

Infections after Bone Marrow Transplantation: Review Article

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ABSTRACT

Background: Bone marrow and stem cell transplantation have become conventional therapy, with the potential to cure a variety of hematologic malignancies and immunologic diseases. Severe infection is still a potentially fatal complication following transplantation, contributes significantly to morbidity, and may demand ICU admission.

Objectives: The present study aims to summarize current evidence on the prevalence, risk factors, and management approaches of infections after bone marrow transplantation.

Methodology: For article selection, the PubMed database and EBSCO Information Services were used. All relevant articles relevant to our topic and other articles were used in our review. Other articles that were not related to this field were excluded. The data was extracted in a specific format that was reviewed by the group members.

Conclusion: the result of the 12 studies included, proves the high risk of infections after bone marrow transplantation and its high mortality effect. Post transplantation patient's immune system is vulnerable, opportunistic infections occur such as viruses and fungi. The highest prevalence recorded in Adenovirus infections reaching 29% of patients throat swaps, urine, and stool samples come positive affirming the diagnosis.

Keyword: Bone marrow, stem cell transplantation, irritable bowel syndrome, Infections.

Introduction

Bone marrow-derived, multipotent hematopoietic stem cells, patients who receive peripheral blood transfusions or umbilical cord blood transplants when doing a hematopoietic stem cell transplant (HSCT) so that they can multiply and create more healthy blood cells [1- 6]. It may be syngeneic (from an identical twin), allogeneic (from a donor), or autologous

(Utilizing the individual's own stem cells) [4, 5]. Patients with bone marrow or blood malignancies such as multiple myeloma or leukemia are the ones who receive it most frequently [5]. The use of a person's stem cells typically shattered undergo chemotherapy or radiation treatments before the transplant. Graft versus host disease and infection are two issues that

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Might arise with allogeneic HSCT [5]. For patients with life-threatening diseases only, HSCT is still a risky procedure with many potential side effects. The application of the procedure was expanded to include autoimmune diseases as its rate of success has risen [7, 8] including malignant infantile osteoporosis and inherited skeletal dysplasia [9, 10]. Conjunction with mucopolysaccharidosis [11]. BMT is recommended for both cancerous and non-cancerous reasons such as multiple myeloma, myelodysplastic syndromes, neuroblastoma, Ewing sarcoma, gliomas, and other solid tumors as well as chronic myeloid leukemia, acute myeloid leukemia, acute lymphoblastic leukemia, and Hodgkin lymphoma (relapsed, refractory), Non-Hodgkin lymphoma (relapsed, refractory). Fanconi anemia, Sickle cell anemia, thalassemia, and other non-cancerous conditions, infantile malignant mucopolysaccharidosis, pyruvate kinase deficiency, osteoporosis paroxysmal nocturnal hemoglobinuria, immune system disorders, multiple sclerosis are examples of several autoimmune diseases [12, 13, 14]. BMT can be allogeneic or autologous. Hematopoietic stem cells (HSCs) from the patient must be removed (via apheresis) and then frozen to do autologous HSCT. The patient is subsequently given high-dose chemotherapy, either alone or in conjunction with radiotherapy, with the intention of completely or partially ablating the bone marrow while destroying the patient's population of cancerous cells. After being transfused into the patient's bloodstream, the patient's stem cells are subsequently employed to replace any damaged tissue and resume normal blood cell production [2]. The patient and the donor are both participants in an allogeneic HSCT procedure. Allogeneic HSC donors must match the recipient's tissue type (HLA). The preferred match at these loci is a perfect match, although matching is done based on variability at three or more HLA gene loci. Immunosuppressive drugs will be required for the recipient to avoid graft-versus-host disease. Related, syngeneic, or unrelated individuals can donate organs allogeneically. A bone marrow donor database, like the National Marrow Donor Program (NMDP) in the US, can help locate unrelated donors [15]. Revaccination is necessary for autologous and allogeneic bone marrow transplant (BMT) recipients because they lose their body's ability to recognize previously exposed infectious pathogens and vaccinations. A major danger of hematopoietic cell transplantation is infection. The two main problems with an infection risk are chronic neutropenia and graft-versus-host disease, and these

consequences differ according to the graft source [16].
Study Objective: The present study aims to summarize current evidence on the prevalence, risk factors, and management approaches of infections after bone marrow transplantation.

Methods

The ENTREQ statement, which promotes greater reporting of the analysis of qualitative research with transparency, was applied in this scientific analysis.

Research plan: To develop a coherent empirical study program that expands existing information, a systematic assessment of the current data on infections following bone marrow transplantation is regarded as a reliable method of locating as well as synthesis the peer-reviewed literature in this area for proof. Only an interpretation could be made from the qualitative material in this review. Additionally, a synthesis of qualitative data aims to generate findings that are relevant, appropriate, accurate, and important to each individual, to guide more effectively influence policy and practices regarding infections after bone marrow transplants, a meaningful research program is needed. The review combined, integrated, and, where appropriate, interpreted the data from the included studies using qualitative synthesis approaches. The evaluation attempts to go beyond the simple collection of data to offer further interpretive insights into infections following bone marrow transplantation and identify areas where more research can advance our understanding.

Criteria for study eligibility: Peer-reviewed qualitative research was included in the review. Mixed method studies' qualitative data was assessed to be included only if the qualitative element is significant, it will be included. Peer-reviewed studies that reported on the prevalence and risk factors of infections after bone marrow transplantation from the perspectives of patients, families, healthcare professionals, and the healthcare delivery system were all published in English. Only studies published between January 2012 and August 2021 were included to maintain the work's currency and provide a broad perspective for identifying developing difficulties.

Study subjects: The study covered all articles that we came to find that discuss infections following bone marrow transplantation using the perspectives of most patient demographics (both adults and kids), families, both healthcare professionals.

Study Inclusion with Exclusion criteria: The papers were chosen for the project based on their applicability, and the English language and Saudi Arabia's geographic restrictions were taken into

consideration. All additional publications, repeated studies, reviews of research, and articles that did not have one of these issues as their primary end were disregarded. Journal articles, conference abstracts, books, grey literature, and unpublished studies that are not available in English were all disregarded by the reviewers. Studies that only provided qualitative data were disregarded.

Search strategy: Headings for medical subjects (MeSH) and restricted language were employed in an approach that was used to find peer-reviewed literature on infections following bone marrow transplants. The databases included Google Scholar, EbscoHost, Scopus/Embase (Elsevier), and PubMed/MEDLINE. The time frame for the search was set from January 2012 to August 2021.

Selection of study: The selection procedures and outcomes were presented following the ENTREQ reporting criteria [11] for qualitative systematic reviews. To help with duplication removal, all studies found were when first imported into the Endnote repository. After eliminating the duplicates, the two reviewers used a shared Endnote library to individually browse the papers by the heading and summary while being led according to the prerequisites. The research that both reviewers would have selected was given a full-text review. Disputes if there are any between the two reviewers were resolved by a third critic. The whole pertinent study texts were read. Independently by both reviewers. The consensus was sought in cases where there were disagreements between the two reviewers by talking about the disagreements with the third reviewer. For the final framework synthesis, the complete texts of all pertinent research that satisfied the inclusion criteria were kept.

Data collection: The information regarding the research population and the pertinent phenomena was filled up on a customized data extraction form by two reviewers who independently collected data from eligible studies. The extracted articles were double-checked and verified by the third reviewer. As research characteristics, the initial author's name, the year of publication, the length of the data collection, and the study's geographic area were all gathered. Then, details about the study itself should be noted, including its demographics, sample size, sampling procedures, and data-gathering methods. There has been substantial research done on infection prevalence and risk factors following bone marrow transplantation.

Data synthesis and analysis: Data analysis was done without the use of any software. The data was organized by theme by the reviewers, who then presented the themes as an analytical table. The rows and columns of (Table 1) represented the research and related topics, allowing us to compare study results across various themes and subthemes.

Results

The result of this study proves the high risk of infections after bone marrow transplantation and its high mortality effect [22]. Post transplantation patient's immune system is vulnerable, opportunistic infections occur such as viruses and fungi. The highest prevalence was recorded in Adenovirus infections reaching 29% of patients [21]. Throat swabs, urine, and stool samples come positive affirming the diagnosis. Respiratory infections among allogeneic SCT patients recorded 3.5% while autologous patients experienced a frequency of 0.4% [19]. Infections of the lower respiratory tract were 2.1% more frequent in allogeneic SCT patients compared to autologous SCT patients (-0.2%). After receiving a diagnosis of a respiratory virus within 28 days, 1.1% of allogeneic SCT patients passed away. However, no patient with an autologous SCT died. Respiratory virus infection was directly responsible for five patient deaths 0.6% [19]. A low prevalence of *Schizophyllum commune* [23], *Mucormycosis* [24], *Stenotrophomonas maltophilia* [25], and *Phialemonium curvatum* [26], as well as toxoplasmosis [28], was investigated.

Discussion

Various hematologic malignancies and immunologic diseases may be cured using traditional therapy such as stem cell and bone marrow transplantation. After transplantation, severe infection is still a potentially fatal complication that increases morbidity and may call for ICU hospitalization. It is predicted that 20–40% of patients will have this condition. Who receive bone marrow transplants, an ICU is a necessary admittance during the first stage of the transplant process. ICU mortality rates have historically been low, particularly when there must be mechanical ventilation owing to breathing difficulty. There have been suggestions to ration or restrict access to critical care facilities and related actions because increased organ involvement worsens the prognosis. Recent investigations have revealed modest but important increases in the course of a critical illness. It is unclear whether better patient selection or altered supportive care levels are to blame for this improvement.

Table1: The included studies:

Author	Year	Causative agent	Participant	Study
Lee et al. [17]	2022	Mucormycosis	Single case	Patient with invasive fungal laryngopharyngitis who complained of a persistent sore throat following BMT. A fungal infection with suspicious mucormycosis was suggested by biopsy and culture. A wide excisional debridement and a partial pharyngectomy with an anterolateral thigh-free flap incorporating the deep fascia were performed.
Kim et al. [18]	2019	Schizophyllum commune	66-year-old man	It is a typical basidiomycete fungus. After receiving allogeneic BMT for myelodysplastic syndrome, pt developed maxillary and ethmoid sinusitis. Filamentous fungal elements were found in the para nasal mucosa debridement tissue. Furthermore, genetic testing on the tissue revealed the presence of S commune.
McDonald et al [19]	2019	Cytomegalovirus Hepatitis	50 transplant patients	Autopsy specimens were examined for CMV-infected cells in five groups of ten, based on the extent of CMV infection during life and at autopsy. Autopsy liver specimens to determine the prevalence of cytomegalovirus hepatitis. CMV-infected cells were found in the livers of 20% of patients.
Heins-Vaccari et al. [20]	2017	Stenotrophomonas maltophilia	44-year-old woman	Because of the repeated bacterial infections caused by hypoplastic myelodysplastic syndrome, the patient underwent allogeneic BMT. Pt was given broad-spectrum antibiotics. Hemorrhagic pneumonia required ventilation support, massive transfusion, and catecholamine administration. She died 8 hours after the onset of hemoptysis.
Yamazaki et al. [21]	2010	Non-tuberculous mycobacteria	33-year-old	Allogeneic BMT was performed on a man with myelodysplastic/myeloproliferative disease. He complained of abdominal pain and diarrhea around day 80 post-transplant. Atrophic villi and mild erosions in the small intestine were discovered during a double-balloon enteroscopy. PCR for Mycobacterium tuberculosis was negative, and an intestinal non-tuberculous mycobacteria (NTM) diagnosis was made.

Infections after Bone Marrow Transplantation Among Irritable Bowel Syndrome Patients: Review Article

Mele et al. [22]	2002	Toxoplasmosis	2 patients	Toxoplasmosis was found in two patients: one with successfully treated cerebral toxoplasmosis after peripheral blood SCT and one with fatal pulmonary toxoplasmosis in a BMT recipient. It is conducted a thorough review of the 110 published cases of toxoplasmosis after BMT. Toxoplasma-related mortality and diagnosis were investigated using statistical analysis. The mortality rate was 80%, and toxoplasmosis recorded 66% of deaths.
Grow et al [23]	2002	Aspergillus	242 patients	IA is still the leading cause of mortality in BMT. During 20 months, 93 allogeneic and 149 autologous transplant recipients, looking for cases of IA. There were no autologous transplant recipients who developed IA, but 15.1% of allogeneic recipients did for a prevalence of 5.8%. Survival was 29% after 100 days from diagnosis.
Ljungman et al [24]	2001	Respiratory Virus	1973 patients	Following BMT community-acquired respiratory virus infections is a significant cause of death. 37 centers participated in a prospective study to assess its prevalence. The prevalence of respiratory infection in allogeneic patients is 3.5%, while in autologous patients 0.4%. Lower respiratory tract infections were 2.1% more common in allogeneic patients than autologous patients 0.2%.1.1% of allogeneic patients died within 28 days after infection diagnosis, however, no autologous patients died.
Runde et al [25]	2001	Adenovirus	130 patients	In a prospective study, the prevalence of adenovirus (AV) infections following SCT was identified. 130 patients who underwent allogeneic were monitored for 6 months. AV infection was found in 35 instances. A total infection risk of 29% resulted from positive samples. The prevalence of AV infection is 19%.
Baldwin et al. [26]	2001	Adenovirus	572 patients	After 18 days after donation, the prevalence of adenovirus was 17%. The prevalence was higher in transplants involving unrelated donors (26%) than in matched sibling donors (9%), and higher in children (21%) than in adults (9%). 6% of adenovirus infection was the direct cause of death.
Steer et al. [27]	2000	Varicella zoster	151 patients	It's found that the prevalence of VZV infection is high. 32 individuals acquired following the transplant. The prevalence of VZV was 13% at 12 months, 32% at 24 months, and 38% at 28 months, with no additional cases past those dates. While receiving acyclovir or ganciclovir, no patient caught VZV.

Furthermore, it might be challenging to identify the risk factors that point to those who will benefit from the most intense form of care. The widespread acceptance of invasive mechanical ventilation is required due to respiratory failure in this patient population, which is associated with a poor prognosis. Early intensivist intervention Managing serious illness in transplant recipients is anticipated to continue to get better patient mortality rates. Bone marrow from the patient must often be destroyed to go through a bone marrow transplant (myeloablation). Before acquiring, patients could go weeks without receiving any new cells having a substantial quantity to combat infection using white blood cells (engraftment). Despite taking preventative antibiotics, this increases a patient's risk of infections, sepsis, and septic shock. Antiviral medications like acyclovir and valacyclovir, however, are particularly effective in preventing HSCT-related outbreaks of the herpetic infection in seropositive individuals. The risk of opportunistic infection is further increased by immunosuppressive drugs used in allogeneic transplants to prevent or cure graft-versus-host disease. Following transplantation, immunosuppressive medications must be taken for at least six months; if graft-versus-host disease is present, the duration may be substantially longer. Patients who undergo transplants lose acquired immunity, including immunity to childhood illnesses like measles or polio. As a result, transplant patients who have stopped taking immunosuppressive medicines need to start receiving childhood immunizations again. The estimated one-year survival rate is around 60%, but this figure includes deaths from both the underlying illness and other causes and the transplant operation. BMT is connected to an important its use is restricted to conditions that are life-threatening because of treatment-related death in the recipient. Serious consequences include graft-versus-host Disease, mucositis, infections (sepsis), veno-occlusive disease, and the appearance of new malignancies are all possible symptoms.

Conclusion

Transplantation of bone marrow is indicated in malignant and unmalignant causes. It is a delicate procedure requiring intensive care after transplantation due to loss of immunological memory from lifetime vaccinations and exposure to infectious pathogens. Through this period many opportunistic infections take place that can be life-threatening to the patient.

Conflict of Interest

None

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None

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