

“How Good Is the Detection of Portal Venous Gas by USG in Diagnosis of Necrotising Enterocolitis”

Dr. Krishna Keshav¹, Dr. Girijanand Jha², Dr. Binod Kr Singh³,
Dr Saroj Kumar⁴

¹Senior Resident, Deptt of Pediatrics, N.M.C.H, Patna

²Senior Resident, Deptt of Pediatrics, N.M.C.H, Patna

³Professor & H.O.D, Deptt of Pediatrics, N.M.C.H, Patna

⁴Assistant Professor, Deptt of Pediatrics, N.M.C.H, Patna

Corresponding Author: Dr Girijanand Jha

Abstract:

Introduction: Necrotising enterocolitis (NEC) is an important cause of neonatal mortality & morbidity. An early diagnosis thus becomes important to institute timely therapy. However, the diagnostic hallmarks & specific X-ray findings- pneumatosis intestinalis (PI) and portal venous gas (PVG) appear rather late in the course of disease. We intended to study if PVG detection by USG would help in earlier diagnosis.

Methodology: We conducted a prospective observational study over 1 year from May 2019 to April 2020 at NICU of N.M.C.H Patna including all consecutively admitted sick neonates. They were screened for PVG by USG either in the course of routinely performed cranial/renal USG and/or when they suffered from symptoms consistent with NEC.

Results: 328 neonates were enrolled in this study. Mean gestational age was 34.2 weeks (S.D=3.9) and mean admission weight was 2.1 Kg (S.D=0.68). Males outnumbered females but this difference wasn't statistically significant. Out of the 328 neonates, 34(10.4%) had features consistent with NEC, 4 of whom had more than one occasion (thus total NEC occurrence=38). NEC stage \geq 2 was found on 18 occasions. None of the 328 neonates demonstrated PVG when screened during routine cranial/renal USG scans. PVG was found in 12 out of 38 episodes of NEC (2 in NEC stage 1, 10 in NEC stage \geq 2). PVG-USG for NEC stage \geq 2 diagnosis had a moderate sensitivity of 56%, high specificity of 90%, high PPV of 83% and a moderate NPV of 69%.

Conclusion: PVG-USG offers a moderate sensitivity and a high specificity for the diagnosis of suspected or definite NEC. PVG-USG is easy, time-saving procedure that can be done bedside even in unstable neonates. PVG-USG should be considered as a helpful diagnostic adjunct to X-ray and should be carried out in every neonate with suspected/definite NEC.

Keywords: Necrotising enterocolitis, pneumatosis intestinalis, portal venous gas, USG, Bell's staging.

Abbreviations: BNPC: benign neonatal peumatosi coli; NEC: necrotising enterocolitis; PI: pneumatosis intestinalis; PVG: portal venous gas, USG: ultrasonography, NICU: neonatal intensive care unit; NPV: negative predictive value; PPV: positive predictive value.

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I. Introduction

Despite advances in neonatology that has led to increased survival of even the very preterm neonates, necrotizing enterocolitis (NEC) remains an important cause of both neonatal mortality and morbidity.^{1,2} It is the commonest gastrointestinal emergency in neonates and affects upto 5% of all NICU admissions and upto 10% of all admitted preterm LBW neonates.³ It carries a high mortality rate, upto 30% in some studies. This toll is higher in those neonates (approx 50%) in neonates requiring surgical treatment due to delayed diagnosis or extensive disease.⁴ There are additional associated long term issues like short bowel syndrome, impaired growth and adverse neurodevelopmental outcomes.⁵ This emphasizes the need for early diagnosis and treatment of this otherwise devastating disease. However, the initial clinical features of NEC are non-specific and considerably overlap with other gastrointestinal problems like feed intolerance, CPAP induced abdominal distension or septic ileus.^{6,7} This leads to a significant delay in the diagnosis of NEC and the diagnosis is established in the presence of specific but late clinical (severe clinical features), lab changes or classic radiological findings of marked intestinal dilatation, pneumatosis intestinalis (PI), portal venous gas (PVG) or free abdominal air. Though X ray findings of PI and PVG are considered highly specific, the sensitivity is not high.⁸ Use of real time USG plays a noteworthy role here in detection of these changes relatively early.⁹ In USG, PI is seen as gas bubbles along the subserosal and submucosal layer. When these air bubbles are absorbed in the vessels, traverse and localize to the

portal vein, these are detected as PVG. Sonologically they appear as lowing echogenic dots. There have been several reports suggesting a role of PVG in abdominal USG as an early diagnostic marker of NEC.¹⁰ However, there have been only few studies in Indian setting on an unselected cohort of neonates so as to determine its sensitivity, specificity and diagnostic value. With this background, we prospectively screened neonates without abdominal problems with an assumption that they will be negative for PVG. We also examined all neonates with G.I symptoms to evaluate if the presence of PVG in them helps in diagnosis of NEC.

II. Aim & Objective

Aim: To study the role of PVG detection by USG in the diagnosis of NEC.

Objective: To study the detection of PVG by USG in specific conditions of neonates.

To study the diagnostic value of such detection in the diagnosis of NEC

III. Methodology

Study design & setting – Prospective observational study done at NICU of a tertiary care teaching hospital, Nalanda Medical College & Hospital, Patna over 1 year from May 2019 to April 2020.

Participants: Ill neonates consecutively admitted to our NICU and staying for more than 24 hours.

Study technique: After obtaining consent and enrolment in the study as per above criteria, the neonates underwent detailed history taking, clinical examination, laboratory investigations & management based on our NICU protocol. All such babies were screened for PVG by USG either in the course of routinely performed cranial/renal ultrasounds and/or when they suffered from symptoms consistent with NEC. All such symptomatic infants were also evaluated for sepsis, acidosis, electrolyte imbalances, CBC picture etc. Abdominal X ray was done in all infants with clinical diagnosis of NEC. Clinically, we suspected NEC when one or more of following symptoms were present: increased gastric residuals before feeds (>20% of feeding volume), moderate to marked abdominal distension, absent bowel sounds, abdominal tenderness with or without discoloration & bloody stool in the absence of a local cause of bleeding (eg rectal fissure). We used Walsh and Kliegman’s modified Bell’s staging for clinical diagnosis & staging of NEC¹¹(Table 1). To definitely diagnose a neonate as NEC of grade ≥ 2 , a suggestive radiological finding was considered mandatory in our study. USG screening was done by the radiologist for minimum 3 minutes so as not to miss PVG. As per established standard, continuous streaming echogenic dots in the bloodstream of portal vein or scattered hepatic echogenic spots were regarded as PVG.

Data collection: Relevant data was recorded in a structured proforma by the attending Doctor during admission, first and subsequent USG for detection of PVG. Additionally during each such screening we also documented all clinical symptoms related to NEC and any medical or surgical procedures that we believed can be associated with air in tissues or circulation (mechanical ventilation or non invasive ventilation, surgical procedure, central and peripheral venous or arterial catheter etc)

Statistical analysis: Data so collected was recorded, tabulated and entered in Microsoft excel sheet, and then analyzed by using statistical software “SPSS ver.20®. Variables were expressed as mean, standard deviation and percentiles as applicable. Cross tables were generated for NEC stage ≥ 2 and PVG. Sensitivity, specificity, positive and negative predictive value were calculated from these cross tables and compared with the clinical diagnosis of NEC. Statistical tests for comparison as appropriate for the parameters were applied. *P*-value <0.05 was taken as significant.

Table 1: Walsh and Kliegman’s (modified Bell’s) classification of NEC:¹¹

Stage	Clinical features	Gastrointestinal findings	Radiological findings
I	Apnea, bradycardia, temperature instability	Gastric residuals, Mild abdominal distension, blood in stools	Normal or mild intestinal dilatation
Ila	Same as stage I	Same as I plus, absent bowel sounds, abdominal tenderness	Dilated bowel loops \pm focal pneumatosis
Ilb	Mild thrombocytopenia, mild metabolic acidosis	Same as I plus absent bowel sounds, definite abdominal tenderness, abdominal cellulitis, RLQ mass	Widespread pneumatosis, PVG, \pm ascites
IIIa	Same as Ilb plus mixed acidosis, coagulopathy, hypotension, bradycardia, oliguria, neutropenia	Signs of II plus features of generalized peritonitis, marked tenderness	As above plus moderate to severely dilated bowel loops, prominent ascites
IIIb	Further deterioration, shock	Same as IIIa	Same as Ilb plus pneumoperitoneum

IV. Observation & Results

During the present study we enrolled 328 sick neonates. Mean gestational age was 34.2 weeks(S.D=3.9) and mean birth weight was 2.1 Kg (S.D=0.68). Males outnumbered females but this difference wasn’t statistically significant (*p*= 0.09). The clinical characteristics of these neonates are depicted in Table 2.

Table 2: Clinical characteristics of the enrolled neonates:

Sl No.	Characteristics	Number	percentage
01	Total number of neonates enrolled	328	100
02	Preterm (GA <37 weeks)	242	73.8
03	Male Gender	179	54.6
04	Birth weight <1500 gram	124	37.8
05	Small for gestational age	34	10.4
06	Perinatal asphyxia	38	11.6
07	Mechanical ventilation	89	27.1
08	Central venous access	85	25.9
09	Major gastrointestinal malformation*	7	2.1
10	Early onset neonatal sepsis	54	16.5
11	Late onset neonatal sepsis	37	11.3
12	NEC, any stage	38	11.6
13	Necrotic bowel other than NEC#	3	1.2

*1 case of gastroschisis, 1 case of omphalocele, 3 cases of volvulus and 2 cases of malrotation

2 cases of volvulus, 1 case of focal intestinal perforation

NEC and USG findings of PVG: Out of the 328 neonates, 34(10.4%) had features consistent with NEC, 4 of whom had more than one occasion (thus total NEC occurrence=38). However, PVG detection was a rare finding in this study as none of the neonates had this finding when PVG-USG screening was requested in the babies undergoing screening cranial/renal USG. It was detected only in cases with confirmed or suspected NEC; no other neonatal disease/condition was found associated with PVG-USG in our study. NEC (any stage) was diagnosed on 38 occasions in these 34 neonates. Out of these, NEC of grade ≥ 2 was found on 18 occasions (16 neonates), whereas NEC stage 1 (NEC suspect) was found on 20 occasions (18 neonates). Surgical intervention was required in 5 neonates with clinical NEC of grade ≥ 2 : 3 due to clinical deterioration and 2 due to pneumoperitoneum. However, among these 5 cases, 3 had no intra-operative findings suggestive of NEC (volvulus: 2, focal intestinal perforation: 1). Interestingly, these 3 cases were negative for PVG by USG. Overall, serum concentration of inflammatory markers was elevated in 7 out of 12 cases where USG showed PVG and all were of grade ≥ 2 . However, 3 neonates with NEC stage ≥ 2 remained negative for inflammatory markers.

Calculations for sensitivity, specificity, positive predictive value and negative predictive value are shown in Table 3. PVG was found in 12 out of 38 episodes of NEC. Surprisingly, we found 2 case with NEC stage 1 who had abdominal symptoms, PVG on USG but no PI on X-ray and negative serum inflammatory markers. The calculation for sensitivity was confounded because 3 of the 18 cases diagnosed as NEC stage ≥ 2 had no intra-operative findings suggestive of NEC and they also had no PVG on USG. Taking this into account, the actual Sensitivity would have been 66.67%. To say this in easy words, PVG detection by USG would have not missed 2 out of 3 cases of NEC stage ≥ 2 .

Table 3: Calculations for Sensitivity, specificity, PPV and NPV

	NEC stage ≥ 2 present	NEC ≥ 2 Absent [#]	Total
PVG present	10	2	12
PVG Absent	8 [*]	18	26
Total	18	20	38

All such neonates were clinically and radiologically stage 1 NEC cases.

*3 had no intra-operative findings suggestive of NEC (volvulus: 2, focal intestinal perforation: 1).

Sensitivity= $10/18 = 55.56\%$;

Specificity= $18/20 = 90\%$

Positive predictive value (PPV)= $10/12 = 83.34\%$;

Negative predictive value (NPV)= $18/26 = 69.23\%$

V. Discussion:

Only few researchers have studied the role of PVG-USG prospectively in an unselected cohort of neonates treated at a tertiary care hospital. Our study indicates that in cases of definite NEC (serious NEC), this modality (PVG detection by USG) has a moderate sensitivity of 56%, high specificity of 90%, high PPV of 83% and a moderate NPV of 69%. However, taking into account the limitation of the clinical criteria used for diagnosis, the sensitivity actually increases to 67%. We reviewed in detail the diagnostic significance of PVG-USG as reported by others. We came across the study of Faingold et al¹² who reported PVG-USG in meager 10% neonates with NEC. However, the study of Meritt et al¹³ reported PVG &/or gas in liver parenchyma in all 12 neonates with NEC and no such abnormality in a control group of 200 neonates with weight <2 Kg.. But none of these studies had reported their findings strictly according to a NEC definition or correlated such findings with the disease severity. This made comparison of our results with other studies rather difficult. Also it has to be kept in mind on the basis of many studies that a coherent relationship between the presence of radiologic PI and PVG on one hand and NEC on the other hand doesn't always exist.^{14,15} Moreover, one can't

rely much on abdominal radiography for PVG which is insensitive and subject to a lot of interobserver variability.

In our study, the specificity of PVG-USG was quite high (90%) and this was demonstrated by the fact that this USG finding was absent in the unselected cohort of 328 neonates screened for this phenomenon in the absence of significant gastrointestinal symptoms, even in medical conditions associated with air in tissue or circulation. As PVG in USG was also seen in 2 neonates (17% of total NEC cases) with NEC stage 1, it can be reasonably said that PVG in USG doesn't always correlate with disease severity. Also, when we did extensive search of literature, we could find 2 conditions: hypertrophic pylorus stenosis (HPS) and “benign neonatal pneumatosis coli”(BNPC) with PVG in USG. BNPC is a poorly understood condition and may be due to cow milk protein allergy or viral enteritis which may mimic NEC in G.I symptoms (blood in stools, PI on X ray) but lack local and systemic signs.¹⁶ As there were no HPS cases in our study population, we wondered if we really encountered BNPC cases in our study which mimicked as NEC. We noted that serum inflammatory markers were absent in 3 neonates with NEC stage ≥ 2 and they had minimal systemic features. This prompted us to doubt if these neonates really suffered from NEC or they were just BNPC. Based on above findings and our experience of treating such babies over the years, we suggest that PVG detection by USG doesn't necessarily indicate a more severe NEC or the need of surgical intervention. Overall mortality was 6/38 (15.8%) and mortality in stage ≥ 2 was 6/18(33%) This was lower than most of the Indian studies. This might be attributed to a relatively early diagnosis due to availability of USG for detection of PVG.

VI. Conclusion

PVG-USG offers a moderate sensitivity and a high specificity for the diagnosis of suspected or definite NEC. However, its absence doesn't rule out this disease. Though its presence indicates NEC, it doesn't always correlate with the severity of disease or stages of NEC. As compared to the standard radiological evaluation, screening for PVG by USG provides a reasonably good efficacy for NEC diagnosis and offers a very high practicability. X-ray changes are often subtle and carry a high interobserver variability but PVG if present can hardly be missed or mistaken even in small quantities. PVG-USG is easy, time-saving procedure that can be done bedside even in unstable neonates. Thus, PVG-USG can improve the diagnosis of definite NEC especially in the absence of a clear radiologic evidence for the same. PVG-USG should be considered as a helpful diagnostic adjunct to X-ray and should be carried out in every neonate with suspected/definite NEC.

VII. Limitation Of The Study

1. Lack of a “Gold standard” diagnostic criteria for NEC hampered the evaluation of role of PVG detection by USG in diagnosis of NEC. Given the myriad presentations it has, some researchers have even hypothesized that NEC might be neither a uniform nor a well-defined disease entity. Infact researchers have proposed that it is time to abandon Bell's criteria¹⁷ and they have suggested a new guideline for the diagnosis of ‘acquired neonatal intestinal diseases’ based on more specific diagnostic criteria. If we take these newer criteria for diagnosis, our sensitivity increases to nearly 90%. This highlights that there is need to develop and use a ‘robust’ criteria for clinical diagnosis of NEC.
2. Second limitation is the small number of neonates with clinical NEC. However, it has been within the commonly reported ranges.
3. We cant rule out inter- and intraobserver variability of PVG-USG

CONFLICT OF INTEREST: None

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