

## Acute Constipation in Children Receiving Chemotherapy for Cancer

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### ABSTRACT

**Background:** The mechanism of gastrointestinal damage (mucositis) induced by cancer chemotherapy remains uncertain. Constipation occurs in children receiving chemotherapy for cancer. **Objectives:** The aim of the study was to determine the rate and various risk factors for the development of constipation in children on chemotherapy for cancer. **Methods:** This observational study was carried out in the Department Pediatrics, Bangladesh Sheikh Mujib Medical University, Dhaka, Bangladesh during October 2012 to March 2013. A total of 100 patients with constipation during chemotherapy for cancer were participated in the study. Statistical analyses of the results were obtained by using window-based Microsoft Excel and Statistical Packages for Social Sciences (SPSS-24). **Results:** Constipation was found 62.3% of children receiving chemotherapy for cancer in this study. The mean age found 7.08+3.8 years with range from 1.5 year to 14 years and male to female ratio was 1.1:1. The mean weight and height were found 23.71+10.53 kg and 118.22+23.59 cm respectively. Nearly two third (63.0%) patients received isolated or combined chemotherapy and rest 37.0% patients had history of constipation. Almost half (45.0%) of the patients had acute lymphoid leukemia, 36.0% lymphomas and 19.0% myeloid leukemia. More than three fourth (77.0%) patients need vincristine chemotherapy, 8.0% patients were methotrexate, 46.0% was Cytosine arabinoside and 4.0% 6-mercaptopurine. **Conclusion:** Constipation developed due to chemotherapy for cancer in most of the children. Majority of them felt constipation related minor problem and had minor impact on lifestyle.

**Keywords:** Gastrointestinal damage, Chemotherapy, Constipation,

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### I. INTRODUCTION

Constipation is a commonly recognized complication in adult patients with chemotherapy and has been the subject of many studies and reviews. [1-3] Our clinical observation suggests that acute constipation is very common in children receiving chemotherapy for cancer. In a survey of 12 pediatric oncology units from the United Kingdom, all units reported constipation as a problem for patients. [4] However, this study did not have any interaction with patients and did not have any data about the prevalence of constipation.

Although both diarrhoea and constipation are well recognized side-effects of cancer treatment very little research has been conducted into the underlying mechanisms. [5-6] Much of the information in the published literature is based on clinical observations with very little basic science existing. Chemotherapy-induced constipation (CIC) is recognized as being a mixture of reduced frequency of bowel action and increased stool consistency; however, the mechanisms of CIC are very poorly defined (Keefe, personal communication).

Mucositis is a major oncological problem, caused by the cytotoxic effect of cancer chemotherapy and radiotherapy. The condition affects the entire gastrointestinal tract (GIT) and causes pain and ulceration in the mouth, oesophagus and small and large intestines. In addition, it causes abdominal bloating, vomiting, diarrhoea and constipation. [7] The absolute percentage of patients that have diarrhoea or constipation as a result of their treatment has yet to be fully defined, although general estimates place 10% of patients with advanced cancer as

being afflicted. [8] Mucositis in general occurs in approximately 40% of patients undergoing standard dose chemotherapy and in almost all patients undergoing high-dose chemotherapy and stem cell or bone marrow transplantation. [9]

## II. METHODOLOGY

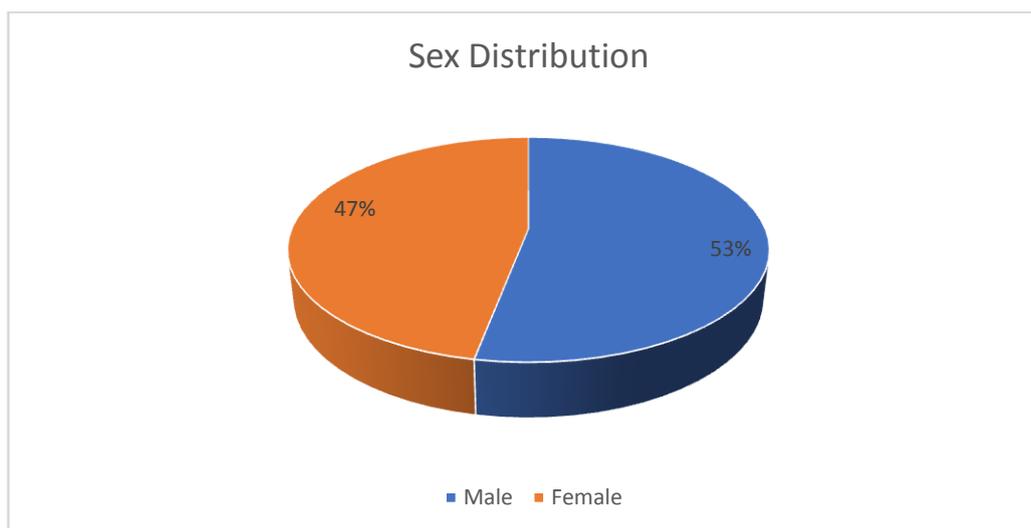
This observational study was carried out in the Department Pediatrics, Bangladesh Sheikh Mujib Medical University, Dhaka, Bangladesh during October 2012 to March 2013. A total of 100 patients with constipation during chemotherapy for cancer were participated in the study. Patients with constipation were selected with convenience sampling type due to chemotherapy for cancer. The primary end point was to investigate the prevalence of constipation in children on chemotherapy for cancer. The secondary end point was determining the associated risk factors for the development of constipation in children on chemotherapy for cancer and also to assess the severity of constipation in this group of children. After taking consent and matching eligibility criteria, data were collected from patients on variables of interest using the predesigned structured questionnaire by interview, observation. Statistical analyses of the results were obtained by using window-based Microsoft Excel and Statistical Packages for Social Sciences (SPSS-24), where required.

## III. RESULTS

**Table-1: Age distribution of the study patients (n=100)**

Age (years)	n	%
≤ 5	41	41.0
6 - 10	33	33.0
> 10	26	26.0
Mean±SD	7.08 3.8 (1.5 – 14)	
Range(min-max)		

A total of 100 patients with constipation were enrolled in this study, majority (41, 41.0%) of the patients belonged to ≤5 years age group and their mean age was 7.08±3.8 years (with range from 1.5 year to 14 years).



**Figure 1: Sex distribution of the study patients (n=100)**

Regarding the sex distribution of the study patients, male was found 53(53.0%) and female was 47(47.0%).

**Table -2 Distribution of the study patients according to weight (n=100)**

Weight (kg)	n	%
≤ 10	8	8.0
11 – 20	35	35.0
21 – 30	35	35.0
31 – 40	17	17.0
> 40	5	5.0
Mean±SD	25.71±10.53	

Range(min-max)	(7.5-50)
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Table 2 shows weight distribution of the study patients, it was observed that, majority patients' weight between 11 kg to 30 kg. The mean weight was found 23.71±10.53 kg with range from 7.5 to 50 kg.

**Table –3 Distribution of the study patients according to height (cm) (n=100)**

Height (cm)	n	%
≤80	8	8.0
81 – 100	21	21.0
101 – 120	23	23.0
121 – 140	29	29.0
141 – 160	17	17.0
> 160	2	2.0
Mean±SD	118.22±23.59	
Range(min-max)	(66-163)	

Table 3 shows height of the study patients, it was observed that, majority 29(29.0%) patients height was 121 to 140 cm. The mean height was found 118.22±23.59 cm with range from 66 to 163

**Table – 4 Distribution of the study patients according to risk factors (n=100)**

Risk factors	n	%
History of constipation	37	37.0
Isolated or combined use of chemotherapy	63	63.0

Table 4 shows risk factors of the study patients, it was observed that nearly two third (63.0%) patients had isolated and combined and rest 37(37.0%) patients had history of constipation.

**Table – 5 Distribution of the study patients according to diagnosis (n=100)**

Diagnosis	n	%
Acute lymphoid	45	45.0
Lymphomas	36	36.0
Myeloid leukemia	19	19.0
Other solid tumor	0	0.0

Table 5 shows the diagnosis of the study patients. it was observed that 45(45.0%) patients had acute lymphoid leukemia followed by 36(36.0%) had lymphomas and 19(19.0%) patients had myeloid leukemia.

**Table – 6 Distribution of the study patients according to chemotherapy (n = 100)**

Chemotherapy	n	%
Vincristine	77	77.0
Methotrexate	8	8.0
Cytosine arabinoside	46	46.0
6-marcaptopurine	4	4.0

Table 6 shows the chemotherapy of the study patients, it was observed that, more than three fourth (77.0%) patients need vincristine chemotherapy, 8(8.0%) patients was methotraxate, 46(46.0%) was cytosine arabinoside and 4(4.0%) 6-marcaptopurine.

**Table-7: Duration of chemotherapy of the study patients (n=100)**

Duration of chemotherapy	n	%
<1 Month	26	26.0
1-2 Months	42	42.0
>2 Months	32	32.0
Mean±SD	1.0 ± 1.3 (25 days-2.5 months)	
Range(min-max)		

Table 7 shows the duration of chemotherapy of the study patients, it was observed that, majority 42(42.0%) patients' chemotherapy during 1-2 months and their mean duration of chemotherapy was found 1.0±1.3 months with range from 25 days to 2.5 months.

**Table-8: Intermittent use of opiates of the study patients (n=100)**

Intermittent use of opiates	n	%
Codeine	7	7.0

Table 8 shows the intermittent use of opiates of the study patients, it was observed that intermittent use of opiates (codeine) was 7(7.0%).

**Table-9: Bowel movement parameters (n=100)**

Bowel movement parameters	n	%
Delayed or difficult defecation for 2 wk	13	13.0
Painful or hard stools	40	40.0
Two or fewer defecations per week	47	47.0

Table 9 shows the bowel movement parameters of the study patients, it observed that, almost half (47.0%) patients two or fewer defecations per week.

**Table-10: Perception of children (n=100)**

Perception of children	n	%
No Problem	16	16.0
Minor	80	80.0
Significant	21	21.0
Major Problem	2	2.0

Table 10 shows the perception of children, no problem perception of children was found 16(16.0%). Minor was found 80(80.0%). Significant perception of children was 21(21.0%) and major problem was found 2(2.0%).

**Table-11: Impact of constipation on lifestyle of children (n=100)**

Impact of constipation on lifestyle of children	n	%
No impact	20	20.0
Minor	76	76.0
Significant	23	23.0
Major impact	2	2.0

Table 11 shows the impact of constipation on lifestyle of children, no impact of constipation on lifestyle of children was 20(20.0%) cases. minor impact of constipation on lifestyle of children 76(76.0%), significant

impact of constipation on lifestyle of children 23(23.0%) and major impact of constipation of lifestyle of children 2(2.0%).

#### IV. DISCUSSION

This prospective observational study was carried out with an aim to investigate the prevalence of constipation in children on chemotherapy for cancer, and to determine the associated risk factors for the development of constipation in children on chemotherapy for cancer and also to assess the severity of constipation in this group of children.

In this current study it was observed that constipation was found 62.3% of children receiving chemotherapy for cancer during the study period. In another study Pashankar et al. [10] reported that diagnosed acute constipation in 57% of children receiving chemotherapy for cancer lasting for 2 or more weeks during chemotherapy. A recent systematic reviewed Berg et al. of [11] pediatric studies reported the prevalence of childhood constipation from 0.7% to 29.69%. In a study Loening-Baucke showed the prevalence of acute constipation (lasting less than 8 wk) in children of 4 to 17 years of age was estimated to be 4.6% in a primary care clinic. In Turkey, Uguralp et al. [12] showed 12.4% of school children (5 to 9 years) had constipation diagnosed by the NASPGHAN criteria. Compared with these studies, children on chemotherapy in this study had much higher prevalence of acute constipation. These results are in agreement with studies in adults that report constipation in 30% to 50% of patients with cancer on chemotherapy. [3]

In this current study it was observed that majority (41.0%) of the patients age belonged to  $\leq 5$  years and their mean age  $7.08 \pm 3.8$  years with range from 1.5 year to 14 years. In Turkey, Uguralp et al. [12] evaluated school children age belonged to 5 -9 years had constipation diagnosed by the NASPGHAN criteria. In another study Loening-Baucke [13] observed the acute constipation in children age range from 4 to 17 years, which are comparable with the current study. On the other hand, Pashankar et al. [10] showed mean age was 10.6 years with range from 1.1 to 20.4 years.

Regarding the sex distribution it was observed in this present study that male was found 53.0% developed constipation and female was 47.0% developed constipation due to chemotherapy. Male to female ratio was 1.1:1. Similarly, Pashankar et al. [10] and Droney et al. [1] showed male to female ratio were 1.3:1 and 1.6:1 respectively, which indicates that constipation is predominant in female subjects, which are closely resembled with the current study.

In this study it was observed that nearly two third (63.0%) patients received isolated or combined chemotherapy and rest 37.0% patients had history of constipation. Pashankar et al. [10] assessed several risk factors for constipation in children. None of the children in their study had gastrointestinal cancer or any other obvious organic cause such as anorectal anomalies or obstruction. The authors also ruled out obesity as a contributing factor in children as obesity was related to childhood constipation in a study done by Pashankar and Loening-Baucke. [13, 14] Children who received both vincristine and opiates were at significant risk of developing constipation.

Pashankar et al. [10] mentioned in their study that 87.5% children with previous history of constipation developed constipation on chemotherapy. Several risk factors reported by the investigators that including age group (below or above 10 years), sex, previous history of constipation, obesity, abdominal radiation, as well as isolated and combined use of medications including vincristine, methotrexate, 6-mercaptopurine, cytosine arabinoside, and opiates were assessed. Use of other medications besides chemotherapy and opiates, and underlying diagnosis of malignancy were also assessed for risk of developing constipation. Only combined use of vincristine and cytosine ( $P < 0.03$ ) in children was significantly related to development of constipation whereas other risk factors were not significant. [15]

In this series it was observed that 45.0% patients had acute lymphoid leukemia followed by 36.0% had lymphomas and 19.0% patients had myeloid leukemia. Pashankar et al. [10] found acute lymphoid leukemia 54.0%, Lymphomas 16.0%, Brain neoplasm 5.0%, Myeloid leukemia 5.0% and other solid tumors 20.0%, which are comparable with the current study.

Pashankar et al, [10] mentioned in their study that children receiving both vincristine and opiates were at high risk for development of constipation. Six children in their study were on prophylactic laxatives before chemotherapy and in the absence of these medications the frequency to constipation could have been higher than what the investigators observed. In this current study it was observed that more than three fourth (77.076%) patients need vincristine chemotherapy, 8.0% patients were methotrexate, 46.0% was Cytosine arabinoside and 4.0% 6-mercaptopurine. Children who received both vincristine and opiates were at significant risk of developing constipation. Similarly, Droney et al, [1] Gibson and Keefe, [2] O'Brien, Fan and Kelleher [16] studies mentioned that both vincristine and opiates can decrease colonic motility and can lead to constipation. Pashankar et al. [10] observed in their study patients that Vincristine 73.0%, Methotrexate 54.0%, 6-mercaptopurine 41.0%, and Cytosine arabinoside 20.0%, which is similar with the current study.

In this present study it was observed that majority (42.0%) patients underwent chemotherapy for 1-2 months and their mean duration of chemotherapy was  $1.0 \pm 1.3$  months with range from 25 days to 2.5 months.

The mean duration of constipation was 2.4 weeks with range from 2 to 6 weeks observed by Ross et al. (2005). In another study Pashankar et al. found the mean duration of chemotherapy was 13 months with range from 1 to 48 months. [10]

In this current series it was observed that intermittent use of opiates (codeine) was 7.0%. Pashankar et al, [10] mentioned in their report that only combined use of vincristine and opiates ( $P < 0.03$ ) in children was significantly related to development of constipation whereas other risk factors were not significant, where the investigators found codeine 6.7%.

In this present series it was observed that almost a half (47.0%) of the patients had two or fewer defecations per week, followed by 40.0% had painful or hard stools and 13.0% had delayed or difficult defecation for 2 weeks. Pashankar et al, [10] obtained in their study that delayed or difficult defecation for 2 weeks (NASPGHAN definition of constipation) 57.0%, painful or hard stools 75.0% and two or fewer defecations per week 43.0%, which is consistent with the current study.

### **Limitations of the study**

The present study was conducted in a very short period due to time constraints and funding limitations. The small sample size was also a limitation of the present study.

## **V. CONCLUSION**

Constipation developed due to chemotherapy for cancer in most of the children. Majority of them felt constipation related minor problem and had minor impact on lifestyle.

## **VI. RECOMMENDATION**

Children on cancer chemotherapy are at high risk of developing acute constipation. Constipation is most often related to the use of vincristine and opiates, and aggressive prophylactic laxative therapy should be considered when both medications are used.

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