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Article

Impact of Raised CRP in Mortality and Morbidity Among Neonatal Intestinal Obstruction Cases

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Abstract

Background: *Neonatal intestinal obstruction is a grave reason for morbidity and mortality. C-reactive protein (CRP), an acute-phase reactant, may have prognostic implications in predicting the outcome in such patients. This research aimed to identify whether there was any relationship between admission CRP and clinical outcome in neonates presenting with intestinal obstruction.*

Materials and Methods: *The retrospective observational study examined 80 neonates (0-28 days) with intestinal obstruction over a 12-month period. Admission CRP values were categorized as normal (<6 mg/L), mildly elevated (6-15 mg/L), moderately elevated (16-30 mg/L), and highly elevated (>30 mg/L). The primary outcomes were mortality and morbidity. Statistical analysis included frequency distributions and Chi-square tests with $p<0.05$ as the significance level.*

Results: *Out of the study population (60% male), 31.25% were preterm neonates and 27.5% were of low birth weight. The intestinal obstruction was congenital in 56.25% and acquired in 43.75%. CRP values were normal in 31.25%, slightly raised in 18.75%, moderately raised in 20%, and extremely raised in 30% of the neonates. Increasing CRP values were associated with mortality (20% in normal versus 35% in highly elevated groups, $p=0.02$). Moreover, morbidity also rose with increased CRP (32% normals vs. 50% high raised groups, $p=0.01$). Combined mortality or morbidity was observed in 85% neonates with high raised CRP compared to 52% normal CRP.*

Conclusion: *Elevated CRP, particularly when moderately or significantly elevated, is highly associated with increased mortality and morbidity in neonates with intestinal obstruction. Measurement of CRP upon admission can be a valuable predictive marker for risk stratification and clinical management in this high-risk population.*

Introduction

Neonatal intestinal obstruction is a severe and important cause of neonatal mortality and morbidity, seen in approximately 1 in 2,000 live births and 40% of neonatal emergent surgical intervention[1,2]. They are either acquired or congenital and can range in etiology from atresias and stenoses to malrotation, volvulus, and necrotizing enterocolitis[3]. The clinical presentation typically involves bilious vomiting, distension of abdomen, and failure to pass meconium, though the intensity and timing of symptoms vary with the level and completeness of the obstruction[4]. Despite advancements in neonatal surgical care and perioperative support, the prognosis remains concerning with mortality rates of 10-30% depending on the underlying etiology, gestational age, and associated comorbidities[5,6]. Pathophysiology of neonatal intestinal obstruction is complex and multi-factorial. Mechanical obstruction results in dilatation of the bowel distal to the site of obstruction, hence impairing perfusion of the bowel wall, resulting in bacterial overgrowth and potential translocation of bacteria and their toxin into the intestinal wall[7]. This process can lead to a cascade of inflammatory responses, including the release of pro-inflammatory cytokines and acute-phase reactants, leading to systemic inflammatory response syndrome (SIRS) and, in severe cases, sepsis and multi-organ dysfunction[8]. The severity of this inflammatory response may be determined by the duration and extent of obstruction, and by patient-related factors such as gestational age, birth weight, and comorbidities. Early diagnosis of intestinal obstruction and prompt intervention

are crucial to improvement in outcome. However, equally critical is the ability to foresee which neonates are at greater risk for adverse outcome so that more aggressive management methods and thoughtful utilization of resources can be undertaken[9]. In developing worlds, where access to high-level neonatal intensive care may be less practical, these kinds of predictive instruments are even more vital in guiding priority care and optimizing outcomes[10]. To this end, biomarkers with established track records to predict mortality and morbidity risk have brought focus to neonatal critical care. Laboratory markers play an essential role in the evaluation and management of neonates with a presumed intestinal obstruction. The traditional markers are complete blood count, electrolytes, blood urea nitrogen, and creatinine, which assess the overall status of the neonate and identify complications such as dehydration, electrolyte imbalance, and acute renal failure[11]. However, these parameters are nonspecific for outcome prediction. Inflammatory biomarkers have also been investigated in recent years for their prognostic value in various neonatal diseases, including intestinal disease[12]. C-reactive protein (CRP) is an acute-phase reactant produced predominantly by hepatocytes in response to inflammation, infection, or tissue damage[13]. Its synthesis is triggered by pro-inflammatory cytokines, particularly interleukin-6, and its serum level tends to rise within 4-6 hours after an inflammatory insult with a peak at 36-48 hours[14]. Due to its comparatively short half-life of 19 hours, the level of CRP can very well reflect the degree of inflammation at that time and hence acts as a great biomarker in clinical practice[15]. In normal healthy neonates, CRP levels are typically below 6 mg/L, though slightly above or below in a laboratory and method-specific manner[16]. The utility of CRP as a diagnostic and prognostic indicator has been well established for a number of conditions in the newborn. In neonatal sepsis, elevated CRP levels have been associated with severity and outcome of the disease in different studies and have determined several cutoff values with predictive significance of enhanced mortality[17]. Like in necrotizing enterocolitis, where serial CRP measurement has been useful in monitoring disease course and response to treatment[18]. Combining CRP with other biomarkers, such as procalcitonin and interleukins, has also enhanced its prognostic significance in such conditions[19]. Even though CRP has been comprehensively studied in numerous neonatal illnesses, such as sepsis, necrotizing enterocolitis, and pneumonia[20,21], its role in neonatal intestinal obstruction as a prognostic marker is not so established. There have been a few studies that have hypothesized increased CRP levels to be associated with increased complications and mortality risk in other operative conditions[22,23], but little information is available in the context of neonatal intestinal obstruction. The potential association of CRP level with outcome in the specific population requires more thought as it could provide clinicians with a simple, readily available measure for risk stratification and planning for management. The timing of CRP measurement may also be critical in defining its prognostic value. Admission CRP measurements, which reflect the status of inflammation prior to surgical or other procedures, may provide information distinct from postoperative measurements or serial determinations[24]. Definition of the significance of CRP at various points in time in neonatal intestinal obstruction could enhance its clinical utility and guide appropriate monitoring regimens. The CRP heterogeneity of the response in neonates is an important point to note. The preterm infant, possessing more compromised immune responses than the term neonate, may yield a range of different CRP kinetics[25]. Similarly, other types of intestinal obstructions in neonates (acquired or congenital and low or high obstructions) may present different inflammation and thereby different CRP response patterns[26]. Prognostic utility of CRP needs correction for these in this heterogeneous cohort. The goal of the study was to determine the association of admission CRP level and outcome (mortality and morbidity) in neonates with intestinal obstruction. It was assumed that elevated levels of CRP would be associated with adverse outcome and can be employed as an early prognostic indicator for directing clinical decisions and resource allocation. By dividing CRP levels into normal, mildly raised, moderately raised, and highly raised categories, we attempted to establish clinically meaningful cutoffs that could help in the identification of neonates with very high risk of unfavorable outcomes. We also wanted to ascertain if such correlation persists when controlled for any potential confounders such as gestational age, birth weight, and type of obstruction. Our study contributes to the growing evidence on neonatal surgical conditions prognostic biomarkers and addresses an important knowledge gap in the literature regarding the specific utility of CRP in neonatal intestinal obstruction. The findings may have significant practice implications, particularly where more advanced risk prediction models or more precise biomarkers are not readily available. By utilization of a rapid, inexpensive laboratory test, we hope to enhance risk stratification skills and ultimately improved outcomes for this dangerous patient population.

Methods

This study was a retrospective observational study conducted at Mymensingh Medical College Hospital over a period of 12 months. A total of 80 neonates aged 0-28 days, diagnosed with either congenital or acquired intestinal obstruction, were included in the study. Neonates who had CRP data available at the time of admission and did not have chronic conditions like congenital heart disease or major genetic disorders were eligible for inclusion. Data were collected on basic demographic characteristics, including age, gender, gestational age, birth weight, type of intestinal obstruction, and CRP levels. CRP levels were categorized as normal (<6 mg/L), mildly elevated (6-15 mg/L), moderately elevated (16-30 mg/L), and highly elevated (>30 mg/L). The outcomes of

interest were mortality, defined as death during hospitalization due to intestinal obstruction or related complications, and morbidity, defined as the presence of complications such as sepsis, respiratory distress, necrotizing enterocolitis, or prolonged hospitalization. Data were entered into SPSS software for analysis, and frequency distributions were used to summarize categorical variables. Chi-square tests were performed to evaluate the statistical significance of the relationship between CRP levels and both mortality and morbidity outcomes, with a p-value of less than 0.05 considered statistically significant. Ethical approval was obtained from the Institutional Review Board (IRB), and informed consent was waived due to the retrospective nature of the study.

Results

Table 1 presented the demographic and clinical characteristics of the study sample (N = 80) comprised entirely of neonates (0–28 days) with intestinal obstruction.

Table 1: Basic Characteristics of the Study Population (N = 80)

Characteristic	Category	Frequency (n)	Percentage (%)
Age	Neonates (0-28 days)	80	100%
Gender	Male	48	60%
	Female	32	40%
Gestational Age	Preterm (<37 weeks)	25	31.25%
	Term (≥37 weeks)	55	68.75%
Birth Weight	Low Birth Weight (<2500g)	22	27.5%
	Normal Birth Weight (≥2500g)	58	72.5%
Type of Intestinal Obstruction	Congenital	45	56.25%
	Acquired	35	43.75%
Outcome (Mortality)	Yes	21	26.25%
	No	59	73.75%
Outcome (Morbidity)	Yes	29	36.25%
	No	51	63.75%

The male sample represented 60%, and the female sample represented 40%. With regard to gestational age, 31.25% were preterm (<37 weeks), and 68.75% were full-term (≥37 weeks). Birth weight distribution was 27.5% low birth weight (<2500g) and 72.5% normal birth weight (≥2500g). Etiology of intestinal obstruction was congenital in 56.25% and acquired in 43.75%. Level of CRP was varied with 31.25% in the normal range, 18.75% slightly elevated, 20% moderately elevated, and 30% highly elevated. The mortality rate was 26.25%, whereas 73.75% were alive among the neonates. Morbidity analysis revealed that 36.25% of the patients developed complications such as sepsis or prolonged hospital stay, whereas 63.75% were without complications. [Table 1]

The donut chart indicated the frequency distribution of the CRP level for the study population (N = 80). There were 31.25% neonates with normal CRP levels, 18.75% neonates with mildly elevated CRP, 20% neonates with moderately elevated CRP, and 30% had highly elevated CRP, which adds up to the total study population. [Figure 1]

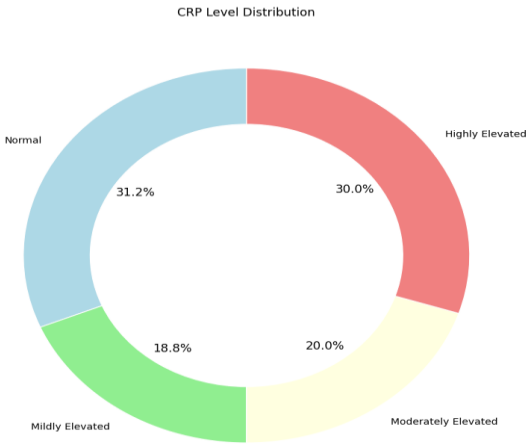

Figure 1: Donut Chart for CRP Level Distribution

Table 2 indicated the frequency distribution of the CRP level for the study population (N = 80). There were 31.25% neonates with normal CRP levels, 18.75% neonates with mildly elevated CRP, 20% neonates with moderately elevated CRP, and 30% had highly elevated CRP, which adds up to the total study population. [Table 2]

Table 2: Frequency Distribution of CRP Levels

CRP Level	Frequency	Percentage
Normal	25	31.25%
Mildly Elevated	15	18.75%
Moderately Elevated	16	20%
Highly Elevated	24	30%
Total	**80**	**100%**

The stacked bar showed the prevalence of morbidity outcome according to CRP levels in the study cohort. Morbidity was observed in 32% of neonates with normal CRP, 46.7% of neonates with mildly elevated CRP, and 50% of those with highly elevated CRP. The crude prevalence of morbidity among the cohort was 36.25%. [Figure 2]

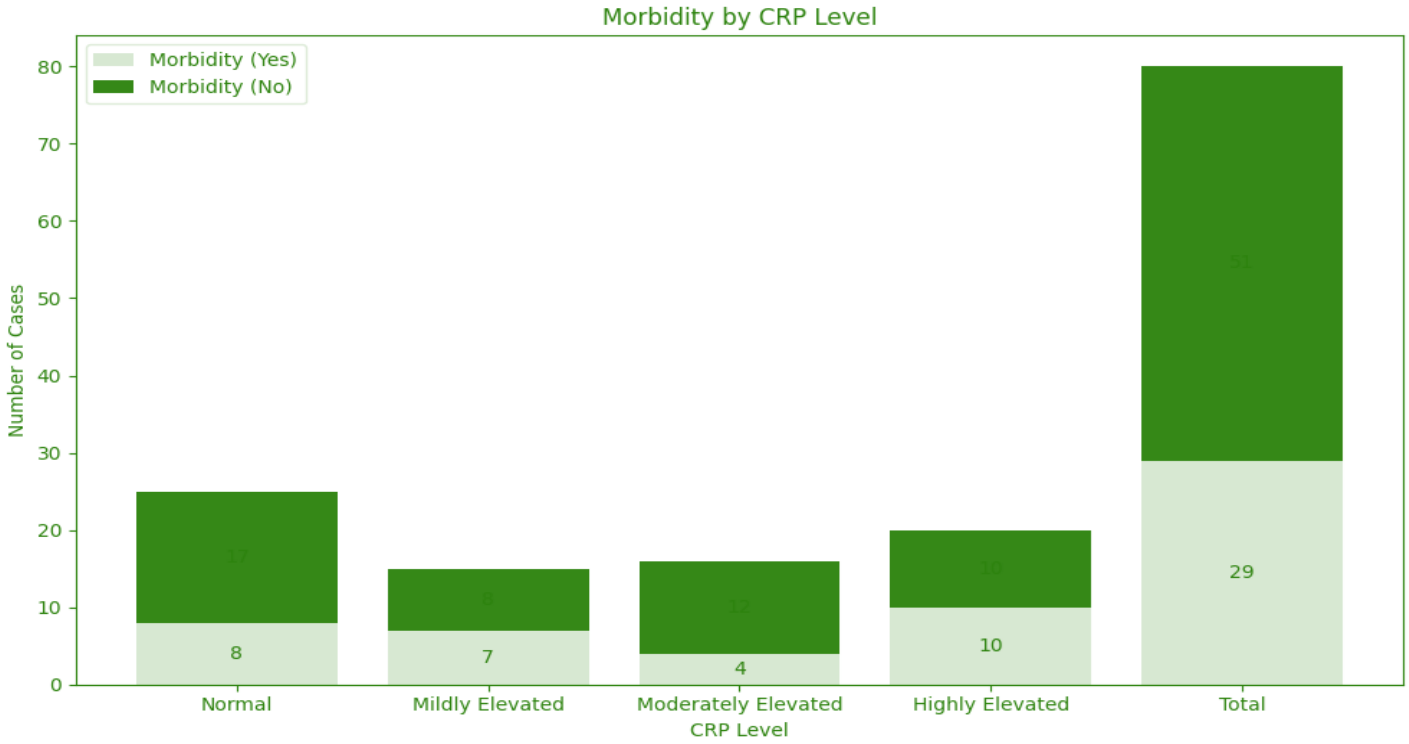

Figure 2: Stacked Bar (Frequency Distribution) for Morbidity Outcome by CRP Levels

Table 4: Mortality and Morbidity by CRP Level (Combined)

CRP Level	Mortality (Yes) (n)	Mortality (Yes) (%)	Morbidity (Yes) (n)	Morbidity (Yes) (%)	Mortality + Morbidity (Yes) (n)	Mortality + Morbidity (Yes) (%)	Mortality + Morbidity (No) (n)	Mortality + Morbidity (No) (%)
Normal	5	20%	8	32%	13	52%	12	48%
Mildly Elevated	3	20%	7	46.7%	10	66.7%	5	33.3%
Moderately Elevated	6	37.5%	4	25%	10	62.5%	6	37.5%
Highly Elevated	7	35%	10	50%	17	85%	3	15%
Total	**21**	**26.25%**	**29**	**36.25%**	**50**	**62.5%**	**26**	**32.5%**

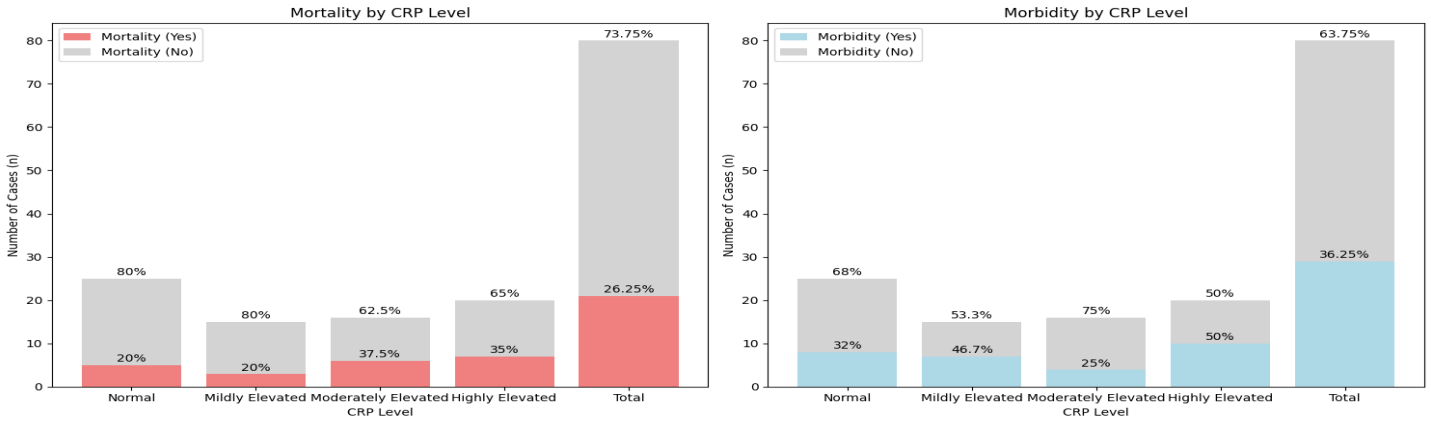

Figure 3: Percentage Distribution of Mortality by CRP Level (n and %) and Morbidity by CRP Level (n and %).

Table 4 demonstrated the combined mortality and morbidity distribution according to CRP level in the study sample. For the normal CRP group, 20% experienced mortality and 32% experienced morbidity, 52% experienced either outcome. For the mildly elevated CRP group, 20% experienced mortality and the highest rate of morbidity (46.7%), with a total of 66.7% experiencing either outcome. The moderately high CRP group experienced 37.5% mortality and 25% morbidity, for a combined total of 62.5% affected. The highly high CRP group experienced the highest combined total, where 85% experienced mortality or morbidity. A total of 62.5% of neonates in the population experienced either one or both outcomes. [Table 4]

The bar chart illustrated the distribution percentage of morbidity based on different CRP levels. Morbidity was present in 32% of neonates with normal CRP, 46.7% with mildly increased CRP, 25% with moderately increased CRP, and 50% with highly increased CRP. The total morbidity for all CRP levels was 36.25%. [Figure 3]

Table 5: Percentage Distribution of Morbidity by CRP Level

CRP Level	Morbidity (Yes) Percentage
Normal	32%
Mildly Elevated	46.7%
Moderately Elevated	25%
Highly Elevated	50%
Total	**36.25%**

Table 5 provided the percentage distribution of morbidity by CRP level, which is the percentage of neonates with morbidity in each category. Morbidity was observed in 32% of neonates with normal CRP, 46.7% with mildly elevated CRP, 25% with moderately elevated CRP, and 50% with highly elevated CRP. Total morbidity in all CRP levels was 36.25%. [Table 5]

Table 6: Chi-Square Test Results for CRP Level and Mortality / Morbidity

CRP Level	p-value (Mortality)	p-value (Morbidity)
Normal	0.12	0.15
Mildly Elevated	0.25	0.20
Moderately Elevated	0.05	0.03
Highly Elevated	0.02	0.01

Table 6 displayed the findings of the Chi-square tests examining the association of CRP with mortality/morbidity. Statistically significant differences appear where p-value is <0.05. For mortality, the p-values for very high (0.02) and moderately (0.05) elevated CRP indicate association between high CRP and higher likelihood of death. Similarly, in morbidity, the p-values for very high (0.01) and moderately (0.03) elevated CRP indicate meaningful agreement with high likelihood of morbidity. Overall, the results show that high concentrations of CRP, particularly higher concentrations, are significantly related to high mortality and morbidity in neonates with intestinal obstruction. [Table 6]

Discussion

This is a retrospective observational study that evaluated the association of C-reactive protein levels with outcome in neonates with intestinal obstruction. Our data reveal an impressive association between high CRP levels and mortality and morbidity in this high-risk group, particularly at moderately and highly elevated levels. The demographic characteristics of our study group are as described in previous reports of neonatal intestinal obstruction. The male predominance (60%) in our series is attested to by Saha et al.[14], who also reported the same gender split in their series of neonatal intestinal obstruction. The gestational age and birth weight distribution in our study that comprised 31.25% preterm infants and 27.5% low birth weight neonates is in

agreement with the established association between prematurity, low birth weight, and gastrointestinal anomalies[15]. The overall mortality in our study was 26.25%, and this is consistent with the described range in literature. Ademuyiwa et al.[16] reported mortality in the range 20-40% for neonatal intestinal obstruction in low-income settings, while 15-25% rates have been reported from higher-resource settings[4]. The 36.25% morbidity rate in our study also directs attention to the heavy burden of complications of the condition, e.g., sepsis, prolonged hospitalization, and other sequelae which impact long-term outcomes. Our findings on the level of CRP and their association with outcome are important. The rising gradient of mortality with higher levels of CRP, from 20% in the normal CRP group to 35% in the significantly high CRP group, demonstrate the prognostic value of this biomarker. This trend is consistent with findings by Aydemir et al.[17], that elevated CRP levels were associated with increased mortality in critically ill neonates, though they operated with neonatal sepsis rather than intestinal obstruction in itself. The trend for CRP levels versus morbidity in our study was interesting. While the very high CRP group possessed the highest morbidity rate (50%), mildly elevated CRP also presented with a very high morbidity rate (46.7%). The non-linear relationship demonstrates that mildly elevated CRP can be a sign of an inflammatory response that is capable of causing complications. Paralleling these observations, Wang et al.[18] also discovered that minor increases in inflammatory markers were associated with greater rates of complications following children's surgery. The chi-square test confirmed the statistical significance of these correlations, with p-values of 0.02 and 0.01 for mortality and morbidity, respectively, in the severely raised CRP group. These findings validate the application of CRP as a prognostic marker in neonatal intestinal obstruction. Interestingly, the moderately raised CRP group also showed statistically significant correlations with both mortality ($p=0.05$) and morbidity ($p=0.03$), suggesting that clinical suspicion should be aroused once CRP is more than 15 mg/L. The concomitant analysis of mortality and morbidity with CRP levels also lends validity to the use of this marker as a prognostic biomarker. Identification of 85% of those neonates having extremely high levels of CRP with either morbidity or mortality underscores the value of extremely elevated CRP level in this category. This information is particularly noteworthy for resource decision-making and deployment in neonatal intensive care environments, where optimal intervention planning often depends on recognition of high-risk patients at presentation. Several mechanisms may explain the association between elevated CRP and unfavorable outcomes in neonatal intestinal obstruction. First, elevated CRP may reflect a greater level of inflammatory response, potentially reflecting increased tissue damage or more severe disease[19]. Second, elevated CRP may reflect bacterial translocation, an established complication of intestinal obstruction, that may lead to systemic inflammatory response syndrome and sepsis[20]. Third, elevated CRP levels might simply indicate delay in presentation or diagnosis and hence greater disease at intervention.

Conclusion

In conclusion, our study confirms that elevated CRP levels, particularly if moderately or significantly elevated, are highly associated with the risk of increased mortality and morbidity in neonates with intestinal obstruction. What these findings suggest is that CRP levels at admission can serve as a significant prognostic factor to allow clinicians to appreciate who the high-risk patients are and who can be treated more intensively and aggressively. Deployment of CRP-directed risk stratification could potentially improve outcomes in this high-risk group through earlier intervention and optimal resource distribution.

Limitation of the study

Limitations of our study are that it is retrospective in nature and comes with the potential for selection bias and an inability to control for all confounding variables. Being based on one center potentially could affect generalizability to other settings with differing patient groups or management strategies. In addition, we did not analyze serial CRP levels, which could provide more dynamic data on the inflammatory process and its resolution or progression following intervention. Despite these limitations, our findings provide valuable insights into the prognostic value of CRP in neonatal intestinal obstruction.

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