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RESEARCH ARTICLE

"CLINICOETIOLOGICAL PROFILE, MANAGEMENT AND OUTCOME OF NEONATAL SHOCK PRESENTING WITHIN FIRST 72 HOURS OF LIFE"

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Abstract

Objective: To study the ethology, presentation, response to treatment and outcome of neonatal shock which is one of the most common causes of morbidity and mortality in neonates while at the same time being amongst the less studied topics in pediatrics, with data from children and adult being extrapolated to the neonates.

Study Design: This was a cross sectional observational study done in a government hospital of north India from 1 January 2023 to 30 April 2023.All the neonates aged 0 – 72 hours who presented to the neonatal intensive care unit (NICU) of the pediatric department of the hospital as a case of shock were included in the study. Shock was defined as decreased perfusion, altered mental status, diminished or bounding pulses, cool extremities or decreased urine output.

Results: Our study included 71 patients (54.9% males and 45.1% females) out of which 77.5 % participants presented within 24 hours of birth. 54.9% babies had normal weight and 47.9% were early term. Babies born via LSCS were more likely to develop and present earlier with shock. 43.7% cases were attributed to respiratory distress syndrome, 32.4% cases to perinatal asphyxia and 27.1% to sepsis. Sepsis and Meconium aspiration were more likely to present earlier. 25.4% required triple inotropic support and 7% had catecholamine refractory shock. Mortality was 18.3% with maximum mortality seen in patients on triple inotropic support, all of whom presented with shock at less than 24 hours of age.

Introduction:-

Shock is a physiologically compromised state due to inadequate oxygen supply to the tissues to support aerobic metabolism, resulting in shift to less efficient anaerobic metabolism. Though there hasn't been a clear-cut consensus on parameters defining shock in neonates, especially in preterms, shock is clinically determined by signs and symptoms like lethargy, irritability, tachycardia, prolonged capillary refill time, oliguria and hypotension. British Association Perinatal Medicine defines hypotension as mean blood pressure less than the neonates Gestational age in weeks, which corresponds to 10th percentile for birth weight and post-natal age[1]. Severe hypotension in preterm neonates has been defined in some studies as a mean arterial pressure of 5 mmHg or more below gestational age[2].

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Understanding the pathophysiology of shock helps to recognise and classify shock during compensated phase itself and initiate appropriate treatment at the earliest. Shock can be classified as distributive (as a result of impaired vasomotor tone as in sepsis, anaphylaxis), cardiogenic (due to congenital cardiac defects, asphyxia or sepsis that cause myocardial pump failure), hypovolemic (caused by decreased circulating blood volume and hence, preload) or obstructive (due to increased afterload in conditions like total anomalous pulmonary venous connection, coarctation of aorta, pneumothorax, etc.)[3]. Myocardial dysfunction as a cause of shock is common in term babies with perinatal asphyxia and in preterm neonates due to myocardial immaturity with poor contractility and loss of vasomotor tone, while hypovolemia is a rare cause in neonates[4].

Shock can be managed by initial volume expansion with 0.9% sodium chloride in neonates with clinical suspicion of hypovolemia. Blood or fresh frozen plasma can be considered in cases of active bleeding[5]. Ionotropic support can be provided in the form of dopamine to increase myocardial contractility and renal blood flow, dobutamine and adrenaline to enhance myocardial contractility and output, or milrinone to increase myocardial contractility and at same time decrease vascular tone in systemic and pulmonary arteries[6,7,8]. Neonates with refractory shock, not responding to fluid resuscitation and inotropes can be due to adrenocortical insufficiency, especially in preterm neonates and with concurrent perinatal stress like respiratory distress syndrome (RDS), mechanical ventilation or surgery[9,10]. Early recognition and management of shock helps in decreasing the mortality as well as morbidities like intraventricular hemorrhage, periventricular leukomalacia, end organ dysfunction and long term neurological complications[12.]

Neonatal shock is one of the most understudied topics. There are only a few studies done for the etiology, time of presentation, mortality, risk factors and management of neonatal shock. Most studies extrapolate data from adults and children onto neonates, who are a very different subset in terms of etiology, risk factors of shock and response to treatment. Our study delineates the risk factors for neonatal shock emphasizing on the need for monitoring, the age group and the risk factors which need to be focused on. This study tries to expand our current knowledge on mortality and factors associated with it in neonatal shock. We tried to determine clinical course and outcome in order to form a common consensus on shock per se in neonatal age group, thus improving overall survival rates.

Methods:-

This was a cross sectional observational study done in a government hospital of north India from 1 January 2023 to 30 April 2023. All the neonates aged 0 – 72 hours who presented to the NICU of the pediatric department of the hospital as a case of shock were taken up for the study. Shock was defined as per American College of Critical Care Medicine as decreased perfusion in the form of capillary refill time of >2sec (cold shock) or flash capillary refill (warm shock), altered mental status, diminished or bounding peripheral pulses, cool extremities or decrease urine output of <1ml/kg/hour. Catecholamine resistant shock was defined as shock despite use of catecholamines [18]. Gender, Age at presentation of shock, gestational age, maternal comorbidities, baseline investigations at the time of shock, management and outcome were all noted. Babies were classified according to birth weight as Extremely Low Birth Weight (<1Kg), Very Low Birth Weight (1-1.5Kg), Low Birth weight (1.5-2.5 Kg), Normal Birth Weight (2.5-3.9 Kg), High Birth Weight (4-4.5 Kg), Very High Birth Weight (>4.5 Kg). Babies were classified according to gestational age into very preterm {Gestational age – 28 weeks 0 days to 31 weeks 6 days), moderate preterm {Gestation age – 32 weeks 0 day to 33 weeks 6 days}, Late preterm {Gestational Age – 34 week 0 days to 36 weeks 6 days}, Early term {Gestational Age – 37 weeks 0 days to 38 weeks 6 days}, Full term {Gestational Age – 39 weeks 0 days to 40 weeks 6 days}. Patients were classified as anemic if they had central venous hemoglobin less than 13g/dl and polycythemic if they had peripheral venous Hemoglobin more than 22 g/dl [19].Leukocytopenia and Leukocytosis was defined as Total leukocyte count (TLC) <5000/µL and >34000/µL respectively. Platelet count less than 1,50,000/µL, <50,000/µL, >4,50,000/µL were defined as thrombocytopenia, severe thrombocytopenia and thrombocytosis respectively.

Statistical analysis –

All the relevant information was collected as per predesigned proforma. All the collected data was entered in Microsoft excel spreadsheet and was analyzed using Jamovi 2.3.21. All the discrete variables were expressed as numbers and percentages and all the continuous data was expressed as mean, standard deviation and z scores. Bar chart was used for representation of data. Relation between categorical variables was analyzed by chi square test. Statistical significance was assessed and p values < 0.05 were considered significant.

Results:-

Gender –
Our study included 71 patients. 39 (54.9%) of them were males and 32 (45.1%) females. However, there was no statistically significant difference (p value – 0.4) in prevalence of shock in either gender.

Age –
Age at presentation ranged from 1 hour to 70 hours of life with mean age at presentation being 15.6 hours with standard deviation of 16.4 hours. Majority of study participants i.e., 31 (43.7%) presented between 4 – 24 hours of birth followed by 24 study participants (33.8%) who presented within 4 hours of birth. 12 (16.9%) participants were in age group of 24-48 hours and 4 (5.6%) were in age group of 48-72 hours. The results were statistically significant with p value of <0.001, χ 2 of 24.6 and df of 3.

Birth Weight –
Majority of the study participants i.e., 39 (54.9%) belonged to normal weight group followed by 18 (25.4%) participants which belonged to low birth weight group. 9 (12.7%) patients were very low birth weight and 2 (2.8%) participants were High Birth weight and extremely low birth weight. Least number of participants i.e., 1 (1.4%) belonged to very high birth weight group. The results were statistically significant with χ 2– 92.5, dF – 5 and p value of <0.001.

Gestational Age –
Majority of study participants i.e., 34 out of 71 (47.9%) were early term followed by 11 out 71 (15.5%) participants who were Full term. The results were statistically significant with χ 2– 35, dF – 4 and p value of <0.001. No statistically significant association was seen between gestational age and age at presentation.

Mode Of Delivery –
44 (62%) patients who presented as neonatal shock were born via Lower segment caesarean section (LSCS) whereas 27 (38%) patients were born via Normal vaginal delivery (NVD). There was statistically significant presence of neonatal shock in babies born via LSCS compared to babies born via NVD (χ 2 – 4.07, dF – 1, and p value of 0.044).

Our study further delineated that babies born via LSCS were more likely to present earlier with shock as compared to babies born via NVD {χ 2 – 9.07, dF – 3, p value of 0.028}.

Maternal History –
Table 1 shows distribution of maternal morbidities in study participants. However, none of these factors showed statistically significant presence in our study group

Table 1:- Frequency Distribution Of Maternal Morbidities In Study Participants.

MATERNAL MORBITIDTY	NO. OF PARTICIPANTS	PERCENTAGE
ABORTION	8	11.3%
DIABETES	6	8.5%
HYPO/HYPER THYROIDISM	5	7%
FEVER	3	4.2%
HYPERTENSION	3	4.2%
LEAKING	2	2.8%

It was observed that LSCS delivery was associated with maternal diabetes and thyroid abnormalities more often than by chance (p value less than 0.05).

Etiology –
31 (43.7%) cases of neonatal shock were attributed to respiratory distress syndrome (RDS), (out of which, 21 cases or 68% received surfactant) followed by 23 (32.4%) cases which were attributed to perinatal asphyxia. Biological plausibility was seen in each of these causes which preceded shock. Thus, in our setting RDS was the most common causes of neonatal shock followed by perinatal asphyxia and sepsis. Further 37 out of 71 (52%) patients had multiple etiological factors to which shock could be attributed. Table 2 shows frequency distribution of etiological factors for shock in study participants.

Table 2:- Etiological Classification Of Shock.

ETIOLOGY	NO. OF PARTICIPANTS	PERCENTAGE
RESPIRATORY DISTRESS SYNDROME (Surfactant Received)	31 (21)	43.7% (29.6%)
PERINATAL ASPHYXIA	23	32.4%
SEPSIS	19	27.1%
MECONIUM ASPIRATION SYNDROME	14	19.7%
PNEUMOTHORAX	11	15.5%
CARDIAC ABNORMALITIES	6	8.5%
BLEEDING	6	8.5%
NECROTIZING ENTEROCOLITIS	2	2.8%

1. It was seen that 26.3% with sepsis presented as shock within 4 hours of birth and 68.4% babies with sepsis presented within first 24 hours of birth. {χ 2- 8.59, dF-3, p value of 0.035}.
2. 64.3% patients with Meconium aspiration presented as shock within 4 hours of birth and 100% patients with Meconium aspiration presented within 24 hours of birth. {χ 2- 12.2, dF-2, p value of 0.002}.
3. 100% patients with Necrotizing enterocolitis presented as shock after 24 hours of birth {χ 2- 10.1, dF-3, p value of 0.018}. No statistically significant association was seen between other etiologies of shock and age at presentation.

Investigations

Table 3:- Investigations Of Study Participants.

	TLC (cells/µL)	L (%)	N (%)	PLATELETS (lakhs/µL)	HB (g/dl)	pH	HCO3 (mmol/L)	LACTATE (mmol/L)
MEAN	16554	37	56.4	2.42	16.1	7.22	16	4.05
MEDIAN	15400	35	58	2.10	15.8	7.23	16	3.7
STANDARD DEVIATION	12343	16.8	15.2	1.82	3.08	0.096	3.98	2.1
MINIMUM	1940	10	18	36,000	7.8	7	4	1.3
MAXIMUM	66900	90.5	85	14.5	22.8	7.42	23	15
L – Lymphocyte percentage N – Neutrophil percentage Hb - hemoglobin								

Table 3 shows statistical variables associated with various investigations in study participants.

12.7% babies had leukocytopenia. 80.3% had normal leukocyte count. 7% had leukocytosis {χ 2- 70.8, dF-2, p value of <0.001}. 42% babies with sepsis had thrombocytopenia {χ 2- 26.9, dF-2, p value of <0.001}.

15.5% babies were anemic. 80% had normal hemoglobin levels. 4.2% had polycythemia.

18.3% participants had thrombocytopenia. Out of these 3 had severe thrombocytopenia. 77.5% had normal platelet count. 4.2% patients had thrombocytosis. {χ 2- 106, dF-3, p value of <0.001}. 36.8% patients with sepsis developed thrombocytopenia and 86% patients with normal TLC didn't have sepsis {χ 2- 7.95, dF-3, p value of 0.047}.

38% participants had abnormal KFT. 11.3% participants had abnormal LFT.

Management And Outcome

All 71 patients were given initial fluid resuscitation for shock. Further 27 participants (38%) required single inotropic support, 26 participants (36.6%) required double inotropic support while 18 participants (25.4%) required triple inotropic support and 5 participants (7%) had catecholamine refractory shock. 17 out of 71 participants (24%) were managed via central line. All patients required some kind of respiratory support; 10patients (14%) were managed on oxygen, 7 (9.8%) on CPAP whereas 54 (76%) required Mechanical ventilation.

13 out of 71 (18.3%) study participants died. Further it was seen that 60% participants with catecholamine refractory shock died and 84.8% participants who didn't have catecholamine refractory shock survived {χ2 - 6.25, dF – 1, p value – 0.012}. It was seen that 44.4% participants on triple inotropic support expired whereas only 3.7% participants on single inotropic support expired {χ 2- 12.2, dF-2, p value of 0.002}. 61% of study participants on

triple inotropic support were less than 4 hours old and 100% patients on triple inotropic support presented before 24 hours of life {χ 2- 13.4, dF-6, p value of 0.038}.

Triple pressor support was required in47.8% patients with perinatal asphyxia {χ 2- 9.08, dF- 2, p value of 0.011} and in 54.5% patients with pneumothorax{χ 2- 6.03, dF-2, p value of 0.049}.

No statistically significant association was seen between mortality and mode of delivery/age at presentation. Further none of the causes of shock were individually associated with increased risk of death.

Discussion:-

This study was an observational study conducted in 71 neonates (39 males and 32 females) admitted in a government hospital in north India who presented as shock within the first 72 hours of birth.

Most (77.5%) of the participants presented within the first 24 hours of life. Thus, it is recommended that if not all, but at least neonates with risk factors including RDS, MAS and sepsis, must be observed in hospital setting for 24 hours.

Majority of the neonates (63.4%) belonged to gestational age of more than 37 weeks whereas 25.3% belonged to 32 to 36 weeks gestational age and only 11.3% were of less than 32-week gestation. This is in contrast to the study conducted by Lee et al[13] which found that preterm infants born at earlier gestational ages were at a higher risk for developing neonatal shock.

It was also seen that shock was more common and presented earlier in babies born via LSCS than NVD. This may be attributed to the fact that LSCS babies were more prone for RDS which was the most common factor associated with shock.

These neonates were also observed for risk factors like respiratory distress syndrome (in 43.7% of our study participants), perinatal asphyxia (in 32.4%) and sepsis (in 27.1%). These findings are in contrast to the retrospective cohort study conducted by Saini et al[14] to study the predictors of mortality in neonatal shock wherein sepsis was the most common cause of shock while Chan et al[15] observed cardiogenic shock to be more common than septic shock. However, these studies didn't solely consider the babies younger than 72 hours of life during which diseases other than sepsis are contributory to the cause.

On studying the patterns of laboratory investigations, it was established, that about 91.5% of the neonates in shock had metabolic acidosis with mean pH of 7.22 (± 0.096), bicarbonate of 16 (± 3.98) and lactate of 4.05 (±2.1).

All the neonates were given initial fluid resuscitation followed by inotropes (dopamine, dobutamine, adrenaline or milrinone), depending on the type of shock. Critically sick neonates (25.4%) required three inotropes for managing shock. Catecholamine-resistant shock was seen in 5 neonates who received hydrocortisone. Hydrocortisone therapy in shock was evaluated by Nichols et al[16] in pediatric shock and by Peeples et al[11] in neonatal refractory hypotension.

Mortality rate of 18.3% was observed in our study with increased mortality rates in neonates on triple inotropic support (44.4%) and catecholamine refractory shock (60%) with perinatal asphyxia and pneumothorax being associated with greater severity of shock (who required triple pressor support). Amongst the 13 mortalities, 53.8% had RDS, 30.7% has sepsis, 15.4% had MAS and 23.1% neonates suffered from air leak with overlap of the associated risk factors seen in many. These findings are similar to those observed by Shah et al[17] where out of the total 119 neonates, 19 neonates (15.9%) expired with 36.8% being due to early onset sepsis.

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