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Letter to the Editor

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Neutrophil to Lymphocyte ratio: A promising tool in neonatal appendicitis diagnosis

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Dear Sir

Neonatal appendicitis (NA) is a very rare disease with a reported incidence rate of 0.04. [1] The delayed diagnosis due to non-specific clinical manifestations often leads to perforation, peritonitis, septicemia, and a mortality rate of up to 28%. [1] I believe Neutrophil to Lymphocyte ratio (NLR) has a potential to be used as a diagnostic marker for this rare condition.

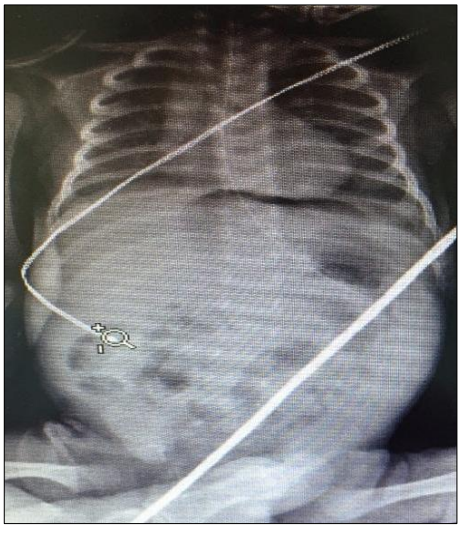

Figure 1: Radiographic view: free air under diaphragm.

An 18-day-old 1490g male, born to a preeclamptic mother at 31 weeks was admitted to Neonatal Intensive Care Unit (NICU) due to prematurity-associated respiratory failure experienced progressive abdominal distention and bilious vomiting. Labs were: White Blood Cell (WBC): 12.300/mm³ (N: 9.300/mm³, L: 2.350/mm³), Hemoglobin (Hb): 11.2g/dL, Platelets (Plt): 590,000/mm³, C-reactive protein (CRP): 88mg/L. Abdominal ultrasonography (AUS) was inconclusive, abdominal X-ray depicted free air (Fig. 1). Laparotomy revealed perforated appendix (Fig. 2). Appendectomy and abdominal irrigation were performed.

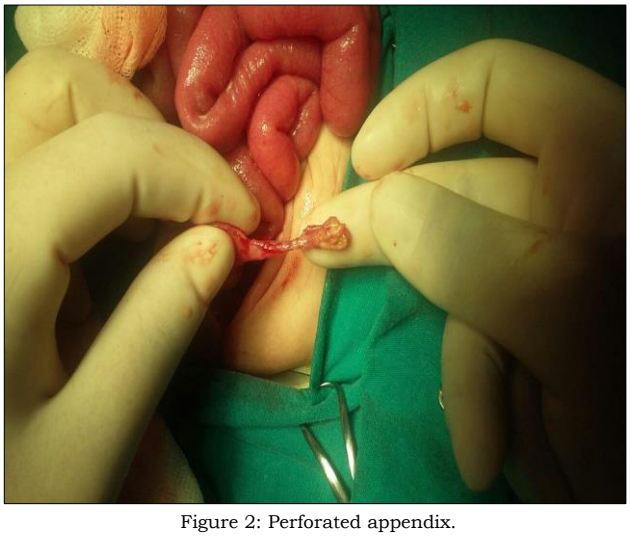

Figure 2: Perforated appendix.

In another 17-day-old, 2950g, term female, with perinatal asphyxia had irritability, abdominal distention, discoloration, and bilious gastric drainage in NICU; Labs were: WBC: 10.800/mm³ [N:7.900/mm³, L:1.800/mm³], Hb: 11.9g/dL, Plt: 197,000/mm³, CRP: 33mg/L. AUS reported right lower quadrant mass. Laparotomy revealed perforated appendix and appendectomy was performed (Fig. 3).

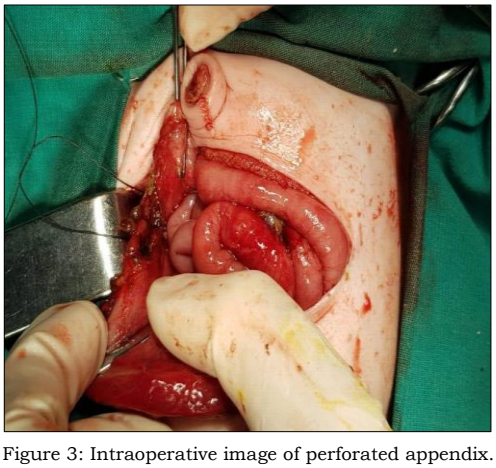

Figure 3: Intraoperative image of perforated appendix.

In another case, a 13-day-old premature 1390g female in NICU delivered at 28 weeks of gestation exhibiting fever, bilious drainage, severe abdominal distention, and discoloration receiving indomethacin for patent ductus arteriosus, the Labs were: WBC: 14,000/mm³ [N: 10,300/mm³, L: 3,300/mm³], Hb: 9.7g/dL, Plt: 379,000/mm³, CRP: 128mg/L. Abdominal X-ray showed absence of gas in the abdomen, AUS reported free abdominal fluid. Urgent laparotomy revealed pelvic pus and perforated appendix. Appendectomy was performed, and the patient was died due to multiple organ failure. Clinical characteristics and outcomes of all patients are detailed in Table 1.

Table 1: Data summary of patients.

Patient Data	Patient 1	Patient 2	Patient 3
Gestational age at birth	31 w+5 d	37w +6d	28w +2 d
Age	18 d	17 d	13d
Sex	male	female	female
Weight	1490	2950	1390
Clinical presentation	Fever Bilious gastric residues Abdominal distention	Irritability, feeding intolerance, abdominal distention, discoloration	Bilious gastric residues Marked abdominal distention. RLQ mass
Associated malformations	Birth asphyxia, preeclampsia	Birth asphyxia, placental anomaly	Patent Ductus arteriosus
Meconium passage in first 24 h	+	+	+
Mechanical ventilation	CPAP	CPAP	Yes
X-ray	Pneumoperitoneum	Dilated intestinal loops	No gas
AUS findings	Distended loops	Distended loops	Mass in RLQ, free fluid in pelvis
Blood workup	WBC:12.3x10⁹/L; NE:9.3x10⁹/L; LY:2.35x10⁹/L; HGB: 11.2 g/dL; PLT, 590x10⁹/L; CRP:88 mg/L	WBC:10.8x10⁹/L; NE:7.9x10⁹/L; LY:1.8x10⁹/L; HGB: 11.9 g/dL; PLT, 197x10⁹/L; CRP:33 mg/L	WBC:14x10⁹/L; NE:10.3x10⁹/L; LY:3.3x10⁹/L; HGB: 9.7 g/dL; PLT, 379x10⁹/L; CRP:128 mg/L
Surgery	Laparotomy, appendectomy	Laparotomy, appendectomy	Laparotomy, appendectomy, drain placement
Postoperative feeding	4d	5d	-
Outcome	Discharged at day 16	Discharged at day 14	Multiple organ failure, Exitus

CRP=C-reactive protein, HCT=hematocrit, HGB=hemoglobin, LY=lymphocytes, NE=neutrophils, PLT=platelet count, RBC=red blood cell count, WBC=blood cell count. AUS: abdominal ultrasound

Acute appendicitis is a common occurrence in children, whereas NA remains exceedingly rare. Prematurity and conditions like perinatal asphyxia, cardiac anomalies, patent ductus arteriosus, and other hypoxic states are considered to lead to neonatal appendicitis through vascular insufficiency. [2] Despite numerous cases and recent advancements on the subject, NA remains a diagnostic enigma in pediatric surgery. Several studies have endeavored to identify sensitive biomarkers or parameters for accurate diagnosis, notably, the NRL has emerged. It is a simple, accessible, and easy to calculate parameter in clinical practice. According to Yazıcı et al., NRL exceeding 3.5 serves as a sensitive indicator for appendicitis diagnosis in children. [3] In a retrospective case control study focusing on preterm newborns with NEC, Mu et al. identified NRL ≥ 1.60 and < 3.20 as indicative cut-off values for diagnosis of NEC in preterm infants. [4] Intriguingly, here all NRL exceeded 3.2 (3.95, 4.38, and 3.22); nevertheless, further investigation is warranted. In addition, none of the above-mentioned patients experienced thrombocytopenia. Since thrombocytopenia is a well-established part of Bell scoring system of NEC, normal platelet values may indicate appendicitis in neonates and could be used in differential diagnosis along with NRL. [5]

To summarize, presentation of neonatal appendicitis demonstrates significant variability and unpredictability. Novel diagnostic biomarkers are imperative to differentiate NA from other neonatal abdominal emergencies, particularly NEC. While further research is

warranted, NRL stands out as a promising additional tool in differential diagnosis of NA when combined with other laboratory results such as thrombocyte values.

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