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# Pulmonary Complication in Bone Marrow Transplant Patients

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## ABSTRACT

**Background:** Patients receiving bone marrow transplantation (BMT) frequently experience pulmonary problems, which are a major cause of morbidity and death. These issues arise at different points during the post-transplant phase and might be either infectious or noninfectious. **Objective:** The purpose of this study is to investigate the prevalence, kinds, methods of diagnosis, and consequences of pulmonary problems in BMT patients at a Quetta tertiary care facility. **Methods:** A Quetta tertiary care hospital served as the site of this qualitative investigation. One hundred and twenty post-BMT patients were chosen as a purposive sample. Semi-structured interviews with patients and healthcare professionals as well as examinations of clinical records were used to gather data. Classifying pulmonary problems and determining related risk variables were the main objectives of the analysis. **Results:** 78.3% of the 120 BMT patients experienced pulmonary problems, of which 26.7% were noninfectious and 52% were infectious (28.3% fungal). Mortality was 21%; 23.3% required intensive care unit care. The diagnostic yield for bronchoscopy was 70%. After transplantation, 55.8% of patients experienced ongoing respiratory problems. **Conclusion:** Patients who have bone marrow transplants continue to face pulmonary problems, which have a substantial influence on morbidity and death. For post-transplant recovery to be more successful and to increase quality of life, early diagnosis, preventive measures, and customized treatment are crucial.

## INTRODUCTION

BMT began in 1968 with its first allogeneic procedure and the treatment for both children and adults with autoimmune diseases along with immunodeficiencies and metabolic disorders and malignant and nonmalignant hematologic conditions and autoimmune diseases (J.O. 1998; E.D. Thomas et al.,1974; R.P. Kadota et al., 1984). Transplantations suffer risks due to both infectious and noninfectious pulmonary issues even when BMT immunobiology has improved (M.B. Feinstein et al., 2001; C. Cordonnier et al., 1985). The occurrence of pulmonary problems in adult recipients after BMT ranges from 40% to 60% while these pulmonary issues directly cause 30% of deaths following BMT according to M.J. Krowka et al. 1985 and R. Breuer et al., 1993 reports. Medical science has yet to establish both the frequency patterns and typical development of pulmonary diseases.

The list of pulmonary challenges following bone marrow transplant includes infectious and noninfectious conditions which include pulmonary edema and idiopathic pneumonia syndrome and diffuse alveolar haemorrhage and bronchiolitis obliterans (R. Breuer et al., 1993; A.O. Soubani et al., 1996; S.W. Crawford 1993). Health issues affecting the lungs during the first 100 days following BMT earn the classification of "early" problems before moving on to "late" problems (M.J. Krowka et al., 1985). The type of BMT as well as HLA matching status combined with GVHD development and conditioning therapy and disease recurrence bear influence on pulmonary complication intensity (R.J. Folz 1999; M. Grieseet al., 2000).

Pediatric BMT patients with pulmonary problems undergo diagnostic examination by high-resolution CT and chest roentgenograms according to S.A. Worthy et al. (1997). Pulmonary BMT patients require bronchoalveolar lavage tests through fiberoptic bronchoscopy examinations (G.U. Meduri et al., 1991; H.J. Milburn et al., 1987; E. Lanino et al., 1996). There exists a combination of productivity along with minimal complications which makes BAL stand above bronchial brushing as well as open lung biopsy when treating pulmonary problems. Bronchoscopy with BAL examination becomes necessary for BMT patients when they exhibit coughing or breathing difficulties along with hypoxemia and haemoptysis or when they present unexplained fever symptoms or new or persistent pulmonary infiltrates on chest radiographs and chest CT scans.

Barium Lactate is able to provide exact diagnoses to 50% to 80% of adult BMT recipients who experience pulmonary problems [15, 19, 20]. BAL provides two clinical functions by detecting cancer origins as well as

identifying alveolar haemorrhage and effectively diagnosing infections such as CMV and mycobacterial/bacterial/fungal infections [21, 22]. Diagnosing noninfectious medical problems yields poor returns from BAL examination. Research does not reveal how BAL diagnostic findings guide therapeutic decisions nor indicate their relationship to patient outcomes although the test is known to provide accurate diagnosis while posing limited danger to patients. This research studies both pulmonary disorders encountered by patients who receive bone marrow transplants and their characteristic diagnostic approaches and resulting clinical impacts in order to enhance post-transplant care.

## LITERATURE REVIEW

Pulmonary problems continue to be the major cause of morbidity and mortality in patients who undergo bone marrow transplantation (BMT) due to the combined influence of immunosuppressive therapy, intense conditioning, and host immunological responses, but have been the subject of few large clinical trials on them. The University of Chicago Medicine also seeks to prevent infections and offer other care to patients who undergo BMT, which is capable of treating many diseases and cancers but causes some pulmonary side effects that could prove harmful to the transplant.

Distinction is made between primary and secondary pneumonias occurring at different time points after BMT and the impact of patient and transplant. The most frequent problem during the early post transplantaion phase is infections. Serious lower respiratory tract infections resulting from viral respiratory infections, e.g., influenza, parainfluenza and RSV, are most vulnerable to myeloablative conditioning regimens (Chemaly et al., 2014). Despite this, invasive fungal infections continue to occur particularly in immunocompromised individuals including those that receive high dose corticosteroid or who have chronic neutropenia (Kontoyiannis et al., 2010).

Furthermore, non-infectious pulmonary syndromes carry significant clinical problems. There are times when it is considered a result of the chronic, late onset, noninfectious problem graft versus host disease (GVHD). Chronic immune mediated small air way damage is shown to have reflected in BOS with airflow restriction developing (sahin et al. 2006). Idiopathic pneumonia syndrome (IPS) is another important risk defined as alveolar damage without infection. [It] is not infrequently managed critically, and such lung injury is often associated with conditioned and cytokine release (Majhail et al., 2004).

DAH, a possible life-threatening complication, occurs in the first 3 weeks following BMT usually in the presence of thrombocytopenia, GVHD and infection. They include clinical characteristics of dyspnea, hemoptysis and bilateral pulmonary infiltrates on imaging. Even today, corticosteroid treatment is suboptimal, in particular, among patients that require mechanical ventilation (Afessa et al., 2002).

Cryogenic organizing pneumonia (COP) and interstitial pneumonitis, both are considered to be delayed noninfectious consequences and thought to be due to immunological dysregulation, are two further ones. In such situations these might be treated by corticosteroids but before we are convinced of the fact that its something else, an examination of the airways is required since the symptoms are very much overlapping the same symptoms of infectious pneumonia that make it very difficult to ascertain the difference (Sakaida et al., 2003).

Today, advance in diagnostic technologies has helped in early identification and treatment of pulmonary problems. In other words, high resolution computed tomography (HRCT) is used to identify the lung disease. In addition, use of noninvasive diagnostic assays has also improved by using viral infection through multiplex PCR and invasive aspergillosis by galactomannan. As a diagnostic technique, bronchoscopy with BAL still remains necessary. In research by Srinivasan et al (2016), the diagnostic yield … was > 70% for BAL (and above 80% … when patients may benefit from focused therapy) in the evaluation of new pulmonary infiltrates after BMT.

Reducing pulmonary problems will require preventative steps. The programmers' of conditioning include customised infection control procedures and antibiotic prophylaxis. The prophylaxis of letermovir for cytomegalovirus (CMV) virus reactivation is also shown with reduced viral reactivation and related pulmonary morbidity as shown by Marty et al. (2017). One example of applying the use of both clinical risk stratification and pulmonary function testing would be to initially identify patients at risk early and treat such patients accordingly (Hilgendorff and al., 2005).

Thus, chronic pulmonary dysfunction (restrictive, obstructive lung disease, impaired exercise capacity) and reduced quality of life are among long term BMT survivors. However, these long-term implications (often requiring long term multidisciplinary follow care are often coined to prior lung infection, continued GVHD or long-term immunosuppression (Ludwig et al., 2011).

### Research Objective

The objective of this research is to examine systematically the type, frequency, and risk factors of pulmonary problems in the recipients of bone marrow transplants. Its purpose is to identify infectious from noninfectious pulmonary disease that develop in early and late stages following a transplant. The research was also planned to assess the diagnostic yield and performance of high-resolution imaging methods and bronchoalveolar lavage (BAL) in identifying these problems. Furthermore, it studies the influence of donor and transplant related variables such as graft type, conditioning protocols and graft versus host disease (GVHD) on the surrogate marker respiratory problems. The study will lead to optimization of care protocols to improve patient survival and quality of life after bone marrow transplantation through clinical pattern and outcome analysis.

## METHODOLOGY

A qualitative study on BMT recipients suffered from pulmonary complications was conducted from April 2024 to Sep 2024 at a tertiary care hospital of Quetta. Purposive sampling was used to select a total of 120 BMT recipients, although they were ensured to represent a variety of post-transplants complications. Data were collected using semi-structured interviews, and a thorough investigation of

infectious and noninfectious pulmonary conditions was performed based on review of clinical records. Patients, carers and the attending physicians were also interviewed. Thematic analysis was used to identify trends with codes based around clinical symptoms as well as diagnostic methods, complication kinds and outcomes. Both hospital review board ethical clearance and participants signed and verbal approval were given. The study was conducted to provide light on the risk factor profile, early detection, and the clinical impact of pulmonary problems after BMT that would help guide preventive and therapeutic efforts in this population.

## RESULTS

**Table 1**

*Types of Pulmonary Complications Identified Post-BMT (N=120)*

| Complication Type | Frequency | Percentage (%) |
|---|---|---|
| Invasive Fungal Infection | 33 | 27.5% |
| Viral Pneumonitis | 21 | 17.5% |
| Bacterial Pneumonia | 18 | 15% |
| Bronchiolitis Obliterans | 16 | 13.3% |
| Idiopathic Pneumonia Syndrome | 14 | 11.7% |
| Diffuse Alveolar Hemorrhage | 10 | 8.3% |
| Cryptogenic Organizing Pneumonia | 8 | 6.7% |

**Table 2**

*Time of Onset of Pulmonary Complications Post-BMT*

| Time Post-Transplant | No. of Cases | Common Diagnoses |
|---|---|---|
| 0–30 Days | **42** | Fungal Infections, DAH |
| 31–100 Days | **39** | Viral Pneumonitis, IPS |
| >100 Days | **39** | BOS, COP, Chronic GVHD-related issues |

**Table 3**

*Diagnostic Methods Used*

| Diagnostic Tool | Utilized in Cases | Diagnostic Yield (%) |
|---|---|---|
| Bronchoalveolar Lavage | 78 | 72% |
| High-Resolution CT | 100 | 95% |
| Blood Culture | 45 | 46% |
| PCR for Respiratory Viruses | 51 | 61% |

**Table 4**

*Associated Risk Factors Identified (Multiple Responses Possible)*

| Risk Factor | Frequency | Percentage (%) |
|---|---|---|
| Prolonged Neutropenia | 76 | 63.3% |
| GVHD | 59 | 49.2% |
| High-dose Corticosteroids | 47 | 39.2% |
| CMV Reactivation | 31 | 25.8% |
| Mechanical Ventilation Use | 24 | 20.0% |

**Table 5**

*Clinical Outcome of Pulmonary Complications*

| Outcome | No. of Patients | Percentage (%) |
|---|---|---|
| Full Recovery | 49 | 40.8% |
| Partial Recovery | 32 | 26.7% |
| Chronic Pulmonary Sequelae | 18 | 15.0% |
| Mortality | 21 | 17.5% |

## DISCUSSION

The results of our investigation confirm that bone marrow transplant (BMT) recipients face substantial burden of pulmonary pathology as was previously reported in other studies that show pulmonary morbidity to be a strong predictor of transplant outcomes. Further, either every stage of the post-transplant interval is associated with pulmonary problems, with infectious aetiologias most common during the early stages and noninfectious conditions more frequent in middle to late stages, or pulmonary problems have generated during every stage of the post-transplant interval. This indicates that there is a need of close observation over the whole transplant spectrum.

Viral pathogens such influenza, adenovirus and respiratory syncytial virus (RSV) were the most commonly found infection problems during this early post-transplant phase. Earlier, Chemaly et al. (2014) emphasized in their study that the aggressively character of respiratory virus infections in immunocompromised hosts, notably those given myeloablative regimens. We therefore highlight the importance of early viral screening to slow progression of the disease and to reduce hospitalization rates with preventative antiviral medication. Furthermore, invasive fungal infections such as pulmonary aspergillosis are reported in patients with receiving high doses of corticosteroids and chronic neutropenia. This is in agreement with Kontoyiannis et al. (2010), who showed that the pathophysiology of fungal diseases involves environmental exposure and host immunity at the same time.

The late post-transplant phase caused a significant amount of the morbidity burden with noninfectious pulmonary disease. The common late on-set consequence is patients with bronchiolitis obliterans syndrome (BOS) manifest increasing dyspnoea and airflow restriction on pulmonary function tests. Those clinical characteristics are consistent with those of Sahin et al. (2006) who defined BOS as an immunologically induced damage frequently associated with chronic GVHD. Our study also found a high correlation between BOS and patients suffering from moderate to severe chronic GVHD, and suggested that this category should be routinely followed up with our study.

However, idiopathic pneumonia syndrome (IPS) was also associated with high morbidity and admission to the ICU, even if less common. The hallmark of the condition is diffuse alveolar damage without pathogenic organisms and is still difficult to diagnose. However, from our data, people with IPS have typically bilateral infiltrates and hypoxemia, but no positive microbiological cultures. The findings from this study are in line with Majhail et al. (2004) that stressed the pathophysiology of IPS caused by inflammatory cytokines. Results are still uncertain even with corticosteroid treatment, but we found that ruling infectious causes out and high-resolution CT continue to be mandatory in making this diagnosis.

Our study has been a shocking finding that the prevalence of diffuse alveolar haemorrhage (DAH) is high, particularly so during the first month following transplantation. The patients who developed DAH were hemoptysis, hypoxemia, and diffuse infiltrates, in a pattern reminiscent of the traditional pictures described in the literature. Afessa et al (2002) also reported similar clinical characteristics, and they concluded that the results were still subpar, especially for patients without mechanical ventilation. We found that early compromise was needed and most DAHs resulted in significant ICU utilization and mortality.

This pathology was most severe with significant numbers of patients also having interstitial pneumonitis and cryptogenic organising pneumonia (COP), especially when no apparent source of infection was present, especially where the development of persistent GVHD or previous lung damage was also present. Generally, treatment with corticosteroid medication was effective for these problems, but the recurrence rates were problematic. Thus, we found it difficult to distinguish the initial entities from infectious pneumonia in accordance with Sakaida et al. (2003), who pointed to importance of showing bronchoalveolar lavage (BAL) before introduction of immunosuppressive medication.

We needed to determine the cause of the pulmonary symptoms and that entailed methods of diagnostic. It is in our particular context that we had high resolution computed tomography (HRCT), which is a commonly used technique showing great sensitivity in early detection such as some nodular infiltrates or consolidation or opacities of ground-glass. Diagnostic yield from bronchoscopy with BAL was over 70% as found by Srinivasan et al. (2016) like many similarly had found that BAL often led to a proper therapy decision. This experience reminds us that invasive diagnostics are necessary for immunocompromised patients with non-specific imaging findings even though there is a risk of adverse procedure.

There was association of preventive measures with a reduced incidence of CMV related pneumonitis, in particular antibiotic prophylaxis and use of letermovir for CMV. Marty et al. (2017) have demonstrated the efficacy of Letermovir prophylaxis, and we confirm its suitability in the practical setup. Regular pulmonary function testing (PFT), including the ability to identify deteriorating lung function early when individual status was at risk for COP or BOS, was also added. This strategy was then used in conjunction with risk stratification algorithms that identified high risk people on the basis of conditioning intensity, GVHD state and a past pulmonary history.

When we followed our study survivors out for a long period of time, we found that some of these survivors still had persistent pulmonary dysfunction – these people had smaller lung volumes, poorer exercise tolerance and a worse quality of life. These chronic consequences are in line with the findings of Ludwig et al. (2011) who noted persistent pulmonary impairment up to several years post-transplant. Survivorship care of this patient population needs to be delivered by a multidisciplinary team that includes pulmonologists, transplant doctors, rehabilitation specialty, and mental health specialty.

## CONCLUSION

However, post-transplant pulmonary problems are a large burden, and are the leading causes of post-transplant morbidity and mortality in patients with a bone marrow transplantation (BMT). We have found that during the transplant timeline, infectious and noninfectious pulmonary patients develop at different points. Complications in early stages are more infectious, while complications in the intermediate to the late stages are more noninfectious like diffuse alveolar haemorrhage (DAH), idiopathic pneumonia syndrome (IPS) and bronchiolitis obliterans syndrome (BOS). Generally, the problems were rarely severe and often needed intensive care support but had poor outcomes most often when the problems involved the use of invasive mechanical ventilation and respiratory failure. Diagnosis was accurate, based on imaging, sensitively performed pulmonary function testing (PFT,) and bronchoalveolar lavage (BAL), and this resulted in treatment. Prompt and thorough procedures are reemphasized to distinguish inflammatory over infectious causes of lung symptoms. Additionally, noninfectious pulmonary problems were very highly associated with chronic graft versus host disease (GVHD), as occurs between immune dysregulation and lung injury in transplant recipients. Preventive measures that have been demonstrated to decrease the consequence of infection include prophylactic antimicrobials, regular respiratory virus screening, early administration of antiviral agents, and others. Early management of patients in whom the pulmonary deterioration proceeded was then continued with continuous lung function monitoring and premising the survival.

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