

## Clinical and Surgical Aspects in Necrotizing Enterocolitis

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### Rezumat

#### *Aspecte clinice și chirurgicale în enterocolita ulceronecrotică*

Scopul lucrării este acela de a stabili dacă parametrii clinici și radiologici pot determina prognosticul și progresia patologiei, necesitatea realizării laparotomiei sau a drenajului peritoneal, precum și mortalitatea în rândul pacienților tratați chirurgical. Un număr de 51 de pacienți diagnosticați cu enterocolită ulceronecrotică internați în clinica de chirurgie a Spitalului de Urgență pentru Copii "Grigore Alexandrescu" în perioada 2005-2011 au fost evaluați, fiind adunate informații cu privire la examenul clinic și radiologic. Mortalitatea în rândul pacienților tratați chirurgical este de 59.9%. Toți pacienții diagnosticați cu enterocolită stagiul III au fost supuși unei intervenții chirurgicale, mortalitatea în rândul acestora fiind crescută. S-a constatat că pentru pacienților la care simptomatologia a debutat mai târziu, patologia a fost mai severă și prognosticul vital al acestor copii a fost unul prost.

**Cuvinte cheie:** stadializare Bell, debutul simptomatologiei, examen radiologic

of the pathology, the necessity of performing laparotomy for patients with peritoneal drain and the mortality in surgically treated neonatal necrotizing enterocolitis patients.

**Material and Methods:** A number of 51 cases with necrotizing enterocolitis from our institution were reviewed (from 2005 to 2011) and information on patient demographics and data about the clinical and radiological parameters was collected. **Results:** Of the 51 patients, 29 were (56.8%) males and 22 (43.2%) females. Age at presentation ranges between 1 and 87 days, with a mean 18.71 days. Birth weight varies between 400-4700g (mean 1979.6 g  $\pm$  1012.5). The mortality rate in our study was 45% (23 patients out of 51).

**Conclusions:** The mortality rate in our series was 45%. Even though Bell stage III patients have clear indications for surgery, the procedure involves high fatality. Patients who undergo surgery are more likely to die than the ones who do not. We found that a later debut of symptoms should be an alarm sign for both the severity of the condition and for its outcome.

**Key words:** Bell's stage, neonatal enterocolitis, debut symptoms, radiological findings

### Abstract

**Background:** The purpose of the paper is to establish whether clinical and radiological parameters can predict the progression

### Introduction

Necrotizing enterocolitis (NEC) is one of the most common surgical emergencies in newborns, with a mortality rate that exceeds that of any other gastrointestinal condition that requires surgical repair (1). NEC diagnosis requires a combination of clinical, laboratory and radiological findings, which were divided into systemic, abdominal and radiological signs by Walsh et al by modifying Bell's original staging criteria (2).

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Various clinical and laboratory parameters have been extensively studied in other series and have been found to be related to the etiology and mortality of the pathology (3). One of the problems in establishing the diagnosis of NEC is the fact that clinical findings can be unreliable because certain systemic and abdominal signs are frequent among sick newborns. The same can be said about certain biochemical abnormalities such as metabolic acidosis or hematological abnormalities (4,5). Most surgeons rely on radiological signs (especially pneumatosis intestinalis) in order to establish the diagnosis of NEC. However, pneumatosis intestinalis has low sensitivity and decreased specificity (6).

NEC can develop in any portion of the gastrointestinal tract, with the small bowel and proximal large bowel being most frequently affected (7).

Mortality in infants with NEC varies between 15% and 30%, with a higher rate in newborns that were surgically treated than in those who only required medical treatment. The surgical management includes resection of the affected part of the bowel and creation of an ostomy, resection and primary anastomosis or peritoneal drainage (8,9).

## Material and Methods

This was a retrospective observational study, carried out in the Department of Pediatric Surgery at The "Grigore Alexandrescu" Emergency Clinical Hospital for Children, between January 2005 and December 2011.

The following criteria were used in order to establish the NEC diagnosis:

- 1) Clinical or radiological evidence of intestinal perforation;
- 2) Abdominal wall erythema/edema indicating gangrene;
- 3) Presence of abdominal, palpable mass;
- 4) Patients failing to respond to conservative management with a rapid decline in their health status.

We have excluded from our series those patients presenting Bell's stage I and those who developed NEC after surgery.

The initial diagnosis of NEC was clinical and based mostly on signs and symptoms such as: abdominal distension, gastric residue, vomiting (feeding intolerance), lack of stool, diarrhea, hematochezia, abdominal wall erythema.

The clinical parameters we followed were: gestational age, birth weight, age of presentation, primary sign/symptom at the time of admission and response to treatment. Plain abdominal radiography was used in order to assess all the patients. The radiographs were interpreted by pediatric radiologists, pertinent date being thus obtained. The radiological criteria we evaluated as predictors of NEC were pneumoperitoneum, intestinal distension, peritoneal fluid, air fluid levels, pneumatosis intestinalis.

Both clinical and radiological parameters were then evaluated in stratified groups and the statistical significance was observed. During the initial assessment of our patients, laboratory tests were also performed, but as these parameters are not the object of this paper, they were not included in our study. As NEC is a severe inflammatory disorder of the gastrointestinal tract, it is our belief that these laboratory

findings could be potentially useful in the diagnosis of this pathology and that this correlation should be further evaluated in another, more extensive study.

We have divided our patients into groups according to the following criteria:

- a) Patients with primary peritoneal drainage (PPD) vs. primary laparotomy;
- b) Survivors and non-survivors;
- c) Operated vs. non-operated patients;
- d) Bell's stage II vs. stage III patients.

By taking into account the health status of the patients and the surgical teams' experience, in 5 cases the management of the newborns was primary percutaneous drainage (PPD), while for rest of the children primary laparotomy performed. The surgical procedures, from the least to the most frequently used ones were: exploration and drainage, intestinal resection with anastomosis, primary perforation closure and intestinal resection with ileo/colostomy.

Some patients were treated conservatively (without any drain) and were kept under observation for 48 hrs.

## Results

A total of 50 patients fulfilled the criteria for inclusion in our series. There were 29 males (56.8%) and 22 (43.2%) females (ratio 1.32:1). Weight at birth varied between 400 and 4700 g (mean 1979.6 g  $\pm$  1012.5). Age at presentation ranged from 1 to 87 days (mean 18.71 days).

There were 38 premature infants, born within 25 to 36 weeks of gestation. Most of our patients were born preterm (74.5%). (Table 1)

Signs and symptoms at presentation are shown in Fig. 1, each according to the stage of NEC as shown by Bell. Most stage II patients presented feeding intolerance (vomiting or gastric residue) and abdominal distension. When examining stage III patients, abdominal distension with wall erythema was encountered. 45% of the patients accused the absence of stools.

A radiological assessment of our patients was done: all patients presented intestinal distension, in 49% of the cases pneumoperitoneum was encountered (25 patients), while 20% of patients were found to have air-fluid levels (10 cases) and 18% pneumatosis intestinalis (9 cases). No fixed loop cases were identified. (Fig. 2) In our series, all patients with pneumoperitoneum underwent surgery, while in only 4 of the 9 patients with pneumatosis intestinalis surgical management was attempted.

**Table 1.** Correlation between the number of cases with NEC and gestational age of the patients

Gestational age	Number of cases
25-30 weeks	17 (33.3%)
31-36 weeks	21 (41.2%)
> 37 weeks	13 (25.5%)
Total	51

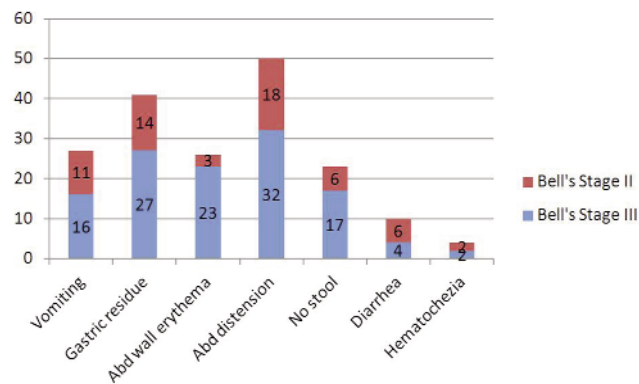


Figure 1. Bar graph showing the various kinds of presentation in patients with NEC

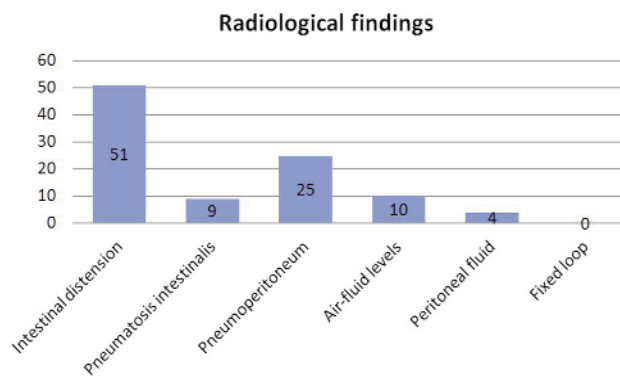


Figure 2. Bar graph showing the radiological findings in patients with NEC

When interpreting the abdominal radiographs from the stage III group, we found that 7 patients (21.87%) did not present pneumoperitoneum. In this case, the surgical indications were the presence of abdominal wall erythema, abdominal distension and laboratory findings. As for the stage II group, the surgical indication was the rapid decline of health status, despite correct medical management.

The appropriate management of each patient was established by taking into account Bell's stage of NEC. 37.25% patients were included in the Bell's stage II group, while 62.75% presented Bell's stage III NEC. In Fig. 3 we have outlined the treatment given to our patients according to the NEC stage that was diagnosed. 14 out of the 51 patients (27.45%) were treated conservatively (without any drain) and after being observed for 48 hrs, these patients were found to be stable. Only 1 death was recorded in this group of children.

All the patients diagnosed as presenting Bell's stage III were operated, while only 5 out of the 19 (26.31%) patients with Bell's stage II underwent surgery. (Table 2)

37 patients (72.55%) were surgically treated. Out of this

Table 2. Management of NEC patients according to Bell's stages II/III

		Management		
		Conservative	Surgical	Total
Bell's Stage	II	14	5	19
	III	0	32	32
Total		14	37	51

group, 32 patients presented Bell's stage III, while the rest were diagnosed with stage II (86.48% vs. 13.51%). The risk of Bell's stage III patients dying is 4.66 higher than that of stage II patients ( $p=0.012$ ). In our group there was a 73.7% cure rate in Bell stage II patients and only 37.5% in stage III patients (Fig. 4)

Even though most of the Bell stage III patients have clear indications for surgery, the procedure involves a high fatality risk. Patients that undergo surgery are 5.37 times more likely to die than those that do not ( $p=0.015$ ). 59.5% of the patients

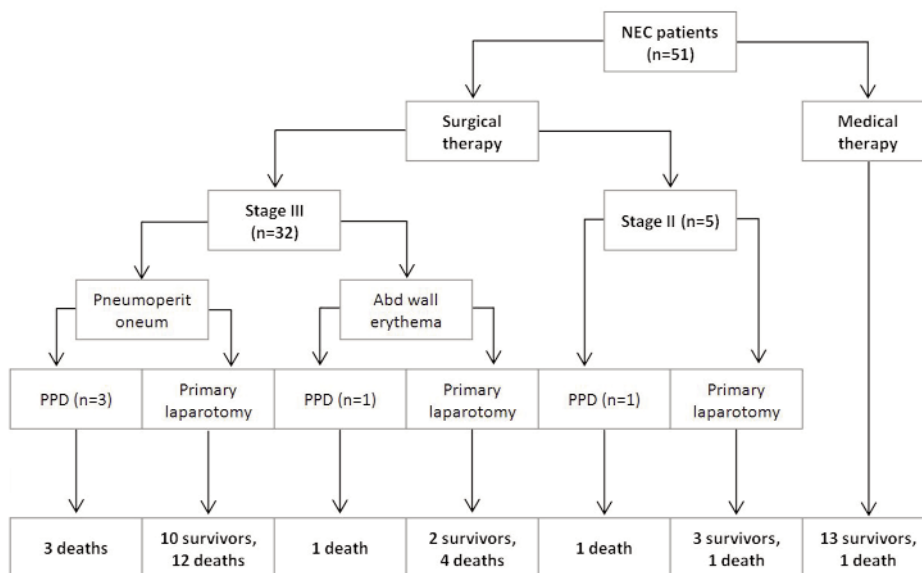


Figure 3. Flow chart showing the treatment and outcome of the 51 patients presenting NEC

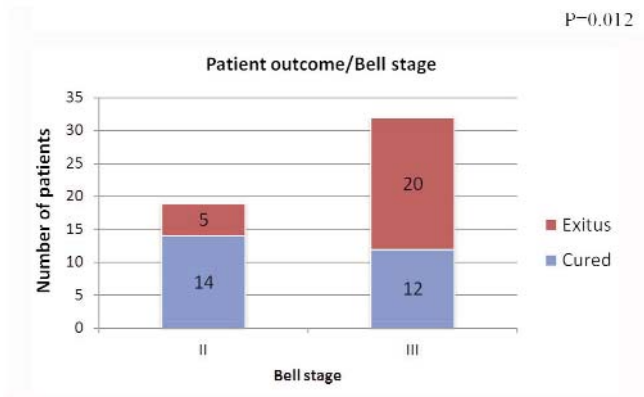


Figure 4. Patient outcome in correlation with Bell's stages

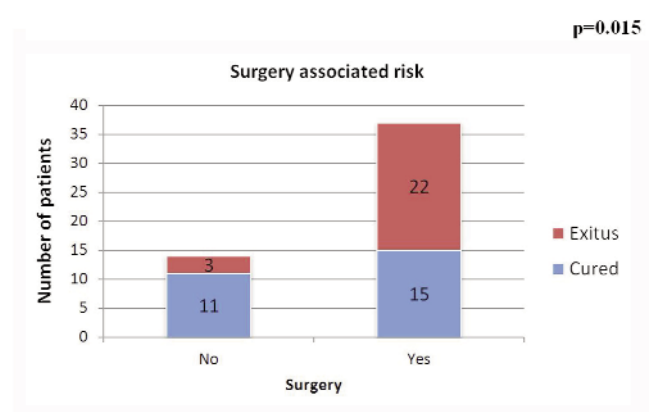


Figure 5. Surgery associated risk

that underwent surgery died. (Fig. 5)

5 patients (13.51%) were managed by primary percutaneous drainage (PPD) and out of them 4 were diagnosed with stage III, while 1 presented stage II NEC. The remaining 32 patients (86.49%) were managed by primary laparotomy, 28 of these children presenting stage III and 4 of them stage II.

The primary laparotomy procedures we used were: exploration and drainage (performed in 4 cases), intestinal resection with anastomosis (5 cases), primary perforation closure (8 cases) and intestinal resection with ileo/colostomy (15 cases).

The mortality rate for the group treated by primary laparotomy was 53.12%. This rate varied for each surgical procedure as follows: 37.5% for the group who underwent primary perforation closure, 50% for the group of patients who had exploratory laparotomy with drainage, 53.33% for those with intestinal resection and ileo/colostomy and 80% for the group with intestinal resection. None of the patients who underwent PPD survived. (Table 3)

We have noticed that patients that survived also had a faster debut of symptoms. The medium time for those who survived was 1.58 days, that for those who did not being 3.76 days, the data being statistically significant (p=0.04). Bell stage II patients also have a longer period for the debut of symptoms (2.56 days) whereas stage II have a faster one (1.11 days). This data is statistically significant (p=0.02). (Fig. 6)

### Discussion

Several large population-based studies have found the incidence of NEC to be 0.7 to 1.1 cases in 1000 live births. Data obtained from other authors have shown no higher prevalence of NEC in either male or females (10). In our series, we have found a slightly higher number of NEC cases in males, with a ratio of 1.32:1.

NEC is considered primarily a pathology related to prematurity. Over 90% of cases occur in preterm infants (10). Gestational age in our patients varied between 25 to 40 weeks, with a mean of 33.04 weeks. Out of the 51 cases we have reviewed, 13 children (25.5%) were born after more than 37

Table 3. Comparison between survivors and non-survivors based on the surgical procedures

	Exitus	Survived	Total
Perforation primary closure	3	5	8
Resection and anastomosis	4	1	5
Resection and stoma	8	7	15
Exploration and drainage	2	2	4
Primary percutaneous drainage	5	0	5

weeks of gestation. This number is higher than the one found in other studies, where only 5-20% of patients had a gestational age higher than 37 weeks (11).

Fixed abdominal masses and erythema of the abdominal wall are strongly predictive of NEC. The problem is that these findings are only present in 10% of the patients (10). In our series, we have found that almost 51% of the patients

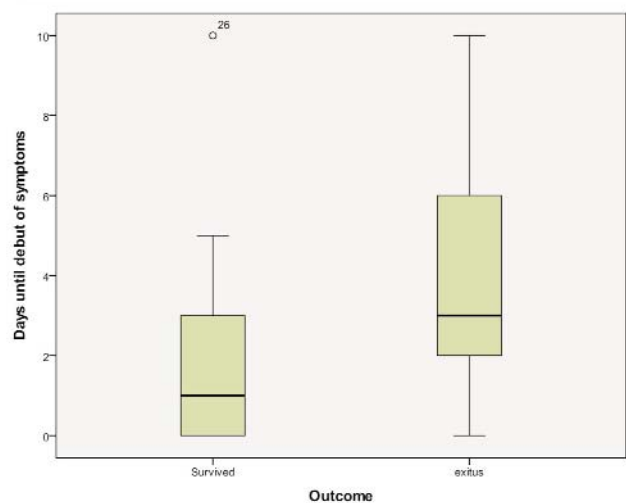


Figure 6. Outcome in correlation with number of days until debut of symptoms

presented erythema of the abdominal wall, while in 90% of cases abdominal distension was present.

Radiological signs play an important part in making the diagnosis of NEC, and while it would be tempting to use the presence/absence of specific signs to establish the diagnosis, the question one has to ask is how reliable these findings are.

The presence of pneumoperitoneum on the abdominal radiograph is widely accepted as an absolute indication for surgical treatment and has been described in 50% to 75% of patients with NEC (13). In 49% of our cases pneumoperitoneum was present.

Intestinal distension is the most frequently encountered radiological sign in patients with NEC (55% to 100% of cases) (10). All the patients included in our series were found to have signs of intestinal distension on the radiographs.

Previous studies have reported the presence of radiological signs suggestive of peritoneal fluid in 11% of cases and have shown a higher incidence of patient mortality in these patients. Our findings were that radiological signs suggestive of peritoneal fluid were positive in only 7.84% of our patients. This number is slightly lower than the one previously reported.

Many studies have investigated the severity NEC and have monitored the patients who were conservatively treated. The results found were that 60-80% of NEC cases are managed medically (10). Of the patients included in our series, only 27.45% were treated conservatively. This number is lower than the one encountered in literature.

Approximately 20-40% of cases with NEC require surgical intervention (12). In our group of patients, 72.55% were surgically treated.

In their study, Moss et al have failed to determine which, between PPD and laparotomy, is the superior treatment option. Even if laparotomy has been considered the established method of dealing with necrosis and perforation, many surgeons turn to peritoneal drainage as the initial and, in some cases, the definitive procedure. Although some investigators have suggested that PPD is an appropriate treatment option, it has been shown that infants treated with PPD often require subsequent laparotomy and have a higher mortality rate (13). In our series, all patients for whom PPD was used as the initial procedure, regardless of the type of NEC (i.e. Bell's stage II or III), died.

Despite the progress in both surgical and intensive care units, NEC is still an important cause of mortality and morbidity in newborns. Mortality ranges from 15% to 30% and is increased when surgical intervention is required (almost 50%) (10). In our study, the mortality in all patients was 45%, which is higher than the rate encountered in previous reports. As for the group of patients who were surgically treated, we have found the mortality rate to be 59.5%.

## Conclusions

The mortality rate in our series was 45%. Even though Bell stage III patients have clear indications for surgery, the procedure involves high fatality. Patients who undergo surgery are more likely to die than the ones who do not. We found that a later debut of symptoms should be an alarm sign for both the severity of the condition and for its outcome.

It is difficult to predict mortality of NEC patients on the basis of either clinical or radiological parameters. In our opinion, in order to find valid results, a larger sample size group should be used.

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