

# Gastrointestinal and Hepatobiliary Complications following Bone Marrow transplantation in the recent years – A Single Centre Study

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## Abstract

**Introduction:** Nausea, vomiting, diarrhea and abnormal liver function tests (LFT) are common following both autologous and allogenic bone marrow transplantation (BMT). The incidence and severity of these complications have decreased in the last few years with the use of less intensive chemotherapeutic and radiation regimens and better supportive care. Nausea, vomiting, diarrhea or abnormal LFTs can occur due to chemo-radiation, infection or graft versus host disease (GVHD). The study aimed to describe gastrointestinal and hepatobiliary complications following BMT at a tertiary care medical centre in the recent years.

**Methods:** Retrospective chart review of patients who presented with nausea, vomiting, diarrhea or abnormal LFTs within 3 months of bone marrow transplantation at Thomas Jefferson University Hospital between November 1, 2016 and October 31, 2018. Baseline demographics, gastrointestinal complications and liver function test were collected.

**Results:** 15 patients underwent bone marrow transplantation between November 1, 2016 and October 31, 2018. Among these patients, 9 patients had gastrointestinal complications or transaminitis. The average age of these 9 patients was 53 years. 7 of them were males and 6 of them were white. Of these 9 patients, 7 patients had nausea, vomiting or diarrhea and 3 patients had abnormal LFTs. Only 2 patients out of 7 patients with diarrhea were positive for *Clostridium difficile* colitis. Others had diarrhea which was thought to be secondary to regimen related toxicity, and one was from an atypical Crohn's flare. Abnormal LFTs were thought to be secondary to sepsis or medication-induced.

**Discussion:** More than half of the patients who underwent BMT had gastrointestinal or hepatic complications. Unlike other studies, we did not have any patients with GVHD. However, *Clostridium difficile* colitis was not uncommon. There were several cases with an unknown etiology. A larger sample size would be helpful in further delineating the incidence and determining trends of various gastrointestinal and hepatobiliary complications following BMT in recent years.

## Introduction

Bone marrow transplantation is done mostly in specialized tertiary care centers for the treatment of various malignant and non-malignant hematological conditions, immunologic and genetic disorders. About 60,000 bone marrow transplants are done worldwide every year [1]. Autologous (stem cells from the patient him or herself) bone marrow transplantation is generally done to treat patients with lymphoma and multiple myeloma while allogeneic (stem cells from persons with very similar but not identical human leucocyte antigen) bone marrow transplantation is usually done for the treatment of patients with leukemia and myelodysplastic syndrome [2]. Graft-versus-host disease (GVHD) and immune-mediated complications are not seen in autologous bone marrow transplantation. Most patients with hematologic malignancy receive high dose chemo-radiation (myeloablative conditioning regimen) before transplantation. Each patient is at risk of developing a wide variety of post-transplant complications. Various infectious and non-infectious gastrointestinal and hepatic complications have been described in the pre-engraftment phase ( $\leq 30$  days after transplantation), early post-engraftment phase

(30 to 100 days after transplantation) and late post-engraftment phase ( $>100$  days after transplantation) [3]. But in the recent years, these complications have been found to low because of administration of less toxic myeloablative conditioning regimen prior to bone marrow transplantation, prophylactic use of antiviral and antifungal therapy to prevent infection, immunosuppressive therapy to prevent GVHD and ursodeoxycholic acid to prevent hepatobiliary complications [4]. Our study was done to find out the trend of various gastrointestinal and hepatobiliary complications following bone marrow transplantation in our institution.

## Methods

We performed a retrospective study with review of electronic medical records from Thomas Jefferson University Hospital in Philadelphia from November 1, 2016 to October 31, 2018. All patients above the age 18 irrespective of sex, race and ethnicity with nausea, vomiting, diarrhea or abnormal LFTs within 3 months of bone marrow transplantation were included in the study. The study was approved by the Institutional Review Board (IRB).

**Results**

A total of 15 patients underwent bone marrow transplantation during the study period of November 1, 2016 to October 31, 2018. Of those 15 patients, 9 patients had gastrointestinal symptoms or abnormal liver function test. On an average, those 9 patients were middle aged and majority of them were white males. Out of those 9 patients, 7 patients had gastrointestinal involvement with nausea, vomiting or diarrhea, and 3 patients had abnormal LFTs. The demographics, gastrointestinal complications and laboratory values are shown in table 1. Stool for Clostridium difficile toxin was positive in 2 out of the 7 patients with diarrhea. One patient had diarrhea due to flare up of her Crohn’s disease. Rest of the patients had diarrhea due to regimen related toxicity. 3 patients had elevated transaminases due to medication side effects or sepsis.

Table 1: Demographics, gastrointestinal complications and laboratory values for patients with bone marrow transplantation

Number of Patients	Patients with GI Complications	Patients without GI Complications
	9	6
Age of BMT,years (average)	53	61
Male gender	7(=7/9, 78%)	3(=3/6,50%)
White race	6(=6/9, 67%)	5(=5/6,83%)
Symptoms		
Nausea	6(=6/9, 67%)	
Vomiting	1(=1/9, 11%)	
Diarrhoea	7(=7/9, 78%)	
Causes of Diarrhoea		
Clostridium difficile colitis	2(=2/7, 29%)	
Atypical Crohn’s flare	1(=1/7, 14%)	
Regimen related toxicity	1(=1/7, 14%)	
unknown	3(=3/7, 43%)	
Abnormal laboratory values		
AST	2(=2/9, 22%)	
ALT	2(=2/9, 22%)	
Alkaline phosphatase	3(=3/9, 33%)	

**Discussion**

Gastrointestinal and hepatobiliary involvements are the major causes of morbidity and mortality following bone marrow transplantation. In the pre-engraftment phase, marrow aplasia, pancytopenia and mucosal damage occur due to pre-transplantation chemo-radiation therapy, and infection can occur secondary to neutropenia [5]. Broad spectrum antibiotics administered during this period can also be a risk factor for developing infection [6]. Nausea, vomiting, oropharyngeal mucositis with dysphagia, diarrhea due to neutropenic enterocolitis (typhlitis) and pseudomembranous colitis (PMC), abnormal LFT due to drug toxicity, sepsis, cholangitis, ischemic hepatitis, sinusoidal obstruction syndrome (SOS) and hepatic veno-occlusive disease (VOD) can be seen during this period [7]. In the early post-engraftment phase, hematopoiesis is restored but both humoral and cellular defense mechanisms remain weak as recovery of lymphocytes occurs slowly. The complications that arise during this period include are viral gastroenteritis (cytomegalovirus, rotavirus, adenovirus), acute GVHD, benign pneumatosis intestinalis, thrombotic microangiopathy and megacolon. In the late post-engraftment phase, chronic GVHD, post-transplantation lymphoproliferative disease (PTLD) and secondary malignancy can occur [8]. Gastrointestinal (GI) bleeding can occur during any engraftment phase. Common etiologies include mucosal necrosis from conditioning therapy, infective enterocolitis (cytomegalovirus, adenovirus, varicella-zoster virus, fungal infection), acute and chronic GVHD, ischemic enterocolitis due to thrombotic microangiopathy, mycophenolate-related ulcerations, gastric antral vascular ectasia (GAVE) and peptic ulcer disease [9]. But with the use of routine anti-viral, anti-fungal and GVHD prophylaxis, GI bleeding has become rare (1%-2%). In our study, majority of the patients with bone marrow transplantation were symptomatic with nausea, vomiting and diarrhea and minority of the patients had abnormal LFT. Most of the patients had diarrhea due to regimen-related toxicity. A minority of them had diarrhea due to infection. Medication and sepsis were the causes of abnormal LFT. No major gastrointestinal or hepatobiliary complications occurred in patients with bone marrow transplantation in our study. This may reflect much improved preventive care before and after bone marrow transplantation in the recent years.

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