

A PROSPECTIVE STUDY OF SEPSIS IN POST – OPERATIVE NEONATES

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Corresponding Author:
Dr. Puppala Santhoshi Keerthi Rao,
Email: keerthi.puppala@gmail.com

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Puppala Santhoshi Keerthi Rao¹, Krishna Rao², Rajesh Mallepalli³, Sai Bhargav Lakkakula⁴

¹Assistant Professor, Department of Paediatric Surgery, Niloufer hospital/Osmania Medical College, Hyderabad, India.

²Assistant Professor, Department of Paediatric Surgery, MR Medical College, Kalaburagi, Karnataka, India.

³Associate Professor, Department of Paediatric Surgery, Govt Medical College, Ramagundam, India

⁴Assistant Professor, Department of Paediatric Surgery, Niloufer hospital/Osmania Medical College, Hyderabad, India

ABSTRACT

Background: Neonatal surgery, the epitome of pediatric surgery, is extremely challenging and has a negligible margin of error. The surgical neonates are more prone to infection due to invasive procedures and contact to pathogenic bacteria in hospital environment. The aim and objective are although the incidence of sepsis is low in many sophisticated centers, postoperative wound infection and sepsis are, nonetheless, still the major causes of mortality and morbidity, which increase the length of hospitalization and the cost of treatment in the developing countries. **Materials and Methods:** It is a prospective study of sepsis in post-operative neonates in Department of Pediatrics Surgery, for a period of 2 years. The study subjects consisted of 75 neonates with a diagnosis of sepsis in post-operative period. Data is analyzed manually by comparing various parameters between sepsis in post-operative neonates and there post-operative clinical findings, pre and post-operative biochemical investigation, type of surgery performed, blood cultures, and pre and post-operative antibiotics used, length of hospital stay, morbidity and mortality. **Result:** Total Neonatal Surgeries are 720 out of which 89 neonatal sepsis were diagnosed (post operatively) which accounted for about 10.4% of total neonatal surgeries performed. Preterm babies are more prone for sepsis which is 66.6% and Term babies 33.4%. 49% in 75 cases who have low haemoglobin levels. Increased in WBC count in sepsis. Next important indicator is platelets counts which is (96%). There is a strong relationship between bad clinical condition of infants during first week of life and elevated plasma LDH. Hypoalbumin levels are more prone to sepsis in our 46 neonates out of 75 have hypalbuminaemia which account for (61%). 36 (48%) are discharge, deaths are 39(52%) of which Gram-positive deaths are 11(42%) gram negative deaths are 14(58%), fungal deaths are 14(56%), Gram positive discharges are 15 (58%), gram negative discharges are 10(42%), fungal discharges are 11(44%). Sepsis is more with gram negative organisms. **Conclusion:** Hypoalbuminemia was frequent among neonates with sepsis. Lower albumin levels might be associated with a poorer prognosis.

INTRODUCTION

Postoperative Neonatal sepsis is a clinical syndrome of bacteremia, which is characterized by systemic signs, and symptoms of infection AFTER 24 Hrs of Procedure.

Sepsis, induced by infection It is a syndrome of abnormalities of physiologic, pathologic, and biochemical results Neonatal surgeries, and postoperative sepsis has been a major problem.

Although the incidence of sepsis is low in many sophisticated centers, postoperative wound infection and sepsis are, nonetheless, still the major causes of mortality and morbidity, which increase the length of hospitalization and the cost of treatment in the developing countries.

Poorly developed cell-mediated and humoral immunities may increase the risk of Sepsis, which poses a major challenge in the newborn, especially in those delivered preterm, and this is compounded by the presence of surgical pathology that may

require invasive intervention, which exposes the neonate to infection. Because of this, the morbidity and mortality of postoperative sepsis have been reported to be particularly high in neonate. Sepsis remains a major challenge to the pediatric SURGEONS in the postoperative neonates.^[1]

Multiple investigations are required in a combined fashion to diagnose postoperative sepsis, which includes quantitative C-reactive protein (QCRP), WBC count, and gold standard blood culture. In order to avoid postoperative sepsis, empirical antibiotic therapy is commonly performed.

Initiation of prophylactic antibiotic(s) before the onset of sepsis has resulted in a considerable reduction in postoperative infections in neonates with excellent surgical outcomes. Thus, a fixed neonatal intensive care unit (NICU) protocol has to be made regarding the use of antibiotics in surgical NICUs. For that, an observational study of BLOOD cultures and a corresponding use of appropriate antibiotics are required, which we have taken care of during this study.^[2,3]

Despite the emergence of newer broad spectrum antibiotics, no single agent has been discovered to give equally effective coverage against all the possible infective bacteria, and this is notably so, in many developing countries, where the rarity of such a single agent requires combinations of antibiotic(s) with proven effectiveness against aerobic and anaerobic bacteria that often cause polymicrobial infections. Therefore, knowledge of adequate combinations of antibiotics that give the best outcome is important when managing surgical neonates. This makes the base for the study of combination antibiotic therapy.

In view of all these and with the availability of fulltime pediatric surgeons/ microbiologist/ neonatologist and a study was carried out in the NICU of Niloufer hospital, Hyderabad, to evaluate the profile of postoperative sepsis in neonates.

MATERIALS AND METHODS

It is a prospective study of sepsis in post-operative neonates in Department of Pediatrics Surgery, Niloufer Hospital for Women and Child Osmania Medical College, Hyderabad.

The present study was carried out for a period of 2 years from November 2019 to 2021.

subjects consisted of 75 neonates with a diagnosis of sepsis in post-operative period.

All neonates admitted in 3 surgical units in the department of pediatrics surgery were involved in this study. Written informed consent was obtained from all the neonates attenders before their enrolment in the study

The study protocol was approved by local ethical committee of this hospital

Criteria of Patient Selection

Inclusion Criteria

All neonates admitted in NICU with established diagnosis of post-operative sepsis

Exclusion Criteria

All neonates admitted in NICU who are stable post operatively

Neonates who presented to acute surgical care unit in the view of surgical emergency like neonatal intestinal obstruction, NNEC, were also excluded

Data collected prospectively and included patients demographics, operating time, post-operative complication data sheet included.

Statistical Analysis: Data is analyzed manually by comparing various parameters between sepsis in post-operative neonates and there post-operative clinical findings, pre and post-operative biochemical investigation, type of surgery performed, blood cultures, and pre and post-operative antibiotics used, length of hospital stay, morbidity and mortality.

RESULTS

There was total 75 neonates who were diagnosed with neonatal sepsis during the study period of 2 years (November 2019 -November 2021) and were included in the study. There was total 720 neonatal surgeries done during the study period. Neonatal sepsis accounted for around 10.4% of total surgical neonatal admissions.

Out of total 75 neonates with neonatal sepsis, males were 44 (67.4%) and females were 31 (32.6%). There were 66 (88%) neonates who presented in the early neonatal period (<7days) and 9 (12%) neonates who presented in the late neonatal period (7-30 days). Mean age of presentation was 4 days with a standard deviation of 6.0479, minimum age of presentation was 1 day, and maximum age was 30 days, median was 2 days. Neonatal sepsis, 29 (39%) were having normal weight (>2.5kgs), 46(61%) were having low birth weight (LBW) (<2.5kgs). Mean weight was 2.25 kgs. with a standard deviation of 0.5488, minimum weight was 1.5 kg and maximum weight was 3.5 kgs., median was 2. Preterm (<37 weeks) were 50(66.6%) and term were 25 (33.4%). There were 6(8%) anorectal malformation,35 cases, 27(36%) neonatal intestinal obstruction cases,28 1(1.33%) gastroschisis case, 6(8%) cases of Hirschsprungs disease, 13(17.33%) of Congenital diaphragmatic defects cases, 3(4%) cases of posterior urethral valves, 19(25.33%) tracheoesophageal fistula with esophageal atresia cases. Neonatal intestinal obstruction was the common indication for surgery constituting 36% of the total cases.

Out of total 75 Neonates with neonatal sepsis, sigmoid loop,35 colostomy was done in all6 cases of anorectal malformation .out of 27 cases of neonatal intestinal obstruction resection and anastomosis end to back was done in 2 cases of duodenal atresia. Sigmoid loop colostomy was done in 2 cases, end

ileostomy was done in 2 cases, redo santullis procedure was done in one case, lads procedure was done in 9 cases of malrotation, levelling colostomy was done in 6 cases of HD diaphragmatic plication was done in 1 case, CDE was done in 1 case, cystoscopic fulguration was done in 3 cases of posterior urethra valves.

Fistula ligation with primary oesophageal anastomosis was done in 19 cases of type 3 c trachea oesophageal fistula, reduction of gastroschisis, 27 was done in one case.

Out of total 75 cases of neonatal sepsis, anastomotic leak was seen in 24 cases accounting. The onset of sepsis was within 3 days after surgery in 60 cases (80%) consistent of majority of the cases and more than 3 days after surgery is 15 cases (20%), 32% of cases, in them nonfunctioning stoma was seen in 3 cases accounted for 4%, surgical site infection was seen in 30 cases accounted for 40% of cases.

Haemoglobin was abnormal in 37 cases accounting for around 49%, Leucocytosis was seen in 83% (62) of cases, thrombocytopenia was seen in 96% of cases, LFT was abnormal in 89% (67) of cases, LDH was abnormal in 61% (46) of cases, CRP was raised in 100% of cases (7%), procalcitonin was raised in 94% (71) of cases, hypoalbuminemia was seen in 61% (46) of cases, RFT was abnormal in 35 of cases (47%).

Out of total 75 cases of neonatal sepsis gram positive organisms were grown in 35% (26) of blood culture, gram negative organisms were grown in 32 % (24) of blood cultures.

Fungal organisms were grown in 33% (25) of blood cultures. Out of 26-gram positive organisms grown in cultures, 14 (54%) were coagulase negative staphylococcus 8 (31%) were enterococcus faecalis, 5 (15%) were staphylococcus hominis. Out of 24-gram negative organisms grown in culture, 13 (54%) were klebsiella species, 8 were pseudomonas pseudomonas species 3 (31%) were Escherichia coli. Out of 25 fungal organisms grown in culture, 16 (64%) were candida non albicans, 9 (36%).

Gram Positive Sepsis: Total: 26/75 Percent: 35%

Out of 26 cases of gram positive sepsis, 54% (24) were coagulase negative staphylococcus, 31% (8) were enterococcus faecalis, 15% (4) were staphylococcus hominis. Out of 24 cultures where coagulase negative staphylococcus was present, 9 (64%) were sensitive to vancomycin, 8 (57%) were sensitive to linezolid, 7 (50%) were sensitive to teicoplanin, remaining antibiotic found to be sensitive were trimethoprim/ sulphamethoxazole 3 (21%), gentamycin 2 (14%), amikacin 3 (21%), ciprofloxacin 3 (21%), colistin 4 (28%).

Fungal Sepsis: Total: 25/75 Percent: 33%

Out of 25 (33%) cases of fungal sepsis, candida albicans constituted 36% (9) cases, candida non albicans 64% (16) cases. candida non albicans were found to be majority.

Out of 16 (64%) cases of candida non albicans 100% (16) were sensitive to fluconazole and amphotericin B 8 (50%) cases were sensitive to voriconazole

.5 (31%) cases were sensitive to flucytosine, 2 (12%) cases were sensitive to capsosungin

Out of 9 (36%) cases of candida albicans 9 (100%) cases were sensitive to amphotericin B and fluconazole, 4 (44%) cases were sensitive to voriconazole, 3 (33%) cases were sensitive to flucytosin.

Gram Negative Sepsis: Total: 24/75 Percent: 32%

Out of 24 cases of gram negative sepsis, 54% (13) were klebsiella sp, 33% (8) were pseudomonas, 13% (3) were e coli.

Out of 13 cases of klebsiella sp. 54% (7) were sensitive for trimethoprim/sulphomethoxazole, colistin, 46% (6) were sensitive for gentamycin, 24% (3) were sensitive for tigecycline, linezolid, teicoplanin, 16% (2) were sensitive for ciprofloxacin, cefotaxim, 8% (1) were sensitive for amikacin, clindamycin.

Out of 8 cases of pseudomonas sp, 50% (4) were sensitive for ciprofloxacin, levofloxacin, 25%, 2 were sensitive for gentamycin, amikacin, linezolid, 12% (1) were sensitive for trimethoprim/sulphomethoxazole. Out of 3 cases of e coli 66% (2) were sensitive for trimethoprim/sulphomethoxazole, amikacin, teicoplanin, 1 (33%) were sensitive for gentamycin, ciprofloxacin, colistin, linezolid.

Total Mortality 39/75 Percentage: 52

Out of 75 cases of study 36 (48%) are discharge, deaths are 39 (52%)

Of which Gram positive deaths are 11 (42%) gram negative deaths are 14 (58%), fungal deaths are 14 (56%). Gram positive discharges are 15 (58%), gram negative discharges are 10 (42%), fungal discharges are 11 (44%). Sepsis is more with gram negative organisms Then fungal then gram positive organism.

Out of 75 cases of sepsis coagulase neg staph contribute 4 (28%) deaths, E. FAECALIS contribute 5 (62%) of deaths, staph hominis contribute 2 (50%), Klebsiella 8 (62%)

Pseudomonas contribute 4 (50%), E. coli contribute 4 (67%), can. albicans 2 (22%), Candida non albicans 12 (75%) deaths. More contribution is with Enter. Faecalis, Klebsiella, Staph hominis, E. coli, Pseudomonas, and Can. non. albicans.

DISCUSSION

Post-operative neonatal sepsis remain a challenging surgical complication, Its Incidence is close to 10% of total neonatal intensive care unit admission in our study. 88% are reported in preterm babies and 12% seen in late neonatal period. Neonatal sepsis depend on weight of the babies, Age of the baby, Type of surgery done, Type of pathology and congenital abnormalities. They are considered as a major factor of morbidity and mortality in the neonatal age groups despite advances in neonatal intensive care units.

In our study Total Neonatal Surgeries undertaken between 2019 -2020 are 720 out of which 89 neonatal sepsis were diagnosed (post operatively) which accounted for about 10.4% of total neonatal surgeries performed. This incidence is comparatively less when compared to other studies of similar topic. In a study by M.Abdel monem tarek et al incidence of post-operative sepsis was 52% of total admission, Other study by Ulf Kessler et al,^[4] the incidence is 6.9% which is less than our study GLOBALLY Incidence of sepsis is 2.9% to 30% in various studies.

Compared to females, Males have high incidence of post-operative sepsis in neonates, when we calculated the ratio males are 67.4% and Females are 32.6% with Male: Female ratio of 2:1 this was nearly comparable to other studies of M:F ratio. In Martin K Angele et al,^[5] study Female gender has been demonstrated to protective because of good cell-mediated Immune response and cardiovascular functions.

When sepsis compared with Age, the mean age of presentation for post-operative sepsis is more in early neonatal period, the is babies who got operated in less than 7 days (88%) for various different surgical conditions than in babies who are in late neonatal period that is 7 to 30 days (12%). In a study by Niels von Rosenstiel et al,^[6] Incidence of sepsis is more in Neonates less than 1 month age. In other study the incidence of sepsis is more in babies who are presented with in 48 hrs, this is called early onset sepsis.

Late onset sepsis account for after 48 hrs, incidence is less So mean age of presentation is 4 days in our study. Weight, Mean Wt at presentation was 2.25 kgs in our study which was compared to other study. Lloyd LG et al study tells us that low birth weight babies that is less than 1 kg are more prone for sepsis if operated. Mayr FB, et al study the mean wt. was 2.54 kg which are more prone to sepsis.^[7]

Good weight babies with term pregnancies have good immunity to fight against infection post operatively. When compared to Term and Preterm in our study preterm babies are more prone for sepsis which is 66.6% and Term babies 33.4% Preterm babies are associated with Low Immunity compared with Term babies.^[8]

In our study Post-operative sepsis is seen more commonly with Gastro intestinal surgeries which are contaminated wounds in them neonatal intestinal obstructions accounts for 30% of total cases, Then comes long operative time surgeries like TEF & CDH So babies with preterm/low birth weight / Males with congenital anomalies of neonatal intestinal obstruction, CDH, and TEF have long operative time which are more prone to high incidence of sepsis. With long operative time and hospitalization leads to surgical site infection. When compared to other study Ulf Kessler et al,^[4] Bowel surgeries, Thoracotomies, diaphragmatic hernia repairs are more prone with sepsis post operatively.

It is also associated with Gestation age/Birth wt. / Sex/Post-natal age / Duration of hospital stay /Operating time/Central venous catheter.

In our study sepsis develops on post-operative day 3 in 60 cases which count for 80% and more than 3 days in 20% cases when compared to a study by Juliana reis mochado et al,^[9] sepsis develop by bacterial invasion and release of toxins which take at least 3 days to develop systemic inflammatory response syndrome. When we go into depth what post-operative complications, which leads to sepsis in our study group. Anastomotic leak is 32% which is the major contributor then comes the Nonfunctioning stomas, were the meconium stasis in bowel (4%), then surgical site infections (40%) in a study by Dora catre et al.^[10] The most common complications were technical (25%), gastrointestinal (22%) and respiratory (21%). They identified four independent risk factors for severe postoperative complications: reoperation, operation for congenital diaphragmatic hernia, preterm birth less than 32 weeks of gestational age and abdominal surgery. Other study by Michelet D et al.^[11] The study included 168 patients. Their postnatal age was 48±48days. Overall, 37 patients experienced major postoperative non-surgical complications.

The most common major complications were hemodynamic compromise (n=19, 11.3%), multiple organ dysfunction syndrome (MODS, n=8, 4.8%) and respiratory failure requiring ventilation (n=3, 1.8%). Surgical complications occurred in 8 cases (4.8%). Four factors were identified as being predictive of non-surgical complications: PCA<40 weeks, a history of cardiac malformation, HMD or NEC, preoperative ICU status and intraoperative fluid bolus administration.

In our study group when we look at investigations most of neonates who are more prone to sepsis have low hemoglobin percentage compared to neonates without sepsis, 64.

We got 49% in 75 cases who have low hemoglobin levels Goobie SM et al,^[12] made a study on Association of Preoperative Anemia with Postoperative Neonates accounted for 2764 children (6%) in the 2012-2013 American College of Surgeons National Surgical Quality Improvement Program databases. Neonates included in the study were predominately male (64.5%), white (66.3%), and term (69.9% greater than 36 weeks' gestation) and weighed more than 2 kg (85.0%). Postoperative in-hospital mortality was 3.4% in neonates and 0.6% in all age groups (0-18 years). A preoperative hematocrit level of less than 40% was the optimal cutoff (Youden) to predict in-hospital mortality. Multivariable regression analysis demonstrated that preoperative anemia is an independent risk factor for mortality (OR, 2.62; 95% CI, 1.51-4.57) in neonates. The prevalence of postoperative in-hospital mortality was significantly higher in neonates with a preoperative hematocrit level less than 40%; being 7.5% (95% CI, 1%-10%) vs 1.4%

(95% CI, 0%-4%) for preoperative hematocrit levels 40%, or greater.

The relationship between anemia and in-hospital mortality was confirmed in our validation cohort (National Surgical Quality Improvement Program 2014). The incidence of postoperative in-hospital mortality in neonates, and the association between preoperative anemia,⁶⁸ and postoperative mortality in US hospitals. Timely diagnosis, prevention, and appropriate treatment of preoperative anemia in neonates might improve survival.

It's a universal indicator of increased in WBC count in sepsis which is same in our study Next important indicator is platelets counts which is (96%) in our study show low platelets. In a study by Abebe Gebreselassie H, et al.^[13] A total of 210 neonates were included in the study, out of which 56.2% were males. The incidence of thrombocytopenia,⁵⁶ was 55.8%. Among neonates with thrombocytopenia, 90.9% had late onset thrombocytopenia and half were in the severe range ($< 50,000/\mu\text{L}$). The presence of sepsis ($P = 0.000$) and atresia ($P = 0.000$) were found to be significantly associated with the development of thrombocytopenia. The mean non feeding hours were found to be significantly longer for patients with thrombocytopenia ($P = 0.000$). There are many studies who support this concept.

When we come to CRP,⁷⁰ levels there is 100% raised in this value All neonates post operatively have raised in CRP levels. In a study conducted by SP sharif et al,^[14] CRP values can differentiate between a normal post-operative response and surgical complications. The post-operative CRP trend was more important than a single result. This study quantified a physiological CRP change in response to surgery in neonates. In particular, there was a significantly different CRP response in neonates who developed a post-operative complication. Fengming Ji et al,^[15] study says that Postoperative CRP level can be used as a reliable marker for predicting the prognosis in neonatal surgeries and other surgeries.

When we talk about procalcitonin 46 neonates have high procalcitonin (94%) which is a diagnostic marker for sepsis. In Ho Park et al,^[16] study PCT, is a highly effective early diagnostic marker of neonatal infection. However, it may not be as reliable as CRP. Mathias Karlsson et al,^[17] Lactate dehydrogenase as an indicator of severe illness in neonatal intensive care patients: a longitudinal cohort study LDH differed significantly between the groups in infants born after 32 gestational weeks. LDH differed with the vitality of the patient ($F = 26.25$, $p < 0.0001$) at admittance and correlated with lactate ($R = 0.496$, $p < 0.0001$). Also, the predictive value for obvious need of intensive care was higher for LDH than for lactate assessed by area under the curve calculated with ROC-curves [0.82 (0.77-0.88) vs. 0.67 (0.60-0.75)].

In our study too there is 46 neonates with raised LDH so out of total 61% is the results. There is a

strong relationship between bad clinical condition of infants during first week of life and elevated plasma LDH. The results suggest that LDH might be a valuable support in decision making in the neonatal period coming to levels of albumin in our study hypoalbumin levels are more prone to sepsis in our 46 neonates out of 75 have hypoalbuminemia which account for (61%). When compared to other studies. Chunyan Yang et al,^[18] among 257 patients, birth weight was 2003 ± 348 g, gestational age was 35.7 ± 2.3 weeks, and 59.1% were male. In addition, 127 (49.4%) were in the low albumin group. There were 32 patients with sepsis, 190 with infections, 35 without infection, and their rates of hypoalbuminemia were 86.0%, 50.5%, and 30.7%, respectively ($P < 0.05$). Albumin levels of the patients who survived were higher than those of the patients who died. In the low albumin group, the number of individual-event-critical NCIS cases and the frequency of multiple organs injuries were 63.8% and 28.3%, respectively, and were higher than in the 2 other groups. Mortality was higher in patients with sepsis. Hypoalbuminemia was associated with severe adverse outcomes (odds ratio=6.3, 95% confidence interval: 3.7– 10.9, $P < 0.001$).

CONCLUSION

Preterm, ELBW, LBW Neonates still pose higher risk of sepsis. Sepsis can be detected in post-operative neonates as early as in the 2nd post-operative period so close monitoring of babies will improve the outcome. Timely convection to culture sensitive antibiotics improve control of sepsis, there by better outcome. Raised CRP, Thrombocytopenia, and Raised procalcitonin are reliable markers to pick up early sepsis in post-operative neonates. Early detection of sepsis with positive blood culture and sensitivity facilitates appropriate usage of antibiotics which improves the outcome and decrease in the hospital stay. The Antibidiograms also are important in formulating institution specific antibiotics protocol.

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