How to Cite:
Agarwal, M., & Agarwal, A. (2022). Prevalence of stress related GI bleeding in children at a tertiary care hospital. *International Journal of Health Sciences*, *6*(S5), 3381–3387.
https://doi.org/10.53730/ijhs.v6nS5.9369

Prevalence of stress related GI bleeding in children at a tertiary care hospital

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***Abstract*---**Introduction: Though the upper gastro-intestinal bleeding is relatively uncommon condition in children who are admitted in paediatric intensive care unit (PICU) but it continues to pose a critical challenge in the management. This present study was undertaken to assess the prevalence of gastrointestinal bleeding due to stress and its associated risk factors. Materials and Methodology: All the available medical records of the children who are younger than 15 years admitted to the PICU were retrospectively studied. The basic indications for the in-patient admission comprised of respiratory/cardiovascular failure, shock, coma, post-operative care and patients requiring intensive monitoring. Demographic data, indications for PICU admission and principal diagnosis as well as basic laboratory investigations were recorded. Cross-tabulations were analysed using the chi square test, represented as the odds ratio and 95% confidence interval, in which $P < 0.05$ was considered statistically significant. Results: A total of 200 charts were eligibly reviewed. There were 89 males (52.4%) with an average age of 3.8 years. The most common indication for PICU admission was respiratory failure (48.8%). GI bleeding complicated 43.5% of cases admitted to the PICU and 5.3% had clinically significant bleeding. Twenty-two percent of patients with CSB were diagnosed as dengue haemorrhagic fever, compared to none in the patients without bleeding. Conclusion: To conclude, the incidence of gastrointestinal bleeding is relatively high in critically ill children. Mechanical ventilation is a significant risk factor for the initiation of gastrointestinal bleeding. Endoscopy is observed to be the best diagnostic and therapeutic option.

***Keywords*---**Gastro-Intestinal Bleeding, Endoscopy, PICU, Coagulopathy.

Manuscript submitted: 27 Feb 2022, Manuscript revised: 9 April 2022, Accepted for publication: 18 June 2022

Introduction

The term 'Upper gastrointestinal (UGI) bleeding' is described as the bleeding in the gastrointestinal tract where the bleeding source is proximal to the ligament of Treitz. The process of UGI bleeding remains an uncommon sign but reported to be an important problem in its management in children who often require frequent hospitalization. Acute UGI bleeding usually presents with hematemesis, melena, or haematochezia. The clinical picture of UGI bleeding in children ranges from asymptomatic microcytic anaemia to hypovolemic shock.[1] Epidemiological studies of UGI bleeding in children are quite few and the exact incidence has not been well-established, but it constitutes about 1% of all inpatient admissions to a paediatric hospital.

Various studies conducted on those hospitalized children have reported that the incidence of UGI bleeding in the paediatric ICU ranged between 6% - 25%.[2,3] In some other studies, an UGI source represented as much as 20% of all episodes of gastrointestinal bleeding reported most commonly in children. Also, many children with haematemesis or melena without haemodynamic instability are being managed without hospitalization or referral and many children usually stop bleeding spontaneously or with certain medication prescribed from the outpatient ward, all these factors usually contributed to be the reporting incidence of UGI bleeding in children.[4]

The diagnosis of about 10-20% of children with UGI bleeding remains undefined even with the application of esophago-gastroduodenoscopy hence the need for newer diagnostic modalities remains increasing interest to the researchers. [5-7] With the advent of the fibre optic endoscopy, it has greatly helped us to understand that the most common aetiologies of UGI in children which may vary depending upon the age and the geological setting.

Stress ulcer bleeding is reported to be one of the common complications in critically ill patients who are admitted to the paediatric intensive care unit. The incidence of UGI bleeding in adults ranges from 0.17% to 14%, based on the diagnostic criteria, patient selection and investigation methods.[8-11] There have been a few observations on this condition in paediatric populations with the incidence ranges from 10% in a paediatric intensive care unit (PICU) to 53% in a neonatal intensive care unit.[12,13] This study was designed to evaluate the frequency and the risk factors of stress-induced upper gastrointestinal bleeding in critically ill children admitted to a paediatric intensive care unit.

Materials and Methodology

All the available medical records of the children who are younger than 15 years admitted to the PICU were retrospectively studied. The basic indications for the in-patient admission comprised of respiratory/cardiovascular failure, shock, coma, post-operative care and patients requiring intensive monitoring. Patients with the reported duration of admission in PICU usually shorter than 48 hrs, previous history of positive GI bleeding, recent GI tract surgery, brain death and epistaxis/oropharyngeal bleeding were excluded from the study. Demographic data, indications for PICU admission and principal diagnosis as well as basic

laboratory investigations including the level of haemoglobin, platelet count, coagulation studies, blood urea nitrogen (BUN), creatinine (Cr) and liver function tests (LFT) were recorded. Upper GI bleeding during PICU admission was categorized as overt and clinically significant bleeding. Overt GI bleeding (OB - major changes in vital signs, namely a decrease in blood pressure greater than 20 mmHg, an increase in heart rate of >20 beats above the baseline value, and a decrease in hemoglobin level of more than 2 g/dL) was noted, if there was a proof of hematemesis, coffee ground gastric content or melena. With the reports available on previous studies observed in adults, potent risk factors were considered in this present study too. These were the use of mechanical ventilation, sepsis, acute respiratory distress syndrome (ARDS), renal insufficiency, coagulopathy, thrombocytopenia, and intracranial pathology.

There are some reported criteria for the diagnosis of these conditions relatively which include: sepsis -body temperature >38 °C or 160/min (infant) or >150/min (child) or >90/min (adolescent), WBC >15 000 or 10% or there was a positive blood culture; ARDS - positive alveolar infiltration in both lungs on chest X-ray and PaO_2/FiO_2 2mg/dL, or requiring dialysis; coagulopathy - prothrombin time (PT) >3s and partial thromboplastin time (PTT) >10 s above the normal range; thrombocytopenia - platelet count <100,000/mm^3. All data were recorded and assessed by SPSS program. Cross-tabulations were analysed using the chi square test, represented as the odds ratio and 95% confidence interval, in which $P < 0.05$ was considered statistically significant.

Results

Over the 12-month period, 240 of 270 medical records were available for review (53 records were missing). Thirty-five cases were excluded for the following reasons: duration of admission shorter than 48 h (n = 28), incomplete medical records (n = 3), epistaxis (n = 2), brain death (n = 1), and recent gastrointestinal surgery (n = 1). Therefore, a total of 200 charts were eligibly reviewed. There were 89 males (52.4%) with an average age of 3.8 years. The total duration of admission was 7.2 d (2-35 d). The most common indication for PICU admission was respiratory failure (48.8%). The demographic data of children with and without bleeding are shown in Table 1. Twenty-five children received stress ulcer bleeding prophylaxis, in which ranitidine was used in 22 cases with a dosage of 3 mg/kg/d; whereas the other three patients received antacids. In the subgroup of children who received stress ulcer prophylaxis, 14 cases developed upper GI haemorrhage (3 CSB and 11 OB); whereas stress ulcer bleeding occurred in 60 of 145 cases who did not receive the prophylactic treatment (6 CSB and 54 OB). GI bleeding complicated 43.5% of cases admitted to the PICU and 5.3% had clinically significant bleeding. Twenty-two percent of patients with CSB were diagnosed as dengue haemorrhagic fever, compared to none in the patients without bleeding.

Among the independent variables, only mechanical ventilation and thrombocytopenia were significantly associated with stress ulcer bleeding using the univariate analysis. The odds ratio and 95%CI were 5.13 (1.86-14.12) and 2.26 (1.07-4.74), respectively (Table 2). Using multivariate analysis, only mechanical ventilation was found to be significantly associated with the development of gastrointestinal bleeding in critically ill patients ($P<0.05$)

Table 1: Demographic data of children with and without stress-induced GI bleeding

Characteristic	Bleeding (n = 90)	No bleeding (n = 110)	P - value
Age (years)	3.84 (0.46)	3.86 (0.48)	0.981
Sex, male	49	53	0.488
Duration of admission (days)	8.26 (0.79)	6.45 (0.61)	0.065
Underlying diseases			
Respiratory diseases	10	17	0.451
Cardiovascular diseases	11	21	
Neurological system	21	28	
Circulatory system	13	13	
Infections	17	11	
Gastrointestinal system	7	8	
Others	10	15	

Table 2: Risk factors for stress-induced GI bleeding in children (n = 200)

Risk factors		N	GI bleeding (%)	Odds ratio (Simple regression)	Odds ratio (Multiple regression)
Mechanical ventilation	Yes	163	49.7	5.132	14.192
	No	37	16.4	P=0.0001	P=0.005
Thrombocytopenia	Yes	43	59.7	2.262	3.472
	No	157	39.6	P=0.030	P=0.089
Renal insufficiency	Yes	153	78.2	4.861	2.772
	No	47	43.3	P=0.038	P=0.359
Prolonged PT	Yes	40	64.9	2.298	1.312
	No	38	44.6	P=0.068	P=0.791
Prolonged PTT	Yes	43	62.8	2.121	1.211
	No	61	44.7	P=0.099	P=0.822
ARDS	Yes	113	62.5	2.062	0.779
	No	63	44.8	P=0.082	P=0.748
Sepsis	Yes	81	47.2	1.488	1.324
	No	119	38.8	P=0.215	P=0.822
Intracranial pathology	Yes	38	46.9	1.189	1.214
	No	162	43.1	P=0.682	P=0.912

Discussion

Various stress-induced gastrointestinal lesions which may include gastritis, erosions, gastric and duodenal ulcers, can eventually result in significant upper gastrointestinal haemorrhage, high rate of morbidity and mortality.[2] The prevalence differs greatly between various studies.[1-6] In this present study, 5% of the cases developed clinically significant bleeding which is reported to be considerably greater than that observed in earlier studies conducted in the paediatric population.[5,14] This may result from a relatively higher prevalence rate of haemorrhagic fever which frequently the major aetiology for the development of

thrombocytopenia and subsequent gastrointestinal bleeding in our study participants. As observed in the study, 22% of the cases with reported CSB were diagnosed as dengue haemorrhagic fever. Also, we did not regularly recommend the administration of stress ulcer prophylaxis in all children and participants reported with ranitidine prophylaxis did not receive the recommended dose of 6 mg/kg/d.[15] This might clearly explain the poor beneficial prophylactic effect observed in our research. Apart from clinically significant bleeding, we also found a high prevalence rate of overt upper gastrointestinal bleeding (38.6%), which is comparable to the retrospective observation revealed from Kuusela et a [16] in neonates. Therefore, this figure could be exponentially high due to a possibility of inclusion of a traumatic nasogastric tube injuries which are impossible to be recorded in such a retrospective study setting and thus we did not regularly perform endoscopy in all children to delineate the aetiology of upper GI bleeding during the proposed study tenure. Although it was believed that the prevalence observed in this study might be over-estimated since it concerns a significant magnitude of the problem that necessitates meticulous medical attention. Similar to earlier studies conducted in adults and children, the mechanical ventilation was observed to be the most significant risk factor which majorly contributed for the stress-induced gastrointestinal bleeding in this study.[1,2,5,6] Moreover coagulopathy is also noted to be a significant independent risk factor in few studies,[1,2,5,7] Unfortunately, this was not revealed in our series using the multivariate analysis. A further prospective study with a larger sample size might be needed in the near future.

An imbalance between protective and destructive factors have been hypothesized as a basic pathophysiology of GI bleeding. Increased acid production and reduced gastric blood flow, secondary to hypotension and metabolic acidosis, are comprised of major physiologic changes that leads to various mucosal injuries. Prophylactic strategies involving H_2RA and cytoprotective agents have been widely prescribed to the critically ill patients admitted to the intensive care unit since the haemorrhagic gastritis majorly affects the gastric mucosa.[4] Lacroix et al[16] have been reported a significant increase in the gastric pH following the administration of cimetidine prophylaxis stress ulcer haemorrhage in children, but no prophylactic benefit was represented in their study. Kuusela et al[17] noted that short-term prophylactic ranitidine treatment could possibly prevent gastric mucosal lesions involving the new-born infants under stress. Cook et al[18] performed a meta-analysis and recorded that H_2RA significantly reduces clinically significant bleeding that is the overt bleeding over sucralfate and antacids. However, overgrowth of Gram-negative bacteria following the increase of gastric pH by antisecretory agents can be relatively associated with ventilator-associated pneumonia (VAP).[19,20] Lopriore et a[l21] observed that 8.4% of mechanically ventilated children develop VAP. Among these, more children who were prophylactically managed with ranitidine tend to be associated with VAP than those in the control group (11.1% vs 6.2%), despite no statistical significance. The use of sucralfate, since its introduction attributed to be logically useful in preventing this complication.[11]

Ben-Menachem et al[22] did a cost-effective analysis on stress induced ulcer prophylaxis and suggested that the expense of prophylactic management is substantial and may be prohibitive in ICU patients since they are at low risk of

developing stress-related haemorrhage. Henceforth, several authors have recently suggested that such prophylaxis should be selective and may be administered only for patients who are relatively at high risk, especially in those with mechanical ventilation and coagulopathy.[2,7]

Conclusion

To conclude, the incidence of gastrointestinal bleeding is relatively high in critically ill children. Mechanical ventilation is a significant risk factor for the initiation of gastrointestinal bleeding. Endoscopy is observed to be the best diagnostic and therapeutic option.

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