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Research Article

# Short-Term Impact of Hematopoietic Stem Cell Transplantation in Leukemia Patients on Bone Bio Markers, Electrolytes and Blood Profile

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**Abstract**

Hematopoietic stem cell transplantation (HSCT) or Bone Marrow Transplantation (BMT) has significantly improved the survival rates of patients suffering from hematological malignancies. However, the cure can only be achieved at the price of morbidity and long-term

complications such as bone diseases leading to fractures and osteopenia. Several studies have reported the impact of organ transplants on bone metabolism, electrolytes and blood profile. This prospective observational clinical study aims at elucidating the effects of HSCT on bone metabolism, electrolytes and blood profile in leukemia patients. Sixty patients were included in this study. The current study aimed to evaluate the short-term (30 days) impact of HSCT on bone biomarkers [osteoprotegerin (OPG) and alkaline phosphatase], electrolytes (calcium, sodium, potassium, and magnesium), and blood profile [hemoglobin, absolute neutrophil count (ANC), platelet, and total leucocyte count (TLC)] in leukemia patients undergoing HSCT from their record files before HSCT (TP1) and after 30 days of HSCT (TP2). Further, the correlation among various parameters at TP2 was assessed using Spearman correlation analysis. At TP2, the level of OPG, alkaline phosphatase, calcium, magnesium and TLC increased significantly compared to TP1. However, no significant change was observed in other parameters at TP2 compared to TP1. A statistically significant positive correlation of TLC with hemoglobin and sodium; and magnesium with alkaline phosphatase was observed. Furthermore, a significant negative correlation between hemoglobin and calcium was observed. Even though there was a statistically significant increase in the level of OPG, alkaline phosphatase, calcium, magnesium and hemoglobin after 30 days of HSCT, the level of bone biomarkers, electrolytes and blood profile were in the normal physiological range. However, additional studies are required to get a detailed understanding of the changes in parameters after HSCT.

**Keywords**
Bone metabolism; hematopoietic stem cell transplantation; osteoprotegerin; blood profile

## 1. Introduction

Bone disorders are the most common complication in patients, receiving Hematopoietic stem cell transplantation (HSCT) or Bone marrow transplantation (BMT) [1, 2]. Osteoprotegerin (OPG) is an important marker for the detection of bone metabolism as it prevents osteoclast differentiation and bone resorption after binding to the receptor activator of nuclear factor kappa beta ligand (RANKL) [3]. Tumor invasion causes an imbalance in osteoblastic and osteoclastic activity leading to loss of skeletal integrity and bone complications. However, the currently available evidence is insufficient to explain bone metabolism immediately post-HSCT. HSCT has significantly improved the survival rates of patients suffering from hematological malignancies. After the infusion, the hematopoietic cells of the host are replaced by the engrafted cells resulting in complete chimerism through the anti-tumor activity of graft and substitution of the donor cells, eventually resulting in curing the disease and preventing malignancy [4]. After high-dose myeloablative chemotherapy, an allogenic bone marrow transplant has become the treatment choice for numerous hematologic, neoplastic and congenital disorders. Allogenic BMT provides 20-90% of the persisting disease-free survival with vast categories of neoplastic diseases [5, 6]. However, this can only be achieved at the price of morbidity and long-term complications.

HSCT is a complex medical procedure involving invasive medical interventions associated with long periods of isolation, extended hospitalizations, adverse effects, long recovery time and risk of mortality or relapse (Rueda-Lara and Lopez-Patton, 2014). Patients often experience substantial changes in their physical functioning due to symptoms such as dry mouth, fatigue, loss of appetite, mucositis and nausea (Rueda-Lara and Lopez-Patton, 2014). Even if the transplantation is successful, patients risk short- and long-term medical consequences such as chronic Graft-vs.-Host Disease (GvHD), secondary malignancies, infections and endocrine dysfunction (Lowe et al., 2007). Several studies have reported metabolic abnormalities leading to changes in serum electrolytes and blood profiles in HSCT patients [7, 8].

Thus, the present study was designed to evaluate the short-term effect of HSCT on bone metabolism, electrolyte level and blood profile in leukemia patients.

## 2. Methodology

### *2.1 Hospital Setting and Study Population*

This prospective observational study was conducted at Rajiv Gandhi Cancer Institute and Research Centre (RGCIRC), a North India hospital providing comprehensive cancer care. The study population comprises 60 patients (M + F) hospitalized for one month to undergo HSCT. No patient had comorbidities or relapsed leukemia. Most patients undergoing BMT were self-reliant and lively. Pre-transplant, no woman enrolled in the study took contraceptives or hormone-replacement therapy. Informed consent was taken from each participant before enrolling in the study. The Scientific Ethical Committee of the Rajiv Gandhi Cancer Institute and Research Center approved the research protocol , Rohini, Delhi.

Inclusion criteria- 1. The patient must have a confirmed diagnosis of one of the following i. Acute Myeloid Leukemia (AML), ii. Acute lymphocytic leukemia (ALL) iii. Chronic myeloid Leukemia (CML) 2. Patients undergoing allogeneic HSCT 3. Both male and female patients 4. Patient capable of giving informed consent 5. Patients willing to participate in study 6. No major organ dysfunction precluding transplantation.

Exclusion criteria- 1. Patients with history of cognitive impairment and Alzheimer's disease 2. Patients having a history of head injury, organ failure, and organ transplant 3. Patients having secondary cancer 4. Patients having neuropsychiatric disorders or neurobehavioral diseases 5. Patients on psychotropic medications 6. Patients using concurrent medication like antidepressant drugs 7. Patients are unable to give informed consent 8. Lactating or pregnant patients 9. Patients are not taking adequate contraception 10. Patients who have a history of undergoing allogeneic or autologous transplant 12. Patients with early complications [especially Graft-versus-host disease (GVHD), hepatic veno-occlusive disease (VOD), infections, etc.] will be excluded.

### *2.2 Assessment of Bone Markers*

Serum OPG was assessed using an enzyme-linked immunosorbent assay (ELISA). Blood samples were collected before chemotherapy or preconditioning (TP1) and after 30 days of bone marrow cell infusion (TP2) in 3 ml vials. It was then centrifuged for 15-20 min at 5000 rpm and was stored at -80°C. Alkaline phosphatase was recorded from the patient’s laboratory reports at TP1 and TP2.

### *2.3 Assessment of Electrolytes*

Levels of electrolytes such as calcium, sodium, potassium and magnesium were recorded from the patient's laboratory reports at TP1 and TP2.

### *2.4 Assessment of Blood Profile*

The blood profile including the level of hemoglobin, platelet, ANC and TLC was recorded from the patient's available laboratory reports at TP1 and TP2.

### *2.5 Ethics Information*

This observational study was approved by the 37$^{th}$ Scientific Committee, Rajiv Gandhi Cancer Institute and Research Centre (RGCIRC). All the documents- Protocol, Informed consent form (ICF), and Case report form (CRF) had been approved by the Institutional Review Board (IRB). REF/2019/12/030223.

### *2.6 Statistical Analysis*

The comparison of mean Hemoglobin (Hb), Platelet count, ANC, Potassium, Sodium Mg, Alkaline phosphatase, Serum calcium, OPG, and TLC was made between pre and post-treatment using the Mann-Whitney U test. The Spearman correlation test assessed the association among various parameters at TP2. All these statistics were accompanied by 95% confidence intervals (CI). All the reported p-values are two-sided and p-values $<0.05$ are considered to indicate statistical significance. All data entries and statistical analyses were performed using SPSS® Version 23.0 software.

### *2.7 Data Handling and Record-keeping*

All the data are recorded manually in hard and soft copies and archived at Rajiv Gandhi Cancer Institute and Research Centre for inspection. Confidentiality will be maintained, the data will be protected with a secure password, and only authorized persons will access the data. Data will be used for research, scientific presentation, and publication without disclosing the subject's identity.

## 3. Results

### *3.1 Demographic Details of the Patients*

Demographic data were collected from patients' interviews and files at the baseline. A total of 60 patients of both gender suffering from different kinds of leukemia or hematological disorder, i.e., 28 AML, 13 CML, and 19 acute lymphocytic leukemia (ALL) were enrolled. The mean age of the enrolled patients was 38.92 ± 12.86. A specific transplant regimen was prepared for each patient, i.e., 50% of the population received fludarabine/busulfan/anti-thymocyte globulin-cyclosporin/methotrexate (FLU/BU/r ATG-CSA/Mtx) regimen and the remaining patients received total body irradiation (TBI) or treosulfan (TREO) in substitutions of BU. 38.33% of patients received matched sibling donor (MSD) type of transplant, 10% of patients got matched family donor (MFD), 31.67% received matched unrelated donor (MUD) and 20% of the total patients received a

Haploidentical transplant. The mean duration of the disease was 6.6 months. As per the comorbidity index, 12% of patients were at low risk, 20% were at intermediate risk and 28% were at high risk. Additionally, about 66.67% of patients were found to be suffering from comorbidities (Table 1).

**Table 1** Demographic and baseline table.

| Item (Measure) | Patient N (%) |
|---|---|
| **Sample Size** | 60 |
| **Gender** | |
| Male | 24 (40) |
| Female | 36 (60) |
| **Avg. Age** | 38.92 ± 12.86 |
| **Avg. BMI** | 24.85 ± 4.05 |
| **Avg. BSA** | 1.68 ± 0.19 |
| **Comorbidity** | |
| Hypertension | 6 (10) |
| diabetes | 4 (6.67) |
| Obesity | 3 (5) |
| Thyroid | 5 (8.33) |
| Others | 22 (36.67) |
| **Habits** | |
| Alcohol | 18 (30) |
| Smoking | 12 (20) |
| No addiction | 41 (68.33) |
| **Type of hematological malignancy** | |
| AML | 28 (46.67) |
| CML | 13 (21.66) |
| ALL | 19 (31.67) |
| **Donor type** | |
| MSD | 23 (38.33) |
| MFD | 6 (10) |
| MUD | 19 (31.67) |
| Haplo | 12 (20) |
| **Mean duration of disease** | 6.6 months |
| **HCT-CI** | |
| 1 (low) | 12 (20) |
| 2 (intermediate) | 20 (33.33) |
| 3 (high) | 18 (30) |
| 4 (high) | 8 (13.33) |
| 5 (high) | 1 (1.67) |
| 6 (high) | 1 (1.67) |

**BMI:** Body mass index; **BSA:** Body surface area; **AML:** Acute myeloid leukemia; **CML:** Chronic myelogenous leukemia; **ALL:** Acute lymphocytic leukemia; **MSD:** matched sibling donor; **MFD:**

matched family donor; **MUD:** Matched unrelated donor; **Haplo:** haploidentical transplant; **HCT-CI:** Hematopoietic cell transplantation-comorbidity index

### *3.2 Effect of HSCT on Bone Markers*

The level of bone biomarkers at TP1 and TP2 are represented in Table 2. There was a significant increase in the level of OPG ($p = 0.001$) and alkaline phosphatase ($p = 0.001$) at TP2 compared to TP1 as shown in Table 3.

**Table 2** Level of biochemical markers at TP1 and TP 2 in leukemia patients.

| | **Bone biomarkers** | | **Electrolytes** | | | | **Blood Profile** | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | OPG (ng/mL) | Alkaline phosphatase (U/L) | Calcium (mg/dL) | Potassium (mEq/L) | Sodium (mmol/L) | Magnesium (mg/dL) | Hemoglobin (g/dL) | Platelet (per mL) | ANC | TLC (per mL) |
| **TP 1** | 0.02 ± 0.02 | 86.19 ± 23.6 | 1.14 ± 0.12 | 4.07 ± 0.4 | 140.5 ± 3.14 | 1.88 ± 0.74 | 9.44 ± 1.93 | 155880.24 ± 126167.97 | 3471.3 ± 3904.8 | 4699.81 ± 3776.16 |
| **TP 2** | 0.05 ± 0.02 | 90.88 ± 22.15 | 1.18 ± 0.12 | 4.09 ± 0.61 | 140.57 ± 3.62 | 2.1 ± 0.77 | 10.0 ± 2.07 | 199578.26 ± 195643.64 | 7024.61 ± 15260.59 | 6592.53 ± 12958.89 |
| **% Change** | 150 | 5.441467 | 3.508772 | 0.4914 | 0.049822 | 11.70213 | 5.932203 | 28.03307 | 102.3625 | 40.27227 |

**TP1:** Time-point 1; **TP2:** Time-point 2; **OPG:** Osteoprotegerin; **ANC:** Absolute Neutrophil Count; **TLC:** Total Leucocyte Count

**Table 3** Distribution of study population according to various parameters.

| Parameters | Rank | Mean Rank | Sum of Ranks | p-value |
|---|---|---|---|---|
| Hb | Negative Ranks | 20.13 | 302.00 | 0.061 |
| | Positive Ranks | 22.26 | 601.00 | |
| Platelet count | Negative Ranks | 21.88 | 350.00 | 0.137 |
| | Positive Ranks | 22.07 | 596.00 | |
| ANC | Negative Ranks | 22.00 | 330.00 | 0.084 |
| | Positive Ranks | 22.00 | 616.00 | |
| Potassium | Negative Ranks | 20.95 | 440.00 | 0.885 |
| | Positive Ranks | 22.05 | 463.00 | |
| Sodium | Negative Ranks | 21.08 | 421.50 | 0.877 |
| | Positive Ranks | 19.93 | 398.50 | |
| Mg | Negative Ranks | 16.73 | 184.00 | 0.001* |
| | Positive Ranks | 23.19 | 719.00 | |
| Alkaline phosphatase | Negative Ranks | 18.35 | 183.50 | 0.001* |
| | Positive Ranks | 22.48 | 719.50 | |
| Serum calcium | Negative Ranks | 20.96 | 272.50 | 0.015* |
| | Positive Ranks | 22.45 | 673.50 | |
| OPG | Negative Ranks | 13.13 | 52.50 | 0.001* |
| | Positive Ranks | 20.25 | 688.50 | |
| TLC | Negative Ranks | 20.80 | 416.00 | 0.049* |
| | Positive Ranks | 23.04 | 530.00 | |

**TP1:** Time-point 1; **TP2:** Time-point 2; **OPG:** Osteoprotegerin; **ANC:** Absolute Neutrophil Count; **TLC:** Total Leucocyte Count

* Indicate significance level

### *3.3 Effect of HSCT on Electrolytes*

The level of electrolytes at TP1 and TP2 are represented in Table 2. Post 30 days of BMT, a significant increase in the level of serum calcium ($p < 0.015$) and magnesium ($p = 0.001$) were observed as compared to baseline levels (Table 3). No significant change in the level of potassium and sodium was observed at TP2 compared to TP1. All measured electrolytes were in the physiological range pre- and post-HSCT.

### *3.4 Effect of HSCT on Blood Profile*

Table 2 represents the hemoglobin, platelet, ANC, and TLC levels at TP1 and TP2. A significant increase in the level of TLC ($p = 0.049$) was observed after 30 days of HSCT (Table 3).

### *3.5 Correlation among Bone Biomarkers, Electrolytes and Blood Parameters*

At TP2, there was a significant negative correlation between hemoglobin with calcium. Furthermore, the Spearman Correlation test showed a significant positive correlation of TLC with

hemoglobin (r = 0.345) and sodium (r = 0.331) using. Additionally, a significant positive correlation between magnesium and alkaline phosphatase was observed at TP2 (r = 0.335) (Table 4).

**Table 4** Correlations between various biochemical parameters assessed at TP 2.

| Correlations (TP 2) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **Hemoglobin** | **Platelet** | **ANC** | **Potassium** | **Sodium** | **Magnesium** | **Alkaline phosphatase** | **Calcium** | **OPG** | **TLC** |
| **Hemoglobin** | **Spearman Correlation** | 1 | 0.004 | 0.045 | 0.268 | -0.155 | -0.074 | -0.016 | -0.356* | 0.274 | 0.321* |
| | **P-value** | | ns | ns | ns | ns | ns | ns | 0.026 | ns | 0.046 |
| | **N** | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 |
| **Platelet** | **Spearman Correlation** | 0.008 | 1 | 0.099 | -0.118 | -0.136 | 0.236 | -0.009 | -0.163 | -0.185 | -0.055 |
| | **P-value** | ns | | ns | ns | ns | ns | ns | ns | ns | ns |
| | **N** | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 |
| **ANC** | **Spearman Correlation** | 0.045 | 0.095 | 1 | 0.000 | 0.016 | 0.177 | -0.153 | -0.110 | 0.109 | 0.050 |
| | **P-value** | ns | ns | | ns | ns | ns | ns | ns | ns | ns |
| | **N** | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 |
| **Potassium** | **Spearman Correlation** | 0.268 | -0.103 | 0.000 | 1 | -0.095 | 0.105 | 0.132 | -0.138 | 0.134 | 0.016 |
| | **P-value** | ns | ns | ns | | ns | ns | ns | ns | ns | ns |
| | **N** | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 |
| **Sodium** | **Spearman Correlation** | -0.155 | -0.129 | 0.016 | -0.095 | 1 | -0.101 | 0.021 | 0.139 | -0.098 | 0.309* |
| | **P-value** | ns | ns | ns | ns | | ns | ns | ns | ns | 0.047 |
| | **N** | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 |
| **Magnesium** | **Spearman Correlation** | -0.045 | 0.230 | 0.180 | 0.124 | -0.113 | 1 | 0.335* | 0.011 | -0.076 | 0.030 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | **P-value** | ns | ns | ns | ns | ns | | 0.030 | ns | ns | ns |
| | **N** | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 |
| **Alkaline phosphatase** | **Spearman Correlation** | -0.016 | -0.004 | -0.153 | 0.132 | 0.021 | 0.335* | 1 | -0.146 | 0.093 | 0.003 |
| | **P-value** | ns | ns | ns | ns | ns | 0.030 | | ns | ns | ns |
| | **N** | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 |
| **Calcium** | **Spearman Correlation** | -0.343* | -0.148 | -0.110 | -0.138 | 0.139 | 0.011 | -0.146 | 1 | -0.191 | 0.014 |
| | **P-value** | 0.026 | ns | ns | ns | ns | ns | ns | | ns | ns |
| | **N** | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 |
| **OPG** | **Spearman Correlation** | 0.274 | -0.171 | 0.109 | 0.134 | -0.098 | -0.076 | 0.093 | -0.191 | 1 | 0.041 |
| | **P-value** | ns | ns | ns | ns | ns | ns | ns | ns | | ns |
| | **N** | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 |
| **TLC** | **Spearman Correlation** | 0.345* | -0.056 | 0.065 | 0.025 | 0.331* | 0.043 | 0.027 | 0.038 | 0.059 | 1 |
| | **P-value** | 0.046 | ns | ns | ns | 0.047 | ns | ns | ns | ns | |
| | **N** | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 |

*. Correlation is significant at the 0.01 level (2-tailed).

**TP2:** Time-point 2; **ANC:** Absolute Neutrophil Count; **OPG:** Osteoprotegerin; **TLC:** Total Leucocyte Count.

## 4. Discussion

The number of long-term survivors of hematological malignancies continuously increases after the HSCT. Thus, HSCT has become the most acclaimed treatment of choice for remission in patients suffering from leukemia. However, bone loss is found to be the most common adverse effect post-HSCT. There are multiple causes of bone loss associated with HSCT. Hence, the exact association between BMT and changes in bone mineral metabolism is yet to be established. A retrospective study showed that 5-15% BMD loss occurs at the lumbar spine (LS) and femoral neck (FN) post 1yr of transplant [9]. Another retrospective study on 7620 patients who received HSCT, reported that only 8% of patients experienced fractures [10]. In a similar study, it was evident that the risk of osteoporosis increased post-HSCT. The study reported that 68.4% of patients after HSCT experienced vertebral fractures [11]. Reduced physical activity, administration of glucocorticoids, cyclosporin to impede graft versus host disease (GVHD), high-dose chemotherapy and traumatic brain injury are the major causes of bone-related disorders [9] in patients after BMT. As reported in a prospective clinical study [1], bone loss on the first 40 days of the transplant was substantial after transplantation. Then it decreased after six months of HSCT in long-term cancer survivors. Furthermore, they reported normal bone formation before and after the transplantation. However, a measurable increase in bone resorption before and after transplantation was observed. As mentioned earlier, RANKL causes osteoclast differentiation whereas OPG inhibits osteoclast differentiation [12]. A study showed that recombinant OPG acts on tissues of the bone and augments BMD and bone volume which is linked with the decrease in the number of osteoclasts in normal rats. Further, the study reported that in OPG deficient mice, severe osteoporosis was developed due to osteoclast formation. These findings discern that under *in vivo* conditions, OPG is the critical biomarker that acts as a negative regulator of osteoclastic bone resorption. Furthermore, a prospective study found that the level of OPG was at its peak post 3 weeks in BMT recipients [13]. Similarly, the current study showed that after 30 days of HSCT, there was a 150% increase in the level of OPG, suggesting normal bone formation. These findings, observed in our study and the facts mentioned above, are in concurrence, depicting improvement in bone resorption after HSCT.

In literature, it is reported that after BMT, alkaline phosphatase increases inorganic phosphate local rates, facilitates mineralization, and reduces the extracellular pyrophosphate concentration, an inhibitor of mineral formation [14]. The current study found a significant increase in the alkaline phosphatase, showing normal mineralization post-allo-BMT. The results are supported by a cross-sectional study that assessed alkaline phosphatase post-allo-BMT and found an accelerated bone turnover in patients following bone marrow transplantation in BMT recipients [15]. However, another clinical study showed that alkaline phosphatase activity in HSCT patients is lower than healthy donors, indicating that the proliferation and differentiation of bone marrow stromal cells are slower in bone marrow recipients than in bone marrow donors [16].

A case study reported hypercalcemia in patients with AML due to the activation of osteoclasts which is associated with the production of cytokines such as tumor necrosis factor [17]. Thus, in the current study we assessed the level of calcium pre-and post-HSCT and found a significant increase post-30 days of HSCT. A retrospective study reported that hypercalcemia post-HCT might be due to the engraftment of osteoclasts, differentiated from the hematopoietic precursors in cancer patients [18]. Further, in the current study, no significant changes in the level of potassium and sodium were observed post-HSCT. However, a study reported that inappropriate antidiuretic hormone secretion

post-HSCT might lead to hyponatremia [19]. Thus, we suggest further studies with a high sample size to ascertain changes in electrolyte levels during HSCT in cancer patients.

The current study found a significant increase in the level of TLC post-30 days of HSCT. Furthermore, an increase in platelet, ANC and hemoglobin level was observed post-BMT. However, the change was not significant. These findings are supported by a clinical study that reported an increased level of hemoglobin, platelet, and neutrophils in HSCT recipients after the BMT [20]. Another clinical study reported a fast recovery of platelet count and TLC post-HSCT compared to ANC after HSCT in cancer patients [21].

Spearman correlation is used to evaluate the relationship between two variables. The positive correlation indicates that as one variable increases, it increases the second variable. A negative correlation shows that as one variable increases, it decreases the second variable. In this study positive correlation of TLC with hemoglobin and sodium; and magnesium with alkaline phosphatase was observed. However, a negative correlation between hemoglobin and calcium was observed. In alignment with our study, a clinical study also found a positive correlation between TLC and hemoglobin, suggesting that these markers could be useful in managing the disease [22]. Furthermore, by our results, a study showed that magnesium affects the level of alkaline phosphatase [23]. However, in contrast, statistical analysis in another study showed a significant negative correlation between magnesium and alkaline phosphatase [24].

The study's main limitation is the small sample size and short follow-up. Another limitation is that a heterogeneous population included in the current study may also affect the outcome. Thus, future studies are required to assess the discussed parameters at different time points in a homogeneous population.

## 5. Conclusion

In conclusion, the present study suggests that post 30 days of HSCT, even though there was a statistically significant increase in the level of OPG, alkaline phosphatase, calcium, magnesium and hemoglobin after 30 days of HSCT, the level of bone biomarkers, electrolytes and blood profile were in the normal physiological range. However, improved short-term survival exposes patients to long-term complications and side effects. The late complications present a great diversity in frequency, time of onset, risk factors, prevention and treatment approaches and outcome. The long-term goal is maintaining health and ensuring the best possible QOL. Thus, further studies are required to check the physiologic changes and impact on QoL post-HSCT for longer.

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## Author Contributions

Rhythm Joshi: Design, Conducted study, manuscript writing; Zehva Khan: Design, Conducted study; Aakriti Garg: Data analysis and manuscript writing; Dinesh Bhurani: Data analysis; Nidhi: Manuscript writing and editing; Ubada Aqeel: Manuscript editing; Mohd. Ashif Khan: Design, Conceptualization of idea, data analysis, final manuscript writing and editing.

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**Competing Interests**

The authors have declared that no competing interests exist.

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