurs because of invasion of microorganism into the blood in the first month of life.4 Basically, the fetuses were still wrapped by layers of amnion adequately shielded from bacterial flora's mother because of the cervical plug, which is the placenta barrier and antimicrobial proteins and peptides in it.5, 6 Even though the probably of microorganism contamination can occurs by a several ways, such as transplacental, or ascending infection from cervical or by the birth canal during the birth process.7 On exposed, the babies are shaping the immune response to maintain their body from the infection.8 Several factors of mother, babies, and environment are contribute to the infection exposed and non optimal of NM immunologic response so as the newborn become susceptible to be infection.9 There is a dilemma on the sepsis management, that if there is a delay of treatment will increase the mortality rate of over 50%. If not be therapy while the over diagnosis happens, due to the non particular of clinical illustration will make the over treatment and harm the patient and his/her family. Hence, the clinic decision by the clinicians against the newborn that is apparently healthy or with a minimal of sepsis symptom. Furthermore, even asymptomatic bacteraemia can be done accuracy and faster with a risk factor consideration considering of several support examine to confirm the diagnosis need a lot of time.10 This study aims to identification the risk factors from the mother and neonate which predispose to development of EONS.

2. Materials and Methods: Figure 1. Flow diagram for study



An observational retrospective cohort study was conducted at our neonatology department over one year period to assess the incidence and identification of the neonatal risk factors relation to the EONS by using a data from patient's medical records. Newborn, aged under or of 3 days birth consecutively recruited. Written informed consent was obtained from the patients' parents or legal guardian following full and detail explanation regarding the study's protocol. Study samples are from all the affordable population that met the inclusion and exclusion criteria. The inclusion criteria are all the newborn from the mother with risk factor treated at SDMH and age under or of 3 days. While, the exclusion criteria are the newborn with congenital abnormalities, birth from the mother with TORCH infection and the patient with incomplete data. Controls were full term newborn with no risk factors. The ways of taking sample is from the patient medical records related to the study. Then it is grouped into two group of neonatal with early onset neonatal sepsis (EONS) and non EONS, and recording of infant infection risk factors. All the data obtained are noted in the study data form, then grouped based on the objectives and types of data. Then, the data is analyzed to assess the relationship of the infection risk factor of the infant with EONS.

Table 1 shows the characteristics of study sample.

Number	Sample characteristics	Percentage (%)
1	Sex: Male Female	56% 46%
2	Maternal fever≥38C Maternal fever <38C	11% 88%
3	PROM≥18hours PROM<18hours	27% 73%
4	Meconium stained liquor No meconium stained liquor	15% 85%
5	Apgar score <7 at one minute Apgar score >7 at one minute	31% 69%
6	Gestational age <37weeks	33%
7	Birth weight <1500 grams	35%

Total of the study samples with EONS was 232, with 130 (56%) male and 102 (46%) female while no EONS reported from control. There are 11.0% neonates with the maternal fever ± foul smelling liquor while PROM >18 hour was noted in 27%. There are 15% neonates with the meconium stained amniotic fluid (MSAF), while rest of them 85% are not. Neonatal sepsis occurring in neonates with apgar score <7 at one minute was 31%, gestational age <37 weeks 33% and birth weight <1500 grams 35%.

Discussion: This study obtained the EONS incidence as 28% from 232 of newborns with risk factors. This incidence is not different with the reported by Canadian Pediatrics Society, which the EONS occurrence prevalence by the mother with infection risk factor about 20%.11 Chacko and Sohi are also report the EONS incidence is 20.6% in newborn.12 Sexual dimorphism from the human immune response is quite clear; female produces the more active of cellular immune reaction and humoral so that they are more resistant to the infection.13 and our result shows there is relationships between the sex to the EONS occurring more frequently in male than female infants. The study in

India also reported that there is no significant between both of the sex with infection rate between male (2.05%) and female (2.08%).12 We also found that the Apgar score <7 at one minute has increased risk significantly with p= 0.001.Chacko and Sohi also reported the EONS occurrence on infants with Apgar score <7 at one minute increased 11.1 times significant with p= 0.001.12 Apgar score <7 in the first minute is also reported by Shah et al., have a significant with each AOR is 5.7 to the EONS occurrence.9 Even the research in America reported the EONS risk increased to 36.25 times if reach to fifth minute of Apgar score <6.14 In general, the Apgar score at the first minute associated with the Hydrogen Potential (pH) cord blood and intrapartum depression and not associate with the outcomes,

whereas the Apgar score then reflects the infants changes condition on the resuscitation performed.15 Perinatal hypoxia-ischemia can caused by several factors, but with the consistent result from the above study shows that the infant infection factor from the perinatal is one of the main factor causes of low Apgar score in the first minute.16 Our study result shows that the gestational age <37 weeks is also the risk factor with p value = 0.001. In Inggris, the infants birth <37 weeks have a risk 12.1 times (95% CI 2.7 to 53.8) obtained EONS because of GBS (group B streptococcus) compared to the term baby.17 The same case also reported from Nepal, with a risk 4.85 times EONS happens on the preterm baby.9 In Mexico reported the preterm baby have a risk of 2.19 times on EONS while on LONS (late onset neonatal sepsis) is not significant.18 This ishappens because of the preterm baby have a limited capacity in increasing the neutrophils production in order to response the infection and the neutrophils dysfunction.19 The impaired neutrophil function have reported apparent when it is <30 weeks of gestation.20 Rebuck et al., found the L-Selectin expression on newborn with >32 weeks of gestation is about 40% of adult.21 This amount is equal to the term infants. Carr et al., also reported the newborn <32 weeks have a low sFcRIII concentration and increase faster when it is 33-36 weeks of gestation.22 sFcRIII is responsible for initiating opsonization and phagocytosis.The decreased of opsonization and complement protein deficiency also occurs whereas both of it are the main component of the non specific immunity which is the first line of defense against microorganisms in neonates. It makes the newborn is susceptible to infectionand often develop into a severe infection.19 Besides, IgG transfers begin since 12 weeks of gestation and reach out the 400 mg/dl in 32 weeks of gestation.23 Bhat and Baby reported the low birth weight have a risk of EONS 10 times compared to the normal birth weight.24 Whereas according to Shah et al., the low birth weights (LBW) have a significant with Odds Ratio 4.85.9 But, Leal et al., shows LBW (≤2500 g) is not a risk factor neither to the EONS or LONS.18 In our study, low birth weight have a significant risk to the EONS occurrence (p= 0.001). This occurs because of the LBW on our samples are dominated by the birth weight 1900-2499 gram which a birth weight of the late preterm baby while the low immunity in the LBW mainly occur on the gestation <32 weeks or among the birthweight <1500 gram. It is strength by the research by Wolkowiez et al., reported there is no significant between the term baby to the late preterm with a lowest birth weight of 1920 gram to EONS (p= 0.126).25.VLBW are more common in a risk factor p value 0.001 (95% CI 1.08-22.25) to the EONS occurrence. In America, the EONS incidences have increases to 10 times higher than the VLBW.26 Benitz et al., found that the EONS risk increase along with a decrease in the birth weight.27 Physical barriers such as skin, the mucosa membrane and chemicals that are antibacterial or inhibit the adhesion of bacteria to the host began mature around 32-34 weeks of gestation and accelerated after the birth. That's why the IgA level is produces by the mucosa protection layer, lowest on the VLBW.23 Seidel et al., found the same levels of sIgA between newborn with 30 weeks of gestation (range of birth weight 1200 grams) with the term baby.28 VLBW also have the ability to decline significantly in the case of actin filament formation and neutrophils plasticity of the transmigration.23 Gahr et al., reported the interference in respiratory burst on newborn <2000 gram.29 VLBW also only had a terminal cytotoxic components value such as C3 and C3b about 10% or less of the content of his mother and difficulty in activating the complement through the lectin and alternative way. Consequently, the result is a complement dysfunction of VLBW, such as a chemotaxis function, opsonization and killed the pathogens through the membrane attack complement. In VLBW also occurs the deficiency of molecular reactants phase such as CRP, inhibitor protein, A amilod protein and several of the coagulation protein which have a function to increase the resistance to the infection.

VLBW had a lot of neutrophil in circulatory pool but it reserves in the bone marrow is only about 20% compared to the term baby and adults so that the state of sepsis occur severe neutropenia.23, 30 The strength of our study is to study the risk factor as an independent factor. The other strength of this study is the risk factor analyzed can be discovered easily by the history and physical examination so that clinicians can easily predict the EONS occurrence. We are still using medical records and may need a further study with a prospective cohort method to obtain a stronger causal relationship and to evaluate further. According to the risk factor mention above, the higher possibility of EONS if more than one risk factor present. We suggest to do some multicenter investigation to include a large sample with a better method to assess the infants risk factor relationship to the EONS.

Conclusions: Based on this study, we concluded that the risk factors of EONS were maternal fever, foul smelling liquor, PROM >18 hours, low APGAR score, gestational age <37 weeks and very low birth weight and were helpful in the early management of sepsis.

The possibility of EONS high if more than one risk factor is present. We suggest to do multicenter investigation to include a large sample with a better methods to assess the neonatal risk factor relationship to the EONS.

Competing interests and funding: none

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