

## PROTOCOL FOR DENTAL TREATMENT BEFORE BONE MARROW TRANSPLANTATION (BMT) IN PAEDIATRIC PATIENTS

<sup>1</sup>SAEEDA ABDULLAH, BDS, MCPS, FCPS

<sup>2</sup>ZAHIDA AHMAD, BDS

### ABSTRACT

*Bone marrow transplant (BMT) provides a chance to life for the patients with end-stage diseases like leukaemia, aplastic anaemia etc. The success of the transplantation procedure depends on the immune reactivity of the recipient patient, which may trigger the rejection. The aim of the present study was, to find out dental treatment needs in patients before BMT in Children's Hospital, Pakistan Institute of Medical Sciences (PIMS, Shaheed Zulfiqar Ali Bhutto Medical University) Islamabad, and also to make the dentists aware of the special needs of BMT patients, the specific medication and the necessity of an effective dental treatment. It was retrospective study done on 44 children who required BMT and were referred from oncology department of Children's hospital. Data of patients were taken from the hospital records. The age of patients ranged from 01-12 years with mean of  $4.69 \pm 2.5$  years. Out of total 44 patients, 12 were females and 32 were males. The difference in ratio between male and female patients is statistically significant ( $P < 0.01$ ). Patients were divided into 2 groups of 1-5 years and 6-12 years. The difference in ratio of males to females in age group of 1-5 years is also significant ( $P < 0.01$ ). Patients who required dental treatment before Bone Marrow Transplant were 29 (65.5%), while 15 (34%) patients did not require any dental treatment. This difference is highly significant ( $P < 0.05$ ). More dental treatment was required in age group of 1-5 years old children as compared to group of 6-12 years old. Total 101 teeth were restored, 13 teeth were extracted and 19 fissure sealants were placed. None of the patient showed dental infection after bone marrow transplant, therefore the protocol of the pre-BMT dental treatment was helpful in minimizing infection during immune-suppression period of post bone marrow transplantation.*

**Key Words:** Bone marrow transplantation, dental treatment in BMT, dental management in immuno-compromised patients, BMT in paediatric patients.

### INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) or bone marrow transplantation (BMT) has become an essential treatment for many patients with malignant and non-malignant haematological diseases, including acute and chronic leukaemia, aplastic anaemia, myelodysplastic syndromes and lymphomas.<sup>1</sup> Although BMT is an effective treatment modality for these patients, successful engraftment after BMT requires adequate immune-suppression of the recipient, which is accomplished with total body irradiation, chemotherapy or a combination of both. Their immune-suppressed status

makes the patients more susceptible to infection, resulting in an increased risk of infectious complications, including the development of severe septicaemia that may be life-threatening.<sup>1,2</sup>

Oral cavity is a potential site of such infectious complications in patients receiving BMT therapy, because it is an important port of entry for agents that can cause systemic infections.<sup>3</sup> To prevent these oral complications, pre-transplant comprehensive oral care has been incorporated into the preparatory steps for patients scheduled to receive BMT therapy. This approach is supported by the National Institute of Health consensus statement on oral complications of cancer therapy, which states, "Dental foci are potential sources of systemic infections that need to be eliminated before commencement of anticancer therapy". Therefore, to prevent significant morbidity, all sources of potential infection should be treated appropriately and the dentist should know the protocol for treating such patients.<sup>1-3</sup>

<sup>1</sup> Assistant Professor, Dental Department (PIMS), Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan.

**Correspondence:** E mail: dr\_saeeda@hotmail.com

<sup>2</sup> Senior Dental Surgeon, Dental Department, PIMS (SZABMU) Islamabad

**Received for Publication:** June 30, 2014

**Revision Received:** August 16, 2014

**Revision Accepted:** September 1, 2014

As the patient is confronting the terminal phase of sickness of an organ, the preventive and therapeutic dental conduct should be established in collaboration with the team who will perform the transplant. There should be a thorough examination of the oro-facial area, for early diagnosis and treatment of any infection/problem which would need a surgical intervention in the immediate post-transplant phase. The prevention of infection is very important because first few weeks after the transplant surgery, the patient will have a low immunity due to the induction of the immune-suppression drugs, which are required for the prevention of the graft's rejection.<sup>4,5</sup>

Hemopoietic Stem Cell Transplantation is the transplantation of multi-potent hematopoietic stem cells, usually derived from bone marrow, peripheral blood, or umbilical cord blood. Specific oral complications can be correlated with phases of HSCT.<sup>1,6-9</sup>

Most of the principles of dental and oral care before the transplant are similar to those for paediatric cancer patient except for 2 differences.<sup>10</sup> The two major differences are: 1) in BMT, the patient receives all the chemotherapy and/or total body irradiation in just a few days before the transplant, and 2) there will be prolonged immune-suppression following the transplant. Elective dentistry will need to be postponed until immunological recovery has occurred at least 100 days following HCT.<sup>5,6</sup> Therefore, all dental treatment should be completed before the patient becomes immune suppressed.

It is preferable to avoid any post-transplant dental treatment for 6 months, due to fatigue in the patient, drugs interaction and side effects of the drugs administered during the post-transplant treatment. As BMT may cause leucopenia or thrombocytopenia, the patient is in general prone to infection, bleeding and delayed healing. The dental treatment should focus on providing an optimal oral health to the patient before the surgical intervention.

Objectives of dental and oral care before the start of bone marrow transplant (BMT) are:<sup>4,5</sup>

- 1 To identify and to eliminate the existing sources of infection in the oral cavity.
- 2 To communicate with the oncology team regarding the patient's oral health status, plan and timing of treatment.
- 3 To educate the patient and the parents about the oral care importance to minimize oral problems before, during and after treatment.

Dental management before transplant – prophylactic and therapeutic treatment.

Dental history review should include fluoride exposure, habits, trauma, symptomatic teeth, previous dental care, preventive dental treatment, oral hygiene and diet assessment.<sup>10</sup>

Oral hygiene includes brushing of the teeth and tongue two to three times daily with regular soft nylon brush or electric toothbrush, regardless of the haematological status.<sup>10-13</sup> Ultrasonic brushes and dental floss should be allowed only, if the patient is properly trained.<sup>6</sup> Patients with poor oral hygiene and/or periodontal disease may use chlorhexidine rinses daily until the tissue health improves.<sup>14</sup> The high alcohol content of commercially available chlorhexidine mouthwash may cause discomfort and dehydrate the tissues in patients with mucositis; thus, an alcohol-free chlorhexidine solution is indicated in this situation.

In patients with good oral hygiene, a special emphasis should be laid on the education for dental health. In patients with a poor oral hygiene and who are not motivated to improve their oral health level, extraction of carious and periodontally involved teeth should be performed.

Dental management of the patient before an organ transplantation may be summarized as follows.<sup>7-10,15</sup> 1. Initial consultation of the patient's physician, in order to discuss the current medical state of the patient, the laboratory blood tests and prescription of the antibiotic prophylaxis or other drugs. 2. Conduct complete series of radiographs for the dentate patients.<sup>16</sup> 3. Attentive oro-maxillo-facial examination, considering the potential development of the malignancies at this level. 4. Patient should be instructed for self-oral care, both by the individualization of the dental brushing technique. The parents of the paediatric patients should be instructed to supervise oral hygiene of their children. 5. Prescribe fluoridated toothpastes and perform topical fluoridation with custom fluoride trays, in case of multiple dental caries. 6. Diet counselling. 7. Remove the microbial dental plaque by scaling/curettage after giving the antibiotic prophylaxis and advise plaque control techniques. 8. Use chlorhexidine 0.12% mouthwash, which may be beneficial as antimicrobial by rinsing before any dental procedures. 9. Try to maintain the teeth by endodontic treatment (preferred over extraction). 10. Restoration of carious teeth with favourable prognosis. 11. Extraction is indicated in non restorable or the teeth with poor prognosis, periodontally involved teeth with > 5-6 mm deeper pockets, teeth with furcation involvement or endo-periodontal lesions, very deep or extensive carious teeth, teeth with periapical lesions and teeth requiring RCT with uncertain prognosis. Use suturing techniques and haemostatic agents in order to ensure the haemostasis after extraction. 12. Use pain management with Acetaminophen (Paracetamol, Ty-

lenol) in adjusted doses. The administration of Aspirin should be avoided, because it increases the bleeding potential. 13. Prescribe antibiotics after consultation with physician of the patient. Antibiotics (erythromycin and clarithromycin), azole anti-fungals (ketoconazole, fluconazole and itraconazole) and NSAIDs can alter the levels of cyclosporine and consequently can increase the levels in serum, rendering patients with a greater immunosuppression. Co-trimoxazole, tetracyclines, aminoglycosides and quinolones increase the risk of nephrotoxicity.<sup>17</sup>

## OBJECTIVES

The aim of the present study was to find out dental treatment needs in patients before bone marrow transplant (BMT) which were to be operated in Children's Hospital, PIMS (Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad) and also to make the dentist aware of the special needs of BMT patients, the specific medication and the necessity of an effective dental treatment.

## METHODOLOGY

It was a retrospective study done on children who were candidates for BMT therapy. Patients were referred during years 2010-13 from the oncology department of Children's Hospital, PIMS (Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad). Only mentally normal patients who received BMT were included in the study. Patients in whom after dental treatment, BMT was not performed due to any reason or patients who had already received any radiation/chemotherapy, or were mentally retarded were excluded from the study. After approval of ethical committee of the hospital, forty four children who fulfilled the inclusion criteria were selected for the study. Data of the patients were taken from the hospital records of dental department of Children's Hospital (PIMS).

Before BMT, the dental status of all patients was evaluated at the initial visit by one experienced dentist. The screening examination consisted of a clinical examination of the hard and soft oral tissues and periapical films for symptomatic teeth only. Bitewing radiographs were not taken for diagnosis of proximal caries. Dental foci were defined as caries, apical and marginal periodontitis.

Teeth with mild or moderate caries were restored and non restorable teeth were extracted. Fissure sealants were placed in patients with high caries rate. All patients, including those without dental foci were given tooth brushing instructions to exfoliate dental plaque. After BMT follow ups for dental examination were done after one month, 03 months and 06 months. Demo-

graphic details, dental treatment provided and follow up were recorded in specially constructed Proformas. Data were entered in SPSS version 20 and analyzed. To compare any difference in treatment need in 2 age groups and in gender, t test was applied. The P value was set at < 0.05. It was also found out how many patients developed post BMT dental infection with and without prior dental treatment.

## RESULTS

Forty four patients were included in the present study. The age of the patients ranged from one to twelve years with mean of 4.69± 2.5 years. Out of these 44 patients, 12 (27.2 %) were females and 32 (72.8%) were males (Fig 1). The difference in ratio between male and female patient is statistically significant (P<0.01). Patients were divided into 2 groups of 1-5 years and 6-12 years and none of the patients was in age of 9 or 10 years (Table 1). The difference in ratio of males to females in age group of 1-5 years was also significant (P<0.01).

TABLE 1: TREATMENT NEEDS BEFORE BMT ACCORDING TO AGE GROUPS AND GENDER

Age	Males	Fe-males	Treat-ment required	Treat-ment not required
1-5 years	24	4**	17	11*
6-12 years	8	8	12	4*
Total	32	12**	29	15**

P < 0.05\* P < 0.01\*\*

TABLE 2: DENTAL PROCEDURES PERFORMED BEFORE BMT

Age	Fillings	Ext due to caries	FS	HCV+
1-5 years	50	1	6	1
6-12 years	51	12	13	3
Total	101	13	19	4

P < 0.05\* P < 0.01\*\*

TABLE 3: POST BMT DENTAL INFECTIONS

	No. of patients	Post BMT Dental infection cases (%)
Cases of BMT without pre-dental evaluation/treatment	30	3 (10%)
Cases of BMT with pre-evaluation/dental treatment	44	Nil (100%)

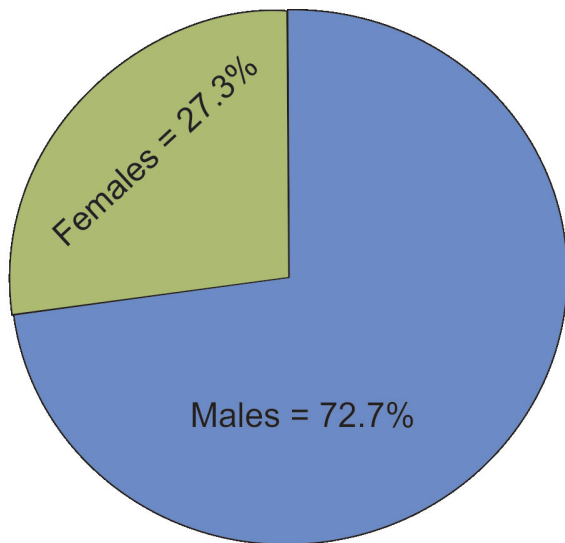


Fig 1: Gender distribution of patients

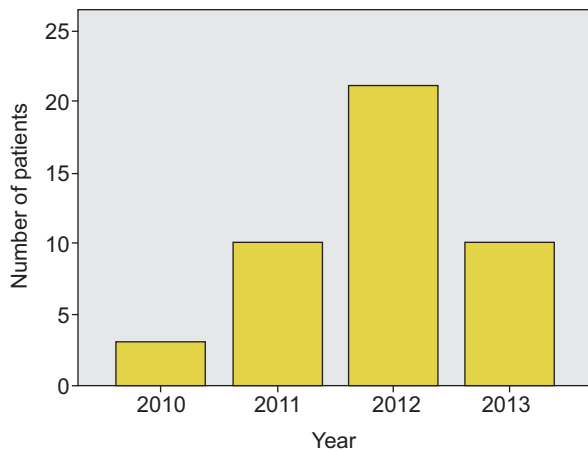


Fig 2: Year wise distribution of patients under gone BMT

Out of total 44 patients, 21 (47.7%) were referred to dental department in year 2012 (Fig 2). Only 03 patients (6.8%) were referred in year 2010. This difference is statistically significant ( $P < 0.01$ ).

Twenty nine patients (65.9%) required dental treatment while 15 (34%) did not require any dental treatment before transplantation (Table 1). This difference is statistically significant ( $P < 0.05$ ). It was found that number of patients who required dental treatment were more in age group of 1-5 years as compared to group of 6-12 years, although percentage of patients required dental treatment was more in age group of 6-12 years (Table 1). It was also observed that although the number of patients required dental treatment in age group of 6-12 years was less, but more dental treatment was required as compared to 1-5 years age group (Table 2). Total 101 teeth were restored. Non restorable 13 teeth were extracted and 19 fissure sealants were placed in 29 patients (Table 2). None of the patient received endodontic treatment.

Four patients were suffering from hepatitis C. One was in age group of 1-5 years and 03 were in age group of 6-12 years (Table 2).

Table 4 shows the summary of post dental infection with and without pre-dental evaluation or treatment. During 2008-09, total 30 patients received BMT without prior dental evaluation and treatment and 03 (10%) cases suffered post BMT dental infection, while no post BMT dental infection was found in 44 cases, which were treated during 2010-13 with pre dental evaluation/treatment.

## DISCUSSION

Oral cavity is highly susceptible to the effects of chemotherapy and radiation. It is the most frequently documented source of sepsis in the immune-suppressed cancer patients. For these reasons, early and definitive dental intervention, including comprehensive oral hygiene measures, reduce the risk for oral and associated systemic complications.<sup>6,7,14,18-21</sup>

Dental screening before BMT/ HSCT to identify and treat potential oral sources of infection has become standard care.<sup>19</sup> The principal aim of screening is to reduce morbidity and mortality, which may arise from oral complications associated with BMT therapy during immune-suppression. The key to success in maintaining a healthy oral cavity during immune-suppression is patient compliance.

In literature review, it is suggested to perform all dental treatment in patients who are candidate for BMT.<sup>16-21</sup> In present study dental treatment was provided to patients before BMT and none of them showed post BMT infection due to dental foci in 6 months period.

Few studies showed no difference of dental treatment on post BMT infections. On comparison between patients with no dental foci or completed dental treatment and those with dental foci or no dental interventions, Yamagata found that the impact of dental foci on the occurrence of post-HSCT infections was not statistically significant.<sup>22</sup> He also suggested that intensive pre- HSCT dental treatment is not necessary. Similarly Toljanic reported that patients with chronic dental pathology were safe to proceed with chemotherapy without dental intervention as the conversion of chronic dental disease to an acute state during chemotherapy occurs infrequently.<sup>23</sup> Toljanic demonstrated that oncologic treatment outcomes were unaffected by acute exacerbations of non treated chronic disease, but majority of the patients in his study received only chemotherapy, which does not require the serious immune-suppression needed for HSCT therapy.<sup>23</sup> These reports are in contrast to present study in which pre BMT dental treatment

minimised the post BMT infection chances. Children's Hospital (PIMS) record showed that before adapting the protocol of pre BMT dental management, the post BMT dental infection had developed in 10% of cases.

Not all previous studies have supported a need for pre- BMT/HSCT dental treatment. Melkos et al reported that there was no significant difference in the occurrence of infection originating from oral disease during and after HSCT therapy between patients, with and without pre- BMT/HSCT dental treatments.<sup>24</sup>

Chronic marginal periodontitis is the most common significant dental infection, which affects BMT/HSCT patients.<sup>25</sup> A retrospective investigation reported that 64% of patients with chronic periodontal disease had positive blood cultures and septicemia during the initial 100 days after BMT/HSCT.<sup>25</sup> However, as little data are available about the effect of pre- BMT dental treatment for chronic periodontitis on the incidence of infectious complications, the treatment modality has varied from observing the affected teeth to removing a symptomatic teeth.<sup>25</sup> Chronic marginal periodontitis was not found in the present study probably because this study was on paediatric patients, which suffer less periodontal problems as compared to adult patients.

In addition to the management of oral diseases, emphasis should be on regular instructions to the patients about oral care during immune suppression.<sup>26</sup> Therefore in present study, repeated verbal instructions on oral care were given to the patients and parents at every visit to minimize dental problems after BMT.

Vaughan found a significant increase in the frequency of caries that can serve as nidus for infection in immune-compromised patients.<sup>27</sup> Interestingly in the present study the frequency of caries was not more as compared to healthy children.

There are no studies to date that address the safety of performing pulp therapy in primary teeth prior to the initiation of chemotherapy and radiotherapy. Many clinicians prefer extraction to avoid pulpal infections during immune-suppression periods which can become life-threatening.<sup>6,20,21,28,29</sup> Literature showed symptomatic non-vital permanent teeth should receive root canal treatment at least one week before initiation of chemotherapy to allow sufficient time to assess treatment success and if that is not possible, extraction is indicated.<sup>33</sup> The extraction should be followed by antibiotic therapy (penicillin or for penicillin-allergic patients, clindamycin) for about one week.<sup>33</sup> Keeping in mind the recommendations of these studies, no endodontic therapy was performed in either primary or permanent teeth in the current study subjects.

## CONCLUSIONS

Organ transplant recipients are growing in number and living longer, thus there is increasing demand for specialized dental treatment.

Effective dental treatment before BMT can play an important part in these patients lives by preventing serious infection.

Children's Hospital (PIMS) is providing good dental care to paediatric patients before and after bone marrow transplantation. The dentists are working in complete coordination with the physicians of the patients when providing dental treatment.

## REFERENCES

- 1 Appelbaum FR. Use of bone marrow and peripheral blood stem cell transplantation in the treatment of cancer. *CA Cancer J Clin* 1996; 46:142-64.
- 2 Centers for Disease Control and Prevention. Guidelines for preventing opportunistic infection among hematopoietic stem cell transplant recipients. *MMWR Recomm Rep* 2000; 49:1-128.
- 3 Barker GJ. Current practices in the oral management of the patient undergoing chemotherapy or bone marrow transplantation. *Support Care Cancer* 1999; 7: 17-20.
- 4 Da Fonseca MA. Long-term oral and craniofacial complications following pediatric bone marrow transplantation. *Pediatr Dent* 2000; 22(1):57-62.
- 5 Hong CH, daFonseca M. Considerations in the pediatric population with cancer. *Dent Clin N Am* 2008; 52(1):155-81.
- 6 Schubert MM, Peterson DE. Oral complications of hematopoietic cell transplantation. In: Appelbaum RF, Forman SJ, Negrin RS, Blume KG, eds. *Thomas' Hematopoietic Cell Transplantation: Stem Cell Transplantation*, 4th ed. Oxford, UK: Wiley-Blackwell; 2009:1589-607.
- 7 Goldman KE. Dental Management of Patients with Bone Marrow and Solid Organ Transplantation. In *The Dental Clinics of North America* 2006 (50):659-76.
- 8 Little JW, Falace AD, Miller CS, Rhodus NL. *Dental Management of the Medically Compromised Patient*, 7th Ed., Mosby Inc. (Elsevier Inc.) 2008:339-59.
- 9 Suzuki JB, Chialastri SM. Dental implications for the immune-compromised organ transplant patient. *Grand Rounds in Oral-Systemic Medicine Magazine*.2007; vol 2(3):2-12.
- 10 American Academy of Pediatric Dentistry. Guideline on Dental Management of Pediatric Patients Receiving Chemotherapy, Hematopoietic Cell Transplantation, and/or Radiation. *Reference Manual* 2013; 35(6 1 3/14): 284-92.
- 11 Lalla RV, Brennan MT, Schubert MM. Oral complications of cancer therapy. In: Yagiela JA, Dowd FJ, Johnson BS, Marriot AJ, Neidle EA, eds. *Pharmacology and Therapeutics for Dentistry*. 6th ed. St. Louis, Mo: Mosby-Elsevier; 2011:782-98.
- 12 Bavier AR. Nursing management of acute oral complications of cancer. *Consensus Development Conference on Oral Complications of Cancer Therapies: Diagnosis, Prevention, and Treatment*. National Cancer Institute Monograph Bethesda, Md: National Institutes of Health 1990 ; (9):23-128.
- 13 Peterson DE, Bensadoun RJ, Roila F. ESMO Guidelines Working Group. Management of oral and gastrointestinal mucositis: ESMO Clinical Practice Guidelines. *Ann Oncol* 2011; 22 (Suppl 6):78-84. Erratum in *Ann Oncol* 2012; 23(3):810.

- 14 Hong CH, Napeñas JJ, Hodgson BD, et al. A systematic review of dental disease in patients undergoing cancer therapy. *Support Care Cancer* 2010; 18(8):1007-021.
- 15 Buzea CM, Cuculescu M, Podoleanu E, Preoteasa C T and Ranga R .Dental treatment considerations for the organ and bone marrow transplant patient. *Wseas Transactions on Biology and Biomedicine* July 2009; 6(3):70-8.
- 16 Ciurescu D, Barabas S, Sangeorzan L, Neica L. Digital Radiography using high dynamic range technique. *Mathematical methods and applied computing*, vol II, WSEAS Press, 2009:599-603.
- 17 Carlos Fabien L, Zavala Estevez C, Carrion Perez MG. Dental management in transplant patients. *Dental management in transplant patients. J Clin Exp Dent* 2011; 3(1):43-52.
- 18 National Cancer Institute: PDQ® Oral Complications of Chemotherapy and Head/Neck Radiation. Bethesda, MD: National Cancer Institute. Modified Feb 28, 2013. Available at:<http://cancer.gov/cancertopics/pdq/supportivecare/oralcomplications/HealthProfessional>." Accessed March 25, 2013.
- 19 Hong CH, Brennan MT, Lockhart PB. Incidence of acute oral sequelae in pediatric patients undergoing chemo-therapy. *Pediatr Dent* 2009; 31(5):420-25.
- 20 Elad S, Thierer T, Bitan M, Shapira MY, Meyerowitz C. A decision analysis: The dental management of patients prior to hematology cytotoxic therapy or hematopoietic stem cell transplantation. *Oral Oncol* 2008; 44(1):37-42.
- 21 American Academy of Pediatric Dentistry. Guideline on pediatric oral surgery. *Pediatr Dent* 2012; 34 (special issue): 264-71.
- 22 Yamagata K , Onizawa K, Yanagawa T, Hasegawa Y, Kojima H, Nagasawa T and Yoshida H.. A prospective study to evaluate a new dental management protocol before hematopoietic stem cell transplantation. *Bone Marrow Transplantation* 2006; (38): 237-42.
- 23 Toljanic JA, Bedard JF, Larson RA, Fox JP. A prospective pilot study to evaluate a new dental assessment and treatment paradigm for patients scheduled to undergo intensive chemotherapy for cancer. *Cancer* 1999; 85: 1843–848.
- 24 Melkos AB, Massenkeil G, Arnold R, Reichart PA. Dental treatment prior to stem cell transplantation and its influence on the post-transplantation outcome. *Clin Oral Invest* 2003; 7: 113–15.
- 25 Lazarchik DA, Filler SJ, Winkler MP. Dental evaluation in bone marrow transplantation. *Gen Dent* 1995; 43: 369–71.
- 26 Majorana A, Schubert MM, Porta F, Ugazio AG, Sapelli PL. Oral complications of pediatric hematopoietic cell transplantation: diagnosis and management. *Support Care Cancer* 2000; 8: 353–65.
- 27 Vaughan M D , Rowland C C , Tong X , Srivastava D K , Hale G A , Rochester R and S C Kaste. Dental abnormalities in children preparing for pediatric bone marrow transplantation. *Bone Marrow Transplantation* 2005; 36: 863–66.
- 28 Lalla RV, Brennan MT, Schubert MM. Oral complications of cancer therapy. In: Yagiela JA, Dowd FJ, Johnson BS, Marrioti AJ, Neidle EA, eds. *Pharmacology and Therapeutics for Dentistry*. 6th ed. St. Louis, Mo: Mosby-Elsevier; 2011:782-98.
- 29 Elad S, Thierer T, Bitan M, Shapira MY, Meyerowitz C. A decision analysis: The dental management of patients prior to hematology cytotoxic therapy or hematopoietic stem cell transplantation. *Oral Oncol* 2008; 44(1):37-42.