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## Risk factors for failure of enema reduction of intussusception in children

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Intussusception is a common surgical emergency in children. Clinical suspicion and radiological evaluation confirm the diagnosis of the disease. Enema reduction is the first line of management. This study aimed to explore the risk factors associated with enema reduction failure. A retrospective analysis of patients diagnosed with intussusception at three different hospitals in different countries from January 2016 to December 2022. Data collected included demographics, presenting symptoms, duration of symptoms, management, outcomes, and follow-ups. A total of 290 cases of intussusception were included in the study. Ages ranged from 1 to 36 months, with a median age of 15 months. All children underwent an enema reduction which was successful in 92.4%. Failure of reduction was seen in 16.7% of females compared to 6.4% of males, and it was significantly seen in children below the age of 1 year compared to older children. Failure of reduction significantly increases with the duration of symptoms and in children who present with bilious vomiting and currant jelly stool. In conclusion, Failure of enema reduction was more prevalent in females, in children below the age of 1 year and who present late, as well as children who had bilious vomiting and currant jelly stool. This study identified several risk factors associated with failed enema reduction in children with intussusception. Recognizing the risk factors can help guide clinicians in the management and anticipation of outcomes.

Intussusception is a common surgical emergency in children, with an incidence rate of approximately one to four cases per 2000 newborns and children<sup>1</sup>. It is a significant cause of intestinal obstruction and a leading cause of abdominal emergency in the pediatric population<sup>1-5</sup>. Intussusception can occur at any age, but it is more commonly observed during the first two years of life. The male-to-female ratio ranges from 3:2 to 2:1, indicating a higher incidence in males<sup>1-3</sup>. Colicky intermittent abdominal pain, vomiting, a palpable abdominal mass, and currant jelly stool are the classic clinical presentations<sup>1,2</sup>. These symptoms are present in approximately 50% of cases. However, 20% of patients are symptom-free at initial clinical presentation<sup>1</sup>. Early recognition and prompt treatment are crucial, as delayed diagnosis and management can lead to significant morbidity and mortality<sup>3,6</sup>. Plain abdominal radiographs may show characteristic findings such as a soft tissue mass, target sign, meniscus sign, absence of air in the ascending colon, and/or small bowel dilatation<sup>1,2</sup>. The diagnosis is usually confirmed by findings of the target or donut sign in the abdomen ultrasonography<sup>1,2</sup>.

Delayed presentation of intussusception reduces the success rate of reduction procedures. Thus, prompt diagnosis and timely initiation of treatment are crucial for favorable outcomes<sup>2,3</sup>. Delayed presentation, characterized by prolonged symptom duration before seeking medical help, can hinder the effectiveness of non-surgical reduction methods. Hydrostatic and pneumatic reduction were monitored fluoroscopically to accurately determine the success of the intervention<sup>3</sup>. Identifying the risk factors associated with failed reduction in cases of delayed presentation is crucial for enhancing management approaches and optimizing patient outcomes<sup>1–3</sup>. Successful

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non-operative reduction can prevent the need for surgical intervention and associated complications<sup>3,4</sup>. While previous studies have identified certain risk factors for failed enema reduction in intussusception, the findings have been inconsistent across different populations and settings<sup>1-4</sup>. There is an ongoing need to better understand the specific factors that contribute to reduction failure, as this can inform treatment protocols and improve outcomes for these pediatric patients. Some studies have reported higher rates of failure in younger infants or those with prolonged symptoms durations, but the strength and consistency of these associations remain unclear<sup>1-7</sup>. Further exploration of the risk profile for unsuccessful non-operative management is warranted to optimize the management of intussusception and reduce the need for surgical intervention. This study aims to explore the risk factors associated with failure of enema reduction as all patients included in the study were hospitalized for monitoring and interventions.

#### Methodology and materials Study design and setting

This is a retrospective, multicenter study conducted at the Department of Surgery at King Saud University Medical City (KSMUC) in Riyadh, Saudi Arabia, Hamad Medical Corporation (HMC) in Doha, Qatar, and AlQasimi Women's and Children's Hospital, Sharjah, United Arab Emirates. The study was approved by the ethical committee of the respective institutions between the years 2016 and 2023. All methods were performed in accordance with the relevant guidelines and regulations.

#### Inclusion criteria

- 1. Children less than 3 years of age.
- 2. Idiopathic Ileo-colic intussusception.
- 3. Confirmed diagnosis of intussusception based on clinical and radiological findings.
- 4. No signs of sepsis or peritonitis.

#### Intussusception examination and reduction protocols

The Ultrasound examinations were performed using a high-resolution machine with a linear transducer probe (L12-5 MHz). Patients were scanned systematically in supine position, focusing on the right upper quadrant where intussusceptions typically present. Doppler imaging was utilized to assess bowel perfusion. Ultrasound findings documented included intussusception size, presence of a lead point, and signs of obstruction or ischemia. The duration of symptoms prior to ultrasound was also recorded<sup>4</sup>.

Pneumatic reduction done under continuous fluoroscopic guidance. A rectal catheter was inserted, and air was slowly insufflated into the rectum. The pressure was gradually increased until the intussusception was reduced, as visualized by the ileocecal valve returning to its normal position, or until a maximum pressure of 120 mmHg was reached. If the initial attempt was unsuccessful, a second attempt could be made after a brief rest period<sup>4,14</sup>. While the hydrostatic reduction, a Foley catheter was inserted into the rectum and connected to a saline-filled bag elevated 60–100 cm above the patient. Saline was slowly infused under fluoroscopic monitoring until the intussusception was reduced, visualized by the return of the ileocecal valve to its normal position. If the initial hydrostatic attempt was unsuccessful, a second attempt could be performed after a short rest period<sup>15</sup>.

In both reduction methods, fluoroscopic images were reviewed by the pediatric radiologist to confirm complete reduction. Based on the available resources, pneumatic reduction is the first choice if equipment available, otherwise hydrostatic reduction is performed.

#### Data collection and analysis

Data collection included information on patients with the final diagnosis of intussusception. Demographics, presenting symptoms, duration of symptoms, management, results, and follow-ups were all collected.

Statistical Package for Social Sciences version 21 (SPSS: An IBM Company) was used for data collection and analysis. All statistical methods were two-tailed with an alpha level of 0.05 and a P-value significance of less than or equal to 0.05. Descriptive analysis was done by prescribing frequency distribution and percentage for study variables, including case age and gender, clinical presentation, and clinical outcome. Intussusception cases were cross-tabulated to determine factors associated with failed reduction performed with a Pearson chi-square test for significance and an exact probability test for small frequency distributions.

#### Results

A total of 290 cases with intussusception were included. Ages ranged from 1 to 36 months with a median age of 15 months, 112 (36.6%) were less than 1 year, 98 (32%) were aged 1 to 2 years, and 80 (27.5%) were aged 2 to 3 years. A total of 190 (65.6%) cases were males. The duration of symptoms was less than 24 h in most cases 189 (65.1%), 24 to 48 h in 48 cases (16.5%), and more than 48 h in 41 cases (13.4%). The most common symptoms were bilious vomiting in 155 cases (53.4%), Currant jelly stool in 77 cases (25.2%), and fever in 20 cases (6.8%) [Table 1].

All cases underwent an enema reduction trial, mainly pneumo-reduction among in 177 cases (61%) and hydro-reduction in 95 cases (32.8%), and 18 (6.2%) of recruited patients needing both. Failure of enema reduction was reported among 22 (7.6%) of patients. All failed cases underwent surgical intervention and seven out of 22 cases who needed surgery for reduction required bowel resection with primary anastomosis or ileostomy due to bowel ischemia [Table 2].

Bio-demographic data	No	%			
Age in years					
<1 year	112	38.6			
1-2 years	98	33.7			
2-3 years	80	27.5			
Gender					
Male	190	65.6			
Female	100	34.4			
Duration of symptom					
Unknown	12	4.1			
<24 h	189	65.1			
24-48 h	48	16.5			
>48 h	41	14.1			
Symptoms					
Bilious vomiting	155	53.4			
Currant Jelly stool	77	25.2			
Fever	20	6.9			

 Table 1. Bio-demographic data (n = 290).

Intervention	No	%			
Enema reduction					
Successful	268	92.4			
Failed	22	7.6			
Enema type					
Pneumo	177	61			
Hydro	95	32.8			
Both	18	6.2			
Surgical reduction (No=22)					
With resection	7	2.4			
Without resection	15	5.1			

 Table 2.
 Intervention for reduction of intussusception.

Failure of reduction was seen in 16 (16.7%) of females compared to 6 (6.4%) of males (P = 0.003). Failure of reduction was significantly seen in children below the age of 1 year compared to children more than two years (P = 0.035). Failure of reduction significantly increased with the duration of symptoms; it was reported among 12 cases (29.3%) who presented with symptoms for more than 48 h compared to 3 cases (1.6%) of others with symptoms for less than 24 h (P = 0.001). Failure of reduction was significantly seen with children who had bilious vomiting (P = 0.048) and currant jelly stool (P = 0.012) but was not significant among those who had fever (P = 0.810) [Table 3].

Logistic regression was carried out for binary variables to determine the predictability of independent variables, namely, age, gender, duration of symptoms (less than 24 h, 24–48 h, and more than 48 h), bilious vomiting, jelly stool, and fever. Predictors with significant odds ratio (OR) are used to perform multiple logistic regressions to determine the predictability of a combination of independent variables. R language programming was used to perform logistic regression utilizing the glm function from the stats library (Dobson and Barnett, 2018<sup>28</sup>; Ripley, 2002<sup>4</sup>). Additionally, to provide visualizations of the data, the ggplot2() library was employed to create the necessary visual representations (Wickham and Wickham, 2016<sup>5</sup>). [Tables 4, 5] illustrated the univariable and multivariable logistic regressions of predictors for surgical intervention versus enema reduction among children with intussusception [Fig. 1].

#### Discussion

Intussusception is a common surgical emergency in children that needs prompt intervention. Cases of intussusception are more commonly seen in males during the first two years of life. The main approach for uncomplicated cases is non-surgical reduction using either hydrostatic or pneumatic enemas. Surgical intervention is usually reserved for cases of peritonitis, perforation, and unsuccessful enema reduction<sup>3</sup>. Diagnosis is confirmed through abdominal ultrasonography, specifically the target or donut sign. Delayed presentation makes non-surgical reduction methods less effective<sup>1</sup>. Therefore, the identification of risk factors related to failed enema reduction

	Failure of reduction					
	Yes		No		1	
Factors	No	%	No	%	p-value	
Gender						
Male	6	3.1	184	96.8	0.003*	
Female	16	16	84	84		
Age						
<1 year	14	12.5	98	87.5	0.035*	
1-2 years	5	5.1	93	94.9	0.033	
2-3 years	3	3.7	77	96.2	]	
Duration of symptom						
Unknown	2	16.6	10	83.8	1	
<24 h	3	1.6	186	98.4	0.001*	
24-48 h	5	10.4	43	89.6		
>48 h	12	29.3	29	70.7	]	
Bilious vomiting						
Yes	8	5.6	135	94.4	0.048*	
No	14	9.5	133	90.5	1	
Currant jelly stool						
Yes	13	17.3	62	82.7	0.012*	
No	9	4.2	206	95.8	1	
Fever						
Yes	2	9.1	20	90.9	0.810	
No	20	7.5	248	92.5		

**Table 3.** Factors associated with failure of reduction among study cases. P: Exact probability test. \*P < 0.05</th>(significant).

	Odds Ratio	Lower CI	UpperCI	P value	Significance
(Intercept)	12.8107	7.7085	22.3469	3.80962856968514e-21	< 0.05
Age	0.9889	0.9782	1.0007	0.0478782115698075	< 0.05
(Intercept)1	14.6923	8.7337	27.1141	6.88318205239369e-21	< 0.05
Gender: female	0.3403	0.1554	0.729	0.00581633661046492	< 0.05
(Intercept)2	21	4.398	376.4856	0.00293443409940027	< 0.05
Duration symptoms: 24-48 h	1.5	0.0775	9.3779	0.713503673083386	NS
Duration symptoms: more than 48 h	0.2063	0.0108	1.2103	0.147015601563829	NS
(Intercept)3	14.5	8.0584	29.4322	2.8596248358567e-16	< 0.05
Bilious vomiting no vomiting	0.4517	0.1963	0.9793	0.050092504792052	NS
(Intercept)4	4.9231	2.8073	9.3455	1.61046817823608e-07	< 0.05
Jelly stool: normal	2.5331	1.1492	5.4793	0.0186460774337029	< 0.05
(Intercept)5	11	3.2431	68.6625	0.00116724269407196	< 0.05
Fever: normal	0.8247	0.1279	3.0074	0.801035834673952	NS

 Table 4.
 Logistic regression of predictors for surgical intervention vs enema reduction.

	ORs	Lower CI	Upper CI	P value	Significance
(Intercept)	10.1814	4.895	23.4816	5.311112e-09	< 0.05
age	0.9867	0.9753	0.9986	0.0236	< 0.05
Gender: female	0.3458	0.155	0.7541	0.008	< 0.05
Jelly stool: normal	3.0655	1.3344	7.0268	0.0077	< 0.05

**Table 5.** Multivariable logistic regression of the predictive variables against surgical intervention vs enema reduction.

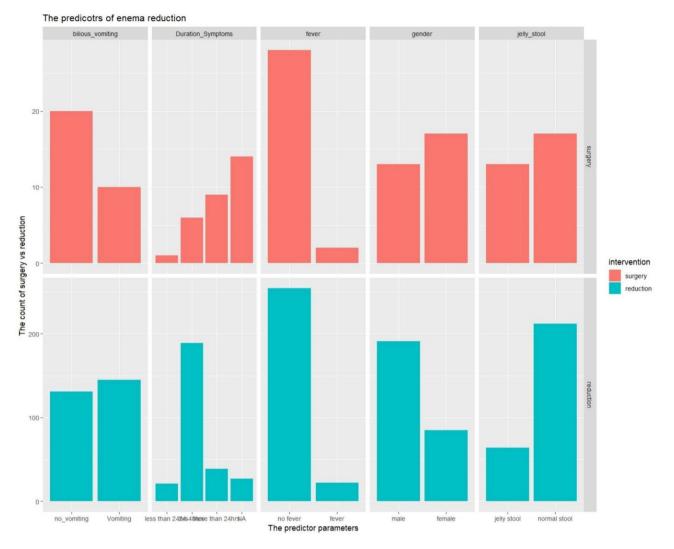


Fig. 1. Frequency of the predictors against intervention, either surgery or reduction.

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is paramount in cases of delayed presentation to optimize management and outcome<sup>1-4</sup>. The current study was conducted to explore the potential risk of enema reduction failure, both pneumatic and hydrostatic.

The age and sex of infants is emphasized in the literature as risk factors for the occurrence of intussusception. Out of 125 patients who underwent attempted enema reduction, nearly 62% were males with an average age of 30 months<sup>5</sup>. Moreover, male infants (54%) more frequently present emergency intussusception, with a male-to-female ratio of 1.19:1 and a peak age of onset at 3–4 years<sup>6–8</sup>. According to a recent study, male patients made up the majority of the study population, accounting for 64% of participants. The male-to-female ratio was observed to be close to 2:1. Additionally, the data revealed that the incidence of intussusception, a medical condition, was notably higher among children aged between 6 months and 2 years, with this age group compromising nearly 60% of the total participants recruited for the study<sup>7</sup>. In the current study, male infants were predominant with a median age of 17 months.

Recent studies have shown a clear relationship between patient age and the success of enema reduction for intussusception, a common pediatric emergency. Infants under 1 year have a significantly lower likelihood of successful enema reduction, while children over 2 years are more prone to recurrence after successful treatment. Geographical variation exist, with earlier median ages observed in Africa (29 weeks) compared to Asia (35 weeks). The current study highlights the critical importance of considering patient age, as failure of enema reduction is strongly correlated with age extremes, while those between 1–2 years have high success rates, underscoring the need for tailored management strategies<sup>8–11</sup>. The regression analysis results show that with each additional month of age, the need for surgery decreases, but this effect is not linear and does not imply a 100% success rate for children older than two years. Therefore, it should be emphasized that the age of onset is an important determinant of enema reduction success and can be a predictor of intervention success.

In one study unsuccessful reduction was 71% in males compared to 28% in females. However, the difference was statistically insignificant<sup>9</sup>. Regarding the debate in the literature on the implications of sex in predicting surgical intervention success, our study showed that enema reduction was significantly higher in females compared

to males. Moreover, 66% of female patients with intussusception had enema reduction success and were less likely to undergo surgery.

Short duration of symptoms presenting less than 12 and 24 h respectively is associated with a high probability of enema reduction success<sup>10</sup>. Further research concurred that infants presenting for 24 h or less after the onset of symptoms were more likely to pass enema reduction successfully<sup>11–15</sup>. The current study matches the results reported in the literature. There was a significantly greater failure rate of enema reduction among patients who presented later compared to those who presented earlier than 24 h. According to the regression analysis, the duration of symptoms (24–48 h, and > 48 h) cannot be considered as predictors for intervention. Consequently, early presentation of infants is considered an important factor for a successful enema reduction approach. Reduction failure is more likely in infants with intussusception accompanied by fever, rectal bleeding, and vomiting; It is also prevalent in infants with ascites, left-sided intussusception, and trapped fluid detected by ultrasound<sup>16–19</sup>. Patients with fever at presentation are less likely to experience a short-term recurrence, whereas those without fever are more likely to do<sup>6,20</sup>.

Bloody stool is significantly associated with unsuccessful enema reduction requiring surgical intervention, but abdominal pain, vomiting, and restlessness are not<sup>20,21</sup>. Consistent with the literature, this current study finds that failure of enema reduction is correlated to vomiting, bloody stool, and fever. Based on logistic regression analysis, bilious vomiting, and temperature were not predictive of success. Yet, a bloody stool was found to increase the likelihood of surgical intervention.

In this context, a systematic review of 15 articles concluded that enema reduction of ileocolic intussusception can be conducted as an outpatient approach<sup>22-25</sup>. Managing intussusception as an outpatient following successful enema reduction leads to shorter hospital stays without any notable difference in the rate of revisiting the emergency, recurrence, need for surgery, or increased mortality rate<sup>26-29</sup>. There were no significant differences in outcomes between patients who were admitted for intussusception management and those who were discharged<sup>30-33</sup>.

#### Strengths and limitations of the study

The main strength of the current study is that it is multidisciplinary, involving three tertiary hospitals in three countries: Saudi Arabia, Qatar, and the United Arab Emirates. A regression analysis was employed to detect the predictability of certain variables pertaining to intussusception. However, this study is limited by the small sample size and its retrospective observational approach. This means that only frequency and correlation can be inferred.

#### Conclusion

The current multicenter study on pediatric intussusception found that failure of enema reduction was more prevalent in females, children under 1 year of age, those with a longer duration of symptoms, and those presenting with bilious vomiting and currant jelly stool. These risk factors should be carefully considered when managing intussusception cases, as they can help guide clinicians towards more expedient surgical intervention in high-risk patients, while allowing for more conservative reduction attempts in low-risk cases. The findings from this large, multinational analysis provide valuable evidence to optimize treatment strategies and improve outcomes for children with this common surgical emergency. Further research is needed to explore additional factors and develop guidelines to reduce delayed presentation and enhance outcomes in intussusception cases.

#### Data availability

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request. The datasets generated and/or analyzed during the current study are not publicly available due to institutions' policies and regulations but are available from the corresponding author on reasonable request.

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#### Author contributions

All authors contributed equally in this study. Tuqa AlSinan and Tariq AlTokhais formulated the study idea and methods. Tuqa AlSinan, Tariq AlTokhais, Fatimah AlShayeb, Amro Hajja, Mohammad AlBoukai, Sulaiman Alsalameh, Renad AlDahleh, Shamah Shabi, and Shams Almubayadh wrote proposal and manuscript, data collection and analysis from Saudi Arabia. Dollis de jesus Rodriquez Ruano and Amani AlAnsari wrote manuscript and data collection and analysis from Qatar. Khalid AlAli wrote manuscript and data collection and analysis from United Arab Emirates. Tuqa AlSinan, Tariq AlTokhais, and Amani AlAnsari reviewed and edited the study.

#### **Competing interests**

The authors declare no competing interests.

#### **Ethical considerations**

The RB Approval of Research Project No. E-23-7774 had waived the informed consent from this retrospective study.

#### Additional information

Correspondence and requests for materials should be addressed to T.A. or A.N.A.

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