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ABDOMINAL ULTRASONOGRAPHY (AUS) AS A MODE OF INVESTIGATION IN THE EARLY EVALUATION OF NECROTIZING ENTEROCOLITIS IN A NEONATAL INTENSIVE CARE UNIT.

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ABSTRACT

INTRODUCTION: Necrotizing enterocolitis (NEC) is the most serious and common gastrointestinal emergency occurring among the neonates. NEC affects 1–5% of all neonates & approximately 7% of preterm infants <1500 grams. The incidence among premature neonates weighing less than 1500 grams is approximately 12% with mortality of 30-35%. NEC is an acute inflammatory injury involving the distal small and often proximal large intestine. Segmental coagulative necrosis of the mucosa with focal haemorrhage can be seen histopathologically. The radiological features appear late in the necrotizing enterocolitis. The delay in diagnosis will lead to increased mortality and morbidity. The features of NEC can be detected early in the ultrasonography of the abdomen.

AIM: The primary objective as Abdominal Ultrasonography (AUS) being investigation of choice in the early diagnosis of NEC and secondary objective of evaluating the morphological features seen in ultrasound and correlation with clinical, X-ray findings.

MATERIAL AND METHODS: This is a prospective study done from March 2016 to August 2017 at a Tertiary care referral centre. The sample size was calculated as 15, using Snedecor and Cochran formula. All the neonates which fulfilled the inclusion criteria were included in the study. The neonates with congenital anomalies and hemodynamic instability were excluded. The outcome was based on the AUS findings. Statistical analysis of data done using the Statistical Package for Social Sciences (SPSS), version 24.0.

RESULTS: The neonates included in the study were from 27 weeks to 38 weeks of gestation and mean age of presentation was 4.80±3.50 days, with the male female ratio 2.7:1. 02 (13%) neonates were of 27 weeks gestation, 01 (6.6%) was of 28 weeks of gestation, 02 (13%) were of 29 weeks of gestation, 02 (13%) were of 30 weeks of gestation, 04 (26%) were of 32 weeks of gestation, 01 (6.6%) was of 33 weeks of gestation and 02 (13%) were of 37 weeks of gestation. The mean birth weight±SD (range) in the study was 1447±601 grams. The neonates presented with features of feed intolerance 15 (100%), abdominal distension 8 (53.3%), lethargy 3 (20%). AUS detected abnormal findings in 10 neonates, in whom there were no radiological abnormalities. There was statistically significant association between the altered temperature and ultrasound findings (p value -0.014).

CONCLUSIONS: Abdominal ultrasonography is more sensitive to detect NEC at early stage.

KEYWORDS : Necrotizing enterocolitis, Abdominal Ultrasonography, Hemodynamic stability, Feed intolerance

INTRODUCTION:

Necrotizing enterocolitis (NEC) is the most serious and common gastrointestinal emergency occurring among the neonates. NEC affects 1–5% of all neonates & approximately 7% of preterm infants <1500 grams. The incidence among premature neonates weighing less than 1500 grams is approximately 12% with mortality of 30-35%. NEC is an acute inflammatory injury involving the distal small and often proximal large intestine. Segmental coagulative necrosis of the mucosa with focal haemorrhage can be seen histopathologically. The radiological features appear late in the necrotizing enterocolitis. The delay in diagnosis will lead to increased mortality and morbidity. The features of NEC can be detected early in the ultrasonography of the abdomen. Long-term effects are seen in surviving neonates, in the form of significant growth delay and adverse neurodevelopmental outcomes.[1,2,3]

Niño et al. (2016) in their study divided risk factors for NEC in two broad categories, i.e. factors related to the infant and factors related to the mother. They described these risk factors as follows:

a. Factors related to the infant - Prematurity (highest risk with lowest gestational age), Very low birth weight (<1,500 g), Low Apgar score at 5 min, Formula feeding, Mechanical ventilation, Congenital defects (Congenital heart disease, Patent ductus arteriosus, Gastroschisis), Pharmacological interventions (Histamine H2 receptor antagonists, Prolonged empirical antibiotic use (≥5 days), Concomitant use of indomethacin and glucocorticoids), Anaemia

b. Factors related to the mother - HIV-positive status, Illicit drug abuse (including opiates, cannabinoids and cocaine), Chorioamnionitis, Vaginal delivery.

The early clinical presentation may include feed intolerance, increased gastric residue and blood in stools. Specific abdominal signs include abdominal tenderness, distension, discoloration, emesis and bilious drainage from nasogastric tube. Non-specific symptoms and signs are akin to neonatal sepsis. In view of these overlapping features, clinical signs and symptoms alone are insufficient to provide a definitive diagnosis of NEC, thus emphasizing the need for other diagnostic modalities. Delay in diagnosis of NEC will lead to increased mortality (more than 10%) and morbidity (more than 25%) requiring surgical intervention. Among VLBW infants, the risk of mortality is much higher and is placed at 30%. Infants with NEC have a higher incidence of nosocomial infections and lower levels of nutrient intake, grow more slowly, and have longer durations of intensive care and hospital stay. The incidence of NEC is inversely related to an infant's birth gestation, but marked variability is evident across NICUs and countries. [1,2,3,4]

The radiological features for NEC appear late, findings are often non-specific. Abdominal Ultrasonography (AUS) has emerged as a sensitive tool in the early diagnosis of NEC. AUS is helpful owing to its ability to visualize intestinal walls, gastrointestinal lumen and neighbouring structures. The Doppler flowmetry helps in assessing the disrupted intestinal wall perfusion. The information provided by USG is superior to X-ray abdomen, augments and substantiates the clinical findings further, thus providing the useful information to plan further management, thus decreasing the mortality and morbidity. [5,6]

METHODOLOGY:

This was a prospective study conducted at a Tertiary care referral centre during March 2016 to August 2017. The sample size was 15, calculated using Snedecor and Cochran formula. The neonates who presented with clinical symptoms suggestive of necrotizing enterocolitis by presence of lethargy, temperature instability, feed intolerance, recurrent gastric residues, abdominal distension, blood in stools, were included in the study. The neonates with congenital anomalies and hemodynamic instability were excluded. Relevant demographic data were noted. Appropriate investigations including CBC, serum electrolytes, blood culture and sensitivity, stool for occult blood, were sent when NEC was suspected. The X-ray and AUS were done simultaneously, were reported by the radiologists and compared (table 2). The data were collected in a predefined Performa and entered in MS Excel 2013. Statistical analysis of data done using the Statistical Package for Social Sciences (SPSS), version 24.0.

Ultrasonographic features:

AUS was done at the department of Radio-diagnosis using GE Logiq P5 apparatus with a 2–2.5 MHz convex probe and 7–14 MHz linear probe. All the 4 quadrants of abdomen were scanned thoroughly to pick up early changes of NEC. The resolution in the near, mid and far fields was optimized independently by adjusting the transducer frequency and the focal zone of the Ultrasound beam. Select images of the bowel and peritoneal free fluid, if present, were acquired. The following are the AUS features suggestive of NEC - presence of wall thickness, hyper echogenicity, obstruction sign, intestinal immaturity, intraperitoneal air/fluid, portal vein air bubbles and peritoneal calcification. Doppler flowmetry was used to assess superior mesenteric artery flow.

Table 1: Demographic Profile and Perinatal history of Neonates Enrolled in the study

Sl No.	Variable	n (%)
1.	Gestational Age	
	27 weeks	02 (13%)
	28 weeks	01 (6.6%)
	29 weeks	02 (13%)
	30 weeks	02 (13%)
	32 weeks	04 (26%)
	33 weeks	01 (6.6%)
	37 weeks	02 (13%)
	38 weeks	01 (6.6%)

2.	Gender	
	Male	11 (73.3%)
	Female	4 (26.7%)
3.	Mode of delivery	
	Vaginal/Forceps delivery	3 (20%)
	LSCS (9 emergency, 3 elective)	12 (80%)
4.	Small for gestational age (SGA) neonates	01 (6.6%)
	Appropriate for age (AGA) neonates	14 (93.3%)
5.	Mean birth weight±SD (range) in grams	1447+601 (630-2400)
	ELBW (extremely low birth weight) babies	04 (26%)
	VLBW (very low birth weight) babies	05 (33%)
	LBW (low birth weight) babies	04 (26%)

Table 2: Comparison of Abdominal Ultrasonographic and Radiological (X-ray) Findings

Sl No.	Abdominal ultrasonography findings			Abdominal X-ray-Radiological findings	
	Variable	n	Percentage	n	Percentage
1.	Intestinal Wall thickness	9	60.0	0	0
2.	Hyperechogenicity indicative of intestinal immaturity	9	60.0	0	0
3.	Signs of obstruction	0	0	0	0
4.	Intraperitoneal air fluid	10	66.7	0	0
5.	Portal Vein Gas	0	0	0	0
6.	Peritoneal calcification	0	0	0	0
7.	Superior mesenteric artery flow (normal flow)	15	100	0	0

Table 3: Association between Clinical findings and Ultrasound findings in early evaluation of NEC

Clinical parameter		USG		Total		
		Present	Absent			
Abdominal Distension	Present	6	2	8	Sensitivity	60%
	Absent	4	3	7	Specificity	60%
					Mc.Nemers test	0.375
Total		10	05	15	p value	0.540

Table 4: Association between Clinical findings and Ultrasound findings in diagnosis of NEC

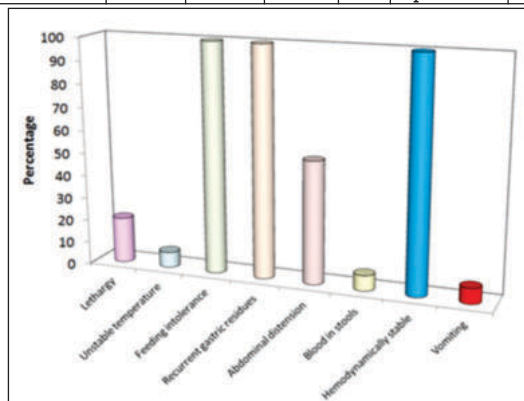| Clinical parameter		USG		Total		
		Present	Absent			
Altered Temperature	Present	3	0	3	Sensitivity	30%
	Absent	7	5	12	Specificity	100%
					Mc. Nemers test	6.03
Total		10	05	15	p value	0.014

Fig. 1: Clinical sign and symptom profile

RESULTS:

The present study was carried out in a total of 15 neonates, who fulfilled the inclusion criteria (Table 1). A total of 02 (13%) neonates were of 27 weeks gestation, 01 (6.6%) was of 28 weeks of gestation, 02 (13%) were of 29 weeks of gestation, 02 (13%) were of 30 weeks of gestation, 04 (26%) were of 32 weeks of gestation, 01 (6.6%) was of 33 weeks of gestation and 02 (13%) were of 37 weeks of gestation. The mean postnatal age of neonates at presentation was 4.80±3.50 days, with the male female ratio being 2.7:1. The mean birth weight±SD (range) being 1447±601 grams. The extremely low birth weight (ELBW) were 04 (26%), very low birth weight (VLBW) were 05 (33%), low birth weight (LBW) were 04 (26%). The mode of delivery with lower segment caesarean section (LSCS) were 12 (80%) and Normal vaginal delivery was 3 (20%). Feed intolerance 15 (100%), abdominal distension 8 (53.3%), lethargy 3 (20%) were the clinical findings predominantly (figure 1). Haemoglobin levels ranged from 13 to 18 g/dl with a mean value of 15.89±1.45 g/dl. Total leukocyte count ranged from 3.2 to 40x103/cumm with a mean of 15.03±9.18x103/cumm. Platelet count ranged from 0.23 lakhs to 5.26 lakhs/cumm with a mean of 2.02±1.36 lakhs/cumm. Mean S. sodium, potassium and calcium levels were 140.53±3.14 mEq/L, 4.77±0.50 mEq/L and 8.17±0.66 mg/dl respectively. Blood culture was positive in 3 (20%) cases while occult blood was detected in 6 (40%) stool samples. The organism grown in blood culture were klebsiella pneumonia, E. coli.

There were 10 (66.7%) neonates having abnormal AUS findings, suggestive of necrotizing enterocolitis, in whom there were no abnormal radiological findings. All the 15 neonates included in the study had no abnormal radiological findings. A total of 9 (60%) cases showed intestinal wall thickness and hyper echogenicity reflective of intestinal immaturity. A total of 10 (66.7%) cases showed presence of intra-peritoneal air/fluid. All the cases had normal superior mesenteric artery flow. None of the cases showed signs of obstruction, portal vein gas and peritoneal calcification. (Table 2). All the cases were managed appropriately, no mortality was reported in our study. In our study it was found that all babies who had alteration in temperature had ultrasonographic features of NEC (p value – 0.014) (table 4).

DISCUSSIONS:

Necrotizing enterocolitis (NEC) is an acute inflammatory injury to the distal small and often proximal large intestine. The segmental coagulative necrosis of the mucosa with focal haemorrhage are the hallmarks of ischemia. The incidence of NEC is inversely related to an infant's birth gestation, but marked variability is evident across NICUs and countries. Low birth weight neonates are at an increased risk of neonatal morbidity and comprise a high proportion of NICU admissions (25-80%) and have several developmental discrepancies. The associated mortality rate for this complication ranges from 10-30%.[1,2] In view of the devastating effects, its early definite diagnosis and immediate initiation of appropriate therapy is crucial.

In the recent years, AUS has emerged as a tool to provide a more detailed estimate of the state of the bowel in patients with NEC and may thus make management decisions easier and potentially change outcome.[1] In our study the cases were from 27 weeks to 37 weeks of gestation. In a study by Staryszak et al, they reported the gestational age of the neonates to be more than 37 weeks. Palleri et al. in their study reported the median gestational age in the cohort was 25.57 weeks (range, 23–35 weeks) and their median birth weight was 824 g (range, 545–3,200 g)25.57 weeks in conservatively treated babies and 25 weeks of gestation in surgically. The median age of onset of symptoms was 28.7 weeks. Wang et al. in their study reported the mean age at onset to be 11.8 and 14.2 days respectively for definite and suspected group of NEC neonates. In the present study, majority of neonates were males 11 (73.3%). A predominance of males over females in clinically suspected cases of NEC has been recorded in different series too. Palleri et al. in their series had a male to female ratio of 2.57. Wang et al. also had a high male to female ratio (2.94). Kamali et al. reported this ratio as 1.83 and Prithviraj et al. found this ratio as 1.4.[7,8] The findings of the present study as well as that of previous studies thus endorse male gender is at a higher risk as compared to females for NEC.

As far as clinical signs were concerned, these were consistent with the modified Bell's criteria for staging of NEC. Feed intolerance 15 (100%) and recurrent gastric residues 15 (100%) were the most common clinical findings. Similar findings were reported by Prithviraj et al, who also found feeding intolerance and recurrent gastric residues as the most common clinical findings in all the stages of NEC in their series. In their study 92% to 100% neonates had presence of these findings. The laboratory investigations revealed a Total leukocyte count ranged from 3.2 to 40x103/cumm with a mean of 15.03±9.18x103/cumm. A high TLC is indicator of an inflammatory activity. Wang et al. in their study found mean TLC count as 9.7±4.8 and 8.9±5.8 X 1000 in the definitive and suspected groups respectively. Relatively higher TLC values in present study could be owing to the fact that present study had patients with a relatively younger age. TLC levels have been shown to change tremendously during the early neonatal life. It has been reported that during first 72 hours of life, a high increasing trend of TLC is observed which reaches at its peak at 72 hours and then shows a gradual decline to normalize between 72 hrs to day 28 of life.[9] Platelet count ranged from 0.23 lakhs to 5.26 lakhs/cumm with a mean of 2.02±1.36 lakhs/cumm. Mean S. sodium, potassium and calcium levels were 140.53±3.14 mEq/L, 4.77±0.50 mEq/L and 8.17±0.66 mg/dl respectively. Abnormal laboratory findings like anemia, left shift of neutrophils, neutropenia, thrombocytopenia, metabolic acidosis and hyponatremia are known indicators of necrotizing enterocolitis as shown in studies by Faix et al and Abramo T et al.[10,11] Blood culture was positive in 3 (20%) cases while occult blood was detected in 6 (40%) stool samples.

In our study there were no radiological features suggestive of NEC in all cases. Prithviraj et al. in their study reported that X-ray fails to diagnose early characteristic features of NEC.[12] In our present study, ultrasonography diagnosed NEC in 10 (66.7%) neonates, in which there were no radiological abnormalities detected. The evidence of intraperitoneal air fluid was seen in 10 (66.7%) cases while intestinal wall thickness and hyper echogenicity indicative of intestinal immaturity were seen in 9 (60%) cases, were the features suggestive of early NEC in abdominal ultrasonography. In all the cases superior mesenteric artery flow was normal. The USG helped to confirm NEC in 10 cases as Definitive. There was statistically significant association between the altered temperature and ultrasound findings (p value -0.014). Hence, in a suspected case of NEC, even the alteration of temperature can be a significant clinical finding.

The findings of this study thus suggested that ultrasonography is more sensitive to detect early changes of NEC. Thick bowel wall is often considered to be predictive of poor outcome. The most common USG finding, i.e. intraperitoneal air fluid is considered to be an indicator of confirmed diagnosis of NEC as per Bell's criteria. The median duration of NICU stay was 30 days with an interquartile range of 14.5 to 55.0 days. There was no mortality. Timely diagnosis and appropriate management of NEC by early diagnosis will decrease both mortality and morbidity, as seen in our study.

CONCLUSIONS:

The ultrasound abdomen is sensitive investigation to diagnose NEC at an early stage. Hence, AUS should be recommended as an early diagnostic tool to diagnose NEC.

Limitation of the Study:

The limitation of our study is the small sample size.

A randomised control study (RCT) with a large sample size should be done in the future.

What Is Known: Nec Has A High Mortality. The Radiological Signs Appear Late.
What Our Study Adds: Aus Is An Investigation To Detect Nec At Early Stage, Even Before Radiological Findings Appear. Thus, Increasing The Survivability And Decreasing The Mortality.

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