

## ORIGINAL ARTICLE

### Assessment of Predictors of Mortality in Neonatal Intestinal Obstruction

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**How to cite:** Ali I, Mufti GN, Bhat NA, Baba AA, Sheikh KA, Hamid R, et al. Assessment of predictors of mortality in neonatal intestinal obstruction. J Neonatal Surg. 2018; 7:2.

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#### ABSTRACT

**Background:** Neonatal intestinal obstruction (NIO) continues to be a life-threatening condition with high mortality rates especially in developing countries. Highly skilled specialized care and facilities are required for survival. This study was conducted to assess various factors responsible for outcome in such neonates, so that extra attention is paid to the ones at high risk, with the idea to bring down the mortality rates in neonates admitted with intestinal obstruction.

**Materials and Methods:** This study was a prospective observational study conducted on all neonates admitted with features of intestinal obstruction in our hospital from February 2014 to August 2016. The patients were followed up for a minimum of 1 month. Data was collected on prescribed proforma and analyzed for age, sex, prematurity, birth weight, clinical features, duration of symptoms, diagnosis, lab investigations, surgical procedure performed, complications etc. using the Statistical Package for Social Sciences (SPSS).

**Results:** There were 120 neonates with intestinal obstruction, of which 92 neonates survived and 28 died. The mortality rate was 23.33%. There were 74 males and 46 females. The mean gestational age was  $38.2 \pm 1.77$  wks with a range between 32 to 41 wks. The mean age at presentation was 5.58 days with a range between 5 hrs to 26 days. The mean weight at presentation was 2510g. Mean duration of symptoms was 3.40 days. Gross congenital anomaly was seen in 22 neonates. Sepsis on admission was noted in 51 patients out of whom 23 died. Twenty-two patients presented with perforation peritonitis, of which 14 expired. Fifty-four neonates experienced significant in-hospital delay in surgery. The mean duration of stay in the hospital was 8.40 days. Overall, 92 neonates were discharged from the hospital.

**Conclusion:** Neonatal intestinal obstruction is still associated with high mortality. After analyzing various factors we conclude, that increased age at presentation, delay in seeking treatment after the onset of symptoms, CRP/ blood culture positive sepsis on arrival, thrombocytopenia, acute kidney injury (raised urea and creatinine), acidosis and coagulopathy on admission, bowel perforation with peritonitis and the need for continued mechanical ventilation after surgery were the statistically significant risk factors for mortality in neonates with NIO in our series. However, sex, mode of delivery, gestational age, weight at presentation, hypothermia on arrival, associated gross congenital anomalies, delay in surgery after admission (in-hospital delay) and duration of stay in hospital were found to be statistically insignificant risk factors for mortality in our series.

**Key words:** Neonatal intestinal obstruction; Mortality; Specialized care; Early diagnosis; Intensive care

#### INTRODUCTION

Neonatal intestinal obstruction (NIO) constitutes a major portion of neonatal surgical problems, and unlike in adults, almost all are due to congenital causes. The pathological sequelae of NIO progress rapidly and is poorly tolerated by the neonates. It is associated with high mortality if not diagnosed promptly and treated adequately in time. [1] The incidence of NIO is approximately 1 in 2000 live

births. [2] There was no data previously recorded from our region about this subject.

These neonates usually require surgical management by trained pediatric surgeons in medical centers equipped with specialized anesthetic and neonatal intensive care. Intestinal obstruction in the neonate may be due to a variety of conditions, like anorectal malformations, bowel atresia and stenosis, malrotation, meconium ileus, meconium plug

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E mail: gowharmufti@yahoo.co.in  
Submitted: 16-08-2017  
Conflict of interest: None

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Accepted: 19-11-2017  
Source of Support: Nil

syndrome, Hirschsprung's disease, and other rarer causes. These diseases have varied etiology and diverse pathophysiology. [3]

Neonates with unrecognized intestinal obstruction deteriorate rapidly. It can result in aspiration of vomit, sepsis, mid-gut infarction or enterocolitis.

The principal features of NIO are bile staining vomiting, abdominal distension and failure to pass meconium (95 % of normal neonates pass meconium in the first 24 hours of life). [1]

Improved obstetric care, neonatal anesthesia, surgical techniques and perinatal support, including neonatal intensive care and appropriate management of associated abnormalities, have all contributed to the improved survival of the surgical neonate. [4] The mortality associated with NIO ranges between 21 and 45% in developing countries, while it is less than 15% in Europe. [5, 6]

## MATERIALS AND METHODS

This study was conducted in the Department of Pediatric Surgery, Sher-i-Kashmir Institute of Medical Sciences, Srinagar (SKIMS) which is the only tertiary care public referral hospital in Jammu & Kashmir state of India, which caters with surgical neonates. Clearance from the ethical committee of the hospital was obtained. This study was a prospective observational study conducted on all neonates admitted with features of intestinal obstruction in the department from February 2014 to August 2016. All of them were followed up for a minimum of 1 month.

Neonates suspected to have intestinal obstruction were admitted in nursery. A detailed clinical and diagnostic workup was done in all cases. Serum electrolytes, complete blood count, arterial blood gas, blood urea, serum creatinine, blood glucose, C-reactive protein, blood cultures (if indicated) etc. were done in all cases. Abdominal x-ray (antero-posterior and lateral) were done in all cases, whereas contrast study (upper GI/contrast enema) and USG abdomen were done when indicated.

General treatment was given, which included warm care, maintenance of fluid and electrolytes, nasogastric suction, appropriate antibiotics, oxygen to maintain saturation when indicated etc. Exploration was done when indicated as early as possible after the baby was properly optimized for surgery. After surgery, the patients were shifted to NICU and standard post-operative care was provided there. Total parenteral nutrition (TPN) was started when

indicated. The babies were followed up till discharge from the hospital or death. The parents were instructed for follow up for 1 month after discharge. Survival 1 month after surgery was taken as end point for data analysis.

Data was collected on prescribed proforma. The standard statistical methods were employed. The two groups were compared using two sample independent t-test, Chi-square and Fisher exact tests. All the results were discussed at 5% level of significance i.e. p-value <0.05 was considered significant. The data was analyzed statistically with the help of statistical software SPSS v.22.

## RESULTS

A total of 120 neonates (101 term and 19 preterm) with intestinal obstruction were included in this study, of which 92 neonates survived and 28 (17 males and 11 females) died. The mortality rate was 23.33%. The mode of delivery was not statistically significant risk factor for mortality (p=0.83).

There were 74 males and 46 females with a male:female ratio of 1.6:1. Sixty-two neonates were born by vaginal delivery and 58 by caesarian section. Antenatal USG was available with only 22 patients, out of which 4 had features suggestive of intestinal obstruction. The mean gestational age was  $38.2 \pm 1.77$  (range 32-41 wks). The mean gestational ages in those who survived and in those who died were  $38.38 \pm 1.51$  and  $37.89 \pm 2.42$  respectively (p=0.20). The mortality rates among term and pre-term babies were 19.8% (20/101) and 42.1% (8/19) respectively (p=0.07). The mean age at presentation in our series was 5.58 days (range 5 hrs.-26 days). The mean ages at presentation in those who survived and in those who died was 5.60 days (range 5 hrs. to 26 days) and 5.49 days (range 12 hrs.-16 days) respectively (p=0.96). Fifty-one patients presented in first 2 days of life and out of those 45 survived (mortality rate 11.76%) and 69 patients presented after 2 days and out of those only 47 survived (mortality rate 31.88%) (p=0.02) (Fig. 1).

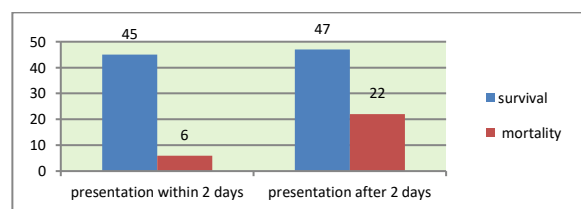


Figure 1: Mortality in neonates who presented within and after 2 days of life

The mean weight at presentation in our series was 2510g (range 1500-3500g). The mean weights at

presentation in those who survived and in those who died were  $2560 \pm 510$ g (range 1500-3500g) and  $2360 \pm 460$ g (range 1500-3500g) respectively ( $p=0.28$ ). Abdominal distention was the most common presenting symptom (Table 1). Mean duration of symptoms in our series was 3.40 days (range 5 hrs-11 days). The mean duration of symptoms in those who survived and in those who died were  $3.29 \pm 2.59$  days (range 1-11 days) and  $3.75 \pm 1.81$  days (range 1-7 days) respectively ( $p=0.38$ ). Twenty-two neonates (18.33%) in our series had associated gross congenital anomalies (GCA), of which 10 expired (45.4%) and 12 survived (Table 2).

Table 1: Frequency of symptoms on arrival in our patients

Symptoms	Survival grp. (n=92)	Mortality grp. (n=28)	Total (n=120)
Abdominal distention	89	28	117
Vomiting	79	25	104
Failure to pass meconium/stools	67	20	87
Refusal of feeds	64	20	84
Lethargy	52	18	70

Table 2: Frequency of congenital anomalies in our patients (n=22)

	Survival grp	Mortality grp
Down's syndrome	3	4
Congenital heart disease	2	4
Spinal abnormality	3	3
Limb deformity	2	3
Renal agenesis	1	1
Hydronephrosis	2	0
Epidermolysis bullosa	1	0

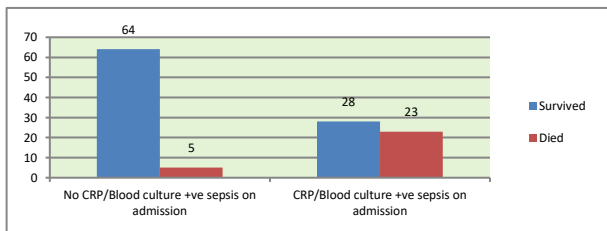


Figure 2: Outcome of patients as per presence or absence of CRP/ blood culture positive sepsis on admission.

However, on statistical analysis, the associated GCA was not a statistically significant risk factor for mortality in our series. Eighty-seven patients presented with hypothermia on arrival, of those 24 died. The mortality rates in the “hypothermia on arrival group” and “no hypothermia on arrival group” were 27.58% and 12.12% respectively. The mortality rates in the “sepsis on admission group” and “no sepsis on admission group” were 45% and 7.2% which was statistically significant with a p-value of 0.0001 (Figure 2).

The laboratory profile on admission was subjected to statistical analysis. Thrombocytopenia ( $\downarrow$  PLT), acute kidney injury ( $\uparrow$  urea,  $\uparrow$  creatinine), metabolic acidosis ( $\downarrow$  pH) and coagulopathy ( $\uparrow$  INR) on admission were statistically significant predictors of mortality in our series (Table 3).

Table 3: Univariate analysis (difference of means) of lab values at admission.

Parameter	Mean		P value
	Survived	Died	
Hemoglobin	$17.30 \pm 2.79$	$17.58 \pm 3.07$	0.645
WBC	$11.40 \pm 5.83$	$11.24 \pm 6.72$	0.900
PLT	$232.79 \pm 109.08$	$169.48 \pm 78.10$	0.005 (s)
Urea	$33.65 \pm 23.15$	$61.78 \pm 61.79$	0.025 (s)
Creatinine	$0.66 \pm 0.246$	$0.96 \pm 0.54$	0.008 (s)
Blood sugar	$76.87 \pm 17.71$	$84.75 \pm 25.59$	0.137
Na	$140.20 \pm 6.87$	$140.28 \pm 8.33$	0.964
K	$3.98 \pm 0.62$	$3.76 \pm 0.73$	0.111
pH	$7.38 \pm 0.08$	$7.34 \pm 0.1008$	0.013 (s)
INR	$1.28 \pm 0.308$	$1.91 \pm 0.608$	0.0001 (s)

s: significant

The causes of NIO in our series are shown in Table 4. ARM was the most common cause of NIO in our series, present in 30 (25%) neonates of which 24 survived and 6 died. Jejuno-ileal atresia (JIA) was seen in 24 (20%) and duodenal atresia (DA) in 15 neonates. Overall, the incidence of associated malformations in DA patients was 73.3% (11/15). DA patients associated with CHD, Down's syndrome and multiple anomalies were associated with worse prognosis. Malrotation was seen in 13 neonates of which 8 had midgut volvulus at laparotomy. Hirschsprung's disease was seen in 12 neonates out of which 6 presented with features of perforation peritonitis and 6 with large bowel obstruction. Overall, 9 neonates with Hirschsprung's disease underwent surgery (colostomy with biopsy) and 3 were managed conservatively with rectal washouts. Necrotizing enterocolitis (NEC) was seen in 10 neonates. Eight out of 10 (80%) NEC patients were preterm. All had advanced disease (stage 3B) with perforation peritonitis and were operated upon. Meconium ileus (MI) was seen in 9, out of which 8 had simple MI and 1 complicated MI. Two out of 8 simple MI patients were managed non-operatively by solubilizing enemas. Overall 7 MI patients were operated and 3 expired due to overwhelming sepsis.

One hundred and eleven (92.5%) of the total of 120 neonates were operated. As regards surgical procedures, stoma formation (colostomy or ileostomy) was done in 46 neonates, resection and anastomosis in 27, entero-enterostomy in 16, Ladd's procedure in 8, peritoneal drainage procedures in 8, anoplasty in 7, chimney procedure in 5, pyloromyotomy in 2, herniotomy in 2, omphalocele repair in 2 and division of omphalo-mesenteric band in 1. Nine (7.5%) patients were not operated as 6 (5%) patients were managed non-operatively with rectal washouts successfully. Three (2.5%) patients were unfit for any surgical procedure and died before any surgical intervention could be done.

Twenty-two patients (18.33%) presented with perforation peritonitis out of which 14 expired (Table 5).

Table 4: Diagnosis (cause of NIO) of patients in our series (n=120)

Sr #	Diagnosis/probable diagnosis	Survived	Died	Total
1	Anorectal malformation	24	6	30
2	Jejuno-ileal atresia	19	5	24
3	Duodenal obstruction	12	3	15
4	Malrotation	11	2	13
5	Colonic obstruction and perforation, peritonitis, ?Hirschsprung's disease	7	5	12
6	Necrotizing enterocolitis	5	5	10
7	Meconium ileus	6	3	9
8	Colonic atresia	3	0	3
9	Pyloric atresia/Antral web	2	0	2
10	Omphalocele minor	2	0	2
11	Obstructed inguinal hernia	2	0	2
12	Infantile hypertrophic pyloric stenosis	2	0	2
13	Omphalo-mesenteric Band	1	0	1

Table 5: Outcome of patients vis-à-vis complication of perforation peritonitis (n=22)

	Survived (%)	Died (%)	Total (%)
No perforation peritonitis	84 (85.7)	14 (14.3)	98 (81.66%)
Perforation peritonitis	8 (36.4)	14 (63.6)	22 (18.33%)
Total	92 (76.6)	28 (23.3)	120 (100)

The mean interval between admission and surgical intervention was 1.59 days (range 0.2-7 days). The mean time interval between admission and surgical intervention in those who survived and in those who died was  $1.50 \pm 1.54$  (range 0.2-7) days and  $1.93 \pm 2.35$  (range 0.2-7) days respectively. The time

interval between admission and surgical intervention was not a statistically significant risk factor for mortality in our series.

Overall, 54 (48.6%) out of 111 neonates operated in our series, experienced significant delay in surgery. Reasons for delay included lack of ventilator (n=27), patient instability (n=18), and non-availability of table in OT (n=9). The mortality rate in those who experienced delay in surgery due to some reason was high (31.4%) as compared to those who experienced no delay in surgery (14%), but this probably also reflects on the fact that to start with, these patients were much sicker. Post-operatively, less than half of the patients (46%; n=51) could be extubated in OT. Of these, 2 eventually needed reintubation and ventilation; both died. The rest 60 (54%) patients had to be shifted (intubated) on ambu to NICU and mechanically ventilated; of these, 23 died (38.3%). Fifty-nine patients received total parenteral nutrition (TPN) when indicated.

Sepsis and its sequelae were seen in many patients (Table 6).

Table 6: Morbidity

Complication	n
Sepsis	50
shock	45
Pneumonia	33
Coagulopathy	32
Subcutaneous edema	29
GI bleed	27
Renal failure	24
Superficial wound infection	18
Pulmonary hemorrhage	15
Anastomotic leak	6
Wound dehiscence	5

The mean duration of stay in the hospital in our series was 8.40 days (range 2-19 days). The mean duration of stay in those who survived and in those who died was 8.21 days (range 4-19 days) and 9.03 days (range 2-17 days) respectively.

Ninety-two neonates were discharged from the hospital. The mean weight at discharge was  $2780 \pm 470$ g. At 1 month follow-up, all the patients who survived were doing fine, with mean weight of  $3300 \pm 540$ g. No major complication was noted in any of these patients.

## DISCUSSION

The mortality rate in our series was 23.33%. Though this is comparable to the outcomes report-

ed in the other published series from Africa and South Asia [7-9], it is much higher than the mortality rates seen in Europe. [6] The male preponderance, noted in our series, has been observed by other too [7,8, 10].

The gestational age and weight at presentation surprisingly didn't affect the survival outcomes; this has been observation of others too [7,10, 11]. However, late presentation after birth beyond 2 days was a statistically significant risk factor for mortality in our series ( $p=0.02$ ). Similarly, the delay in presentation after two days of the onset of symptoms was a significant risk factor for mortality in our series ( $p=0.01$ ). The late presentation was mostly due to delay in recognition of illness because of ignorance and lack of awareness, delay in seeking and accessing care due to financial constraints, lack of adequate means of transportation and sometimes because of poor parental motivation. Also on many occasions, there was delay in referral from primary first contact physicians because of delay in diagnosis.

We noted thrombocytopenia, acute kidney injury, metabolic acidosis and coagulopathy on admission to be statistically significant predictors of mortality in our series). More or less similar observations were also made by Manchanda et al. [12] in his series.

Hypothermia on arrival when subjected to statistical analysis, surprisingly was not statistically significant risk factor for mortality with a p-value of 0.092 as was also noted by Manchanda et al [12] in his series. Sepsis on admission, however, was a statistically significant predictor for mortality with a p-value of 0.0001. Similar observations were made by other authors also. [7,8,10,13]

ARM was seen in 30 (25%) neonates out of which 24 survived. Four out of 6 ARM patients who died presented to us late (after 4 days of life) with colonic perforation and peritonitis. Had these patients presented to us earlier, before perforation peritonitis, the results could have been different. Thus, routine examination of every baby's perineum at birth, observing passage of meconium by 24 hours of life and prompt referral when indicated cannot be over-emphasized.

The incidence of perforation peritonitis (18.33%) in our series and the mortality rates in this subgroup of patients were comparable to others reporting from third-world countries [9,10].

Those neonates in our series who were born with GCA had more likelihood of mortality (45.4%) than those who were born without one (18.3%). However, this difference was not statistically significant. These is similar to the earlier observations made by Osifo et al. and Manchanda et al. [9, 12] The time interval between admission and surgical intervention was not a statistically significant risk factor for mortality in our series. Ilori et al. had similar observations. [11] The complications noted in our patients were similar to those noted by other authors. [7,10,13,14,16]

Continued post-operative mechanical ventilation after surgery was a significant risk factor for mortality in our series. The reason for bad prognosis in such patients who needed continued post-operative mechanical ventilation was the fact that this reflected their bad general condition prior to surgery. The patients who are too sick are more likely to need post-operative mechanical ventilation. Second reason off course would be the complications associated with mechanical ventilation. Thus, every effort should be made, to make patient breath spontaneously without ventilatory support post-operatively, by proper pre-op optimization, avoiding unnecessary delay in surgery, dedicated anesthetic care including warm care during surgery and decreasing operative time by doing minimum that is necessary in sick neonates. The duration of stay in the hospital was not a statistically significant risk factor for mortality in our series as noted by Aljarrah et al. also. [10]

Early diagnosis and timely intervention, and dedicated neonatal surgical and intensive care are undoubtedly the crucial factors in improving outcome in NIO. Pediatricians are usually the first attending physician for early diagnosis in most instances. So, both pediatricians and surgeons have a contributing role in reducing neonatal mortality within existing facilities. Education of all birth attendants in recognition of signs of NIO (e.g. bilious vomiting, abdominal distension, failure to pass stools, imperforate anus) and early referral and improvement in facilities may reduce mortality from NIO in developing world. Based on Gadchiroli model of home-based newborn care that led to significant decline in neonatal mortality in rural areas, we recommend village health workers who conduct home visits be also trained to identify signs of NIO to provide for early referral. [15] We also recommend nasogastric suction, fluid resuscitation, intravenous antibiotics and warm care should be provided by first contact physician in suspected cases of NIO before referral.



**Authors' contribution:** All authors equally contributed in concept, design, manuscript writing, and approved final version.

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