ASSOCIATION OF NEONATAL BIRTH WEIGHT AND NEONATAL SEPSIS ALONG WITH PATHOGEN DISTRIBUTION IN KARACHI POPULATION

Summayya Kanwal[1], Ishrat Younus[1]*, Muhammad Liaquat Raza[2], Shagufta Nesar[1], Farzana Malik[3] and Sidra Khan[4]

[1]Department of Pharmacology, Faculty of Pharmacy, Hamdard University, Karachi.
[2]Iqra University, Karachi.
[3]Liaquat College of Nursing & allied health sciences, Karachi.
[4]Abdus Samad Hospital, Karachi
*Corresponding author: ishratyounas@gmail.com

ABSTRACT

Neonatal mortality rates are high in infants with low or very low birth weight (VLBW) as they are prone to sepsis. Early-onset sepsis (EOS) which occurs at 48hr of life remains an important cause of illness and death in VLBW infants. The objective of the study is to analyze the association between Neonatal birth weight and neonatal sepsis in the Karachi population and to study their pathogen distribution in positive isolates. A prospective cross-sectional study took place in Karachi's leading hospitals, Darul Sehat hospital and Abdus Samad hospital. Neonatal birth weight and neonatal blood culture sensitivity tests were studied for positive sepsis. Data were analyzed using SPSS applying the Chi-square test Results out of 120 neonates' blood culture sensitivity test 12 neonates had positive sepsis. The weight of 6 neonates out of 12 positive was 2.1-3kg and the other 6 neonates' weight was 3kg. 3 isolates were *Streptococcus pneumonia* and 9 were *Staphylococcus aureus*. Infants with positive sepsis are of healthy weight. Therefore, results were found to have no significant relation between neonatal birth weight and neonatal sepsis. EOS remains an uncommon yet important cause of morbidity and mortality among VLBW infants.

Keywords: Neonatal, very low birth weight (VLBW), early onset sepsis (EOS), *S. pneumonia, S. aureus.*

INTRODUCTION

2.6 million Neonatal deaths were reported by UNICEF in 2016 highlighting it as a global issue **[1-4]**. Neonatal death rate is more in developing countries than in developed countries which are 34 and 5 per 1000 live births respectively **[5, 6]**. 50% of neonatal deaths report in Asian countries

with which Pakistan contributes 10% [3, 7]. Among causes of neonatal deaths, infections predominate that is 36% [1, 7, 8]. Sepsis has the highest mortality rate reported that is 400,000/year [8-10]. The sepsis incidence rate varies on multiple factors such as race, geographical location, and advanced medical resources. Asia ranges between 7.1-38 cases of sepsis per 1000 live birth [11].

Any systemic infection that may develop in an infant within 90 days of birth is neonatal sepsis [9, 12]. An infant having sepsis within 7 days period of birth is early-onset sepsis [13, 14] usually starting within 48hrs of birth [15]. Sepsis after 7 days of birth is late-onset sepsis [9, 11, 12, 16]. EOS complications may lead to permanent hearing loss, seizures, neurological defects, and death in neonates [17]. Due to normal appearance at the time of birth EOS [6] diagnosis is questionable and often shows delayed clinical signs [14, 18] and is often recommended with empiric treatment to infants having risk factors [19, 20]. The culture/sensitivity test of blood and CSF of neonates remains the gold standard for EOS [3, 6, 19] diagnosis.

Group B *streptococcus* and *Escherichia coli* are common pathogens isolated with positive EOS [20].

However, positive EOS isolates show varying gram-positive pathogens such as *Staphylococcus aureus, Streptococcus pneumonia,* Group B *streptococci* (GBS), or *Streptococcus agalactiae* and *Escherichia coli, klebsiella pneumonia* and *Acinetobacter* are predominate gram-negative pathogen causing EOS [6, 8, 9, 17]. Early-onset sepsis is accompanied by various obstetric complications that may include premature rupture of membrane, amniotic fever, preterm labor, and low birth weight infant [16, 21]. Infants having birth weight very low are likely to have EOS therefore EOS incidence rate increases from1- 4.6 to 11-36 cases per 1000 births of infants weighing less than 1.5kgs [7, 21].

Low birth weight infants (LBW) are those having weight less than 2500g at the time of birth and weight under 1500g consider very low birth weight (VLBW) infants [22]. VLBW infants are more at risk of having sepsis which may lead to death therefore mortality rate of VLBW infants is high [23, 24]. 20% of death is reported in VLBW infants with sepsis [25].

METHOD

A cross-sectional study was designed of 6-8 months duration and took place in Darul Sehat hospital and Abdus Samad hospital of Karachi. IRB approvals were taken. Neonatal profiles were studied data filed in Performa containing gender, weight, birth route, gestational period, medical condition, and blood culture sensitivity profile. 117 live infants completing 28 weeks gestation were included in the study.

Study parameters include neonatal birth weight and blood culture/sensitivity profile of neonates with positive isolates. Two techniques were used to obtain results. Automated (BacTec) Technique and Conventional (broth) technique. Data will be analyzed by applying the chi- square test

with the help of SPSS for statistical significance. The neonatal birth weight would be the independent variable and positive/negative sepsis is the dependent variable p < 0.05 is considered significant.

Parents with proper counseling signed informed consent, confidentiality ensured with intact participant's identity and complete ethical consideration.

Data availability

Due to privacy and ethical concerns, supporting data can only be made available to bona fide researchers subject to a non-disclosure agreement. Details of the data and how to request access are available from summayya.sk@gmail.com.

RESULT

This study includes 120 neonates. During the study, their maternal history is taken and maternal factors that may be contributing to antibiotic resistance in neonates are noted. Medical history depicts 83 (69.2%) have no co-morbidity whereas 37 (30.8%) had hypertension and diabetes. Medicine history of all mothers shows intrapartum / Antepartum antibiotic administration for multiple reasons 72 (60%) urinary tract infections, upper respiratory tract infections PROM.

Vaginal discharge, and Amnionitis. Among them, 108 (89.3%) took prophylactic antibiotics due to cesarean delivery. Amoxicillin clavulanic acid, Cefixime, Cefotaxime, cefoperazone + salbactum, ceftizoxime, and ceftriaxone are antibiotics administered to them. Mothers gave birth to live infants completing 28 weeks gestation

.22 neonates were born via natural vaginal delivery rest of 112 were delivered through cesarean.

Neonatal birth weight of 120 infants are 2 (1.7%)1kg, 8 (6.6%) 1-2kg, 83 (63.6%) 2.1-3kg and 27 (22.3%) greater than 3 kg. These 120 neonates undergo blood culture sensitivity testing for positive early-onset sepsis 12 (9.9%) results with positive sepsis and 108 (89.3%) with negative sepsis. The weight of 12 neonates with positive sepsis was noted as 6 (50%) 2.1-3kg and 6 (50%) greater than 3kg ($\chi2$=6.301, p=0.098) which shows no significant relationship between positive neonatal sepsis and neonatal birth weight.
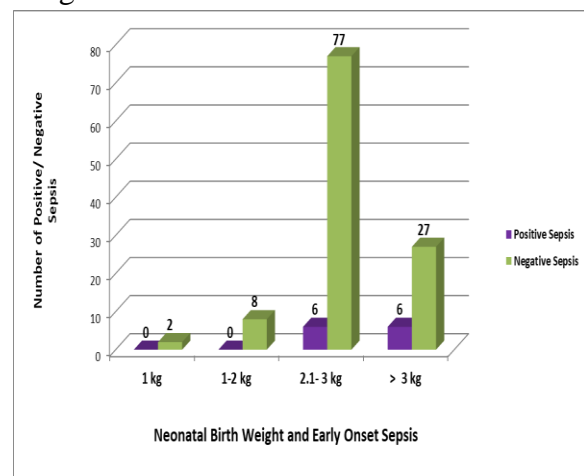

Figure 1. Birth weight of neonates born to 120 mothers and number of blood cultures positive /negative results.

In figure 1. Each bar represents the number of positive/ negative sepsis in neonates of particular birth weight with p=0.098.

In these 12 positive sepsis, 3 species isolated were *Streptococcus pneumonia* and 9 were *S. aureus*.

DISCUSSION

In this study birth weight of infants associated with neonatal sepsis was analyzed showing no significant relation. Two gram-positive pathogens were isolated staphylococcus aureus and streptococcus pneumonia. Mothers of these neonates are exposed to different types of antibiotics for their multiple intrapartum/Antepartum complications.

Studies reveal the birth weight of infants as contributing factor for EOS and found positive. EOS with ampicillin-resistant E. coli in VLBW infants [26], whereas this study couldn't conclude significant relation between neonatal birth weight with positive EOS as all infants included in the study were of healthy weight and resulted in positive EOS.

Another study reveals an inverse relationship between neonatal birth weight and neonatal sepsis. An increase in the rate of early-onset sepsis infection takes place with low-birth-weight infants. The most common species isolated were group B streptococci (GBS) in term infants and *Escherichia coli* in preterm infants [27]. On the other hand, this study's culture sensitivity results show early-onset sepsis in twelve neonates all were having healthy weights. Pathogens isolated were *Streptococcus pneumonia* and *Staphylococcus aureus*.

One more study shows *Escherichia coli* major cause of neonatal early-onset sepsis-related deaths among low-birth-weight infants and the second common cause in term infants [28]. Whereas in this study among positive sepsis no *Escherichia coli* pathogen was isolated.

Limitations

This study highlighted important aspects in identifying risk factors associated with EOS but, limited sample size, limited population, and reluctant participation from mothers to allow their infant blood culture test limit a definite conclusion. The current study recommends further multicenter prospective study with a longer duration and larger sample size and inclusion of infants of all birth weight.

CONCLUSION

Concluding low or very low birth weight neonates as a risk factor to develop sepsis draw attention to empiric treatment initiation resulting in a decreased mortality rate. Empiric Antibiotic treatment to neonates with risk of EOS decreases the mortality rate of neonates but increased the risk of developing resistance against antibiotics thus limiting their ability to fight infections and therefore complete understanding of the distribution of pathogens responsible for EOS in VLBW and LBW infants needed and antibiotic use should be rationalized.

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