Variability of contribution of 1,25 (OH)2D3 (vitamin D) level to hematopoietic stem cell transplantation outcome

Azza Kamel (azza.kamel@nci.cu.edu.eg)
NCI, Cairo University

Eman Radwan
Faculty of Medicine, Cairo University

Ashraf Zeidan
South Egypt Cancer Institute, Assuit University

Amen Zaky
South Egypt Cancer Institute, Assuit University

Abeer Ibrahim
NCI, Cairo University

Raafat Abdelfattah
NCI, Cairo University

Maged Abdelfattah
South Egypt Cancer Institute, Assuit University

Research Article

Keywords: 1, 25(OH)2D3, Vitamin D, HSCT, GVHD

Posted Date: March 31st, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2723254/v1

License: © This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Abstract

**Background:** The impact of vitamin D status on the outcome of allogeneic hematopoietic stem cell transplantation (HSCT) has recently been the focus of interest with a lot of controversy. In this study we aimed to evaluate the impact of pre-transplant vit. D level on the outcome of HSCT. We also wanted to find an explanation of the controversy in the literature.

**Methods:** In this study, we evaluated the impact of vitamin D level on the risk of development of graft versus host disease (GVHD) and survival after HSCT. The study included 97 patients who received allogeneic HSCT from an identical sibling. Serum vitamin D level was measured before conditioning using ELIZA.

Student t- test, Mann-Whitney U test, ANOVA F-test and Kruskal-Wallis H tests were used to determine significance of difference for quantitative data. Pearson correlation, Spearman correlation and Chi-square test were used to determine correlations and associations. Kaplan-Meier and Log rank (Mantel-Cox) tests were used for analysis of survival.  P value ≤ 0.05 was considered significant.

**Results:** Vitamin D level showed a range of 18.24 - 84.6 with a mean of 38.14 ± 9.73 and a median of 36.26 ng/ml. Two patients had vitamin D level <20 and 17 had a level <30 ng/ml. Acute GVHD occurred in 33 (34%) and chronic GVHD in 29 (29.9%) patients. Vitamin D level had no impact on frequency or severity of GVHD; either did it impact survival. This might be attributable to the relatively normal level in the majority of our patients on account of the sunny weather of Egypt. This might also be a potential explanation for the inconsistency of the different studies with variable levels of vitamin D. **Conclusions:** The current study failed to demonstrate an impact of pre-transplant vitamin D level on the outcome of HSCT. This might be attributed to the low prevalence of vitamin D deficiency in our population on account of our almost always sunny weather. The marked variability in the level of vitamin D that is considered sufficient interferes with objective comparison between studies; a consensus on what is considered sufficient, insufficient, or deficient is essential.

Background

Hematopoietic stem cell transplantation (HSCT) is a standard therapeutic modality for many hematological disorders. Ideally, the recipient's immune system tolerates donor cell engraftment and donor immune effector cells engraft without inducing fatal graft versus- host disease (GVHD). Eventually, a stable chimeric state predominates, with reconstitution of functional immune cells capable of performing graft versus tumor (GVT) effect [1]

In allogeneic HSCT, graft rejection is not a major problem; yet GVHD is still a major complication. In spite of all efforts to unravel the causes of GVHD, the situation is far from settled. Among the factors claimed to contribute to GVHD is vitamin D level. Apart from its known role in bone metabolism and calcium homeostasis, vitamin D has a well-recognized role in the regulation of immune responses and prevention of autoimmunity [2]. The presence of vitamin D receptor (VDR) on activated lymphocytes suggests a role
for vitamin D in immune modulation on differentiated cells [3]. Stimulation of the VDR receptor is claimed to favor the Th2 response by suppressing interferon gamma (IFN-γ) and this underlies the immune-modulatory effects of Vitamin D [4].

The immune regulatory role of vitamin D is mediated, in part, by its effect on dendritic cells (DCs); it inhibits their maturation resulting in the accumulation of immature DCs with a potentially immunosuppressive phenotype [5]. Furthermore, vitamin D was reported to enhance apoptosis of mature DCs resulting in inhibition of T-cell allo-reactivity [6] and suppressing their capacity to present antigens to T cells [7]. Accordingly, vitamin D may inhibit DC-mediated expansion of allo-reactive T cells. Hence vitamin D deficiency could be a potential risk factor for the development of GVHD after allogeneic HSCT [8]. Also, vitamin D is reported to have possible effects on cytokine levels [9] which might contribute, as well, to the occurrence of GVHD.

In the current study we evaluated 25(OH)₂D₃ level in 97 allogeneic HSCT recipients to verify if vitamin D level would affect the transplantation outcome or complications especially acute and chronic GVHD.

**Methods**

**Patients:**

A total of 97 patients who received peripheral blood allogeneic HSCT from an identical sibling at the Bone Marrow Transplantation Centre, Nasser Institute, Cairo, Egypt, were enrolled. They included 71 males and 26 females with an age range of 18–56, median 31 years. The study was approved by the Institutional Review Board and a written informed consent was obtained from all patients before transplantation. Patients were followed up for, at least, 12 months. Neutrophil engraftment is defined as the first day of three consecutive days where the neutrophil count is ≥ 0.5 x 10⁹/L. Platelet engraftment is defined as ≥ 20 x 10⁹/L unsupported by platelet transfusion. Progression-free survival (PFS) is defined as the time from stem cell infusion to progression or death from any cause. Overall survival (OS) is defined as the time from stem cell infusion to death from any cause.

**Measurement of 25-hydroxyvitamin (OH) Vitamin D**

Pre-transplant serum samples were obtained before the start of conditioning and stored in liquid nitrogen. 25-hydroxyvitamin (OH) vitamin D concentrations were measured by enzyme-linked immunoassay (ELISA) using 25(OH) Vitamin D ELISA ASSAY [Enzo Life Sciences’ Catalog No. ADI-900-215]. According to guidelines from the Endocrine Society, we defined vitamin D deficiency as ≤ 20, insufficiency as 20.1–29.9 and sufficiency as ≥ 30 ng/ml (10).

**Statistical Analysis**

Data were analyzed by SPSS version 21 (IBM Inc., USA). Quantitative data were summarized as mean ± standard deviation (SD) if it is normally distributed and as median (range) if it is not. Qualitative data were described as frequencies and percentages.
Student t-test, Mann-Whitney U test, ANOVA F-test and Kruskal-Wallis H tests were used to determine significance of difference for quantitative data.

Pearson correlation was used to determine relation of two normally distributed data, while Spearman correlation was used for quantitative data which are not normally distributed. Relations of qualitative data were determined using Chi-square test.

Survival analysis was done using Kaplan-Meier method to determine OS and PFS. Log rank (Mantel-Cox) test was used to examine difference between survivals of different groups. P value $\leq 0.05$ was considered significant.

## Results

Vitamin D level showed a range of 18.24–84.6 with a mean of $38.14 \pm 9.73$ and a median of 36.26 ng/ml. Only two patients had vitamin D deficiency with a level $< 20$ ng/ml; both males, one 22 years old (19.31 ng/ml) with AML (M5) and the other 49 years old (18.24 ng/ml) with SAA. Fifteen out of the 97 patients had vitamin D insufficiency with a level $> 20 < 30$ng/ml. Accordingly, patients were categorized as $< 30$ (deficient/insufficient) and $\geq 30$ ng/mL (sufficient). Patient’s characteristics in context of vitamin D level are presented in table [1].

Table (1) Characteristics of 97 patients subjected to allogeneic stem cell transplantation in context of serum vitamin D level
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Vitamin D &lt; 30 ng/ml</th>
<th>Vitamin D ≥ 30 ng/ml</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
</tr>
<tr>
<td>Age: Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>18–49</td>
<td>100</td>
<td>18–56</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12</td>
<td>70.6</td>
<td>59</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>29.4</td>
<td>21</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- SAA</td>
<td>5</td>
<td>29.4</td>
<td>21</td>
</tr>
<tr>
<td>- AML</td>
<td>4</td>
<td>23.5</td>
<td>35</td>
</tr>
<tr>
<td>- ALL</td>
<td>3</td>
<td>17.6</td>
<td>10</td>
</tr>
<tr>
<td>- Biphenotypic</td>
<td>2</td>
<td>11.8</td>
<td>6</td>
</tr>
<tr>
<td>- CML</td>
<td>2</td>
<td>17.6</td>
<td>1</td>
</tr>
<tr>
<td>- MDS</td>
<td>1</td>
<td>5.9</td>
<td>3</td>
</tr>
<tr>
<td>- Others</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conditioning regimen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- BY/CY</td>
<td>8</td>
<td>47.1</td>
<td>40</td>
</tr>
<tr>
<td>- TBI/CY</td>
<td>3</td>
<td>17.6</td>
<td>11</td>
</tr>
<tr>
<td>- FLU/CY</td>
<td>5</td>
<td>29.4</td>
<td>22</td>
</tr>
<tr>
<td>- Others</td>
<td>1</td>
<td>5.9</td>
<td>7</td>
</tr>
<tr>
<td>CMV status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Negative</td>
<td>0</td>
<td>0.0</td>
<td>2</td>
</tr>
<tr>
<td>- Positive &lt; 250</td>
<td>14</td>
<td>82.4</td>
<td>58</td>
</tr>
<tr>
<td>- Positive ≥ 250</td>
<td>3</td>
<td>17.6</td>
<td>20</td>
</tr>
<tr>
<td>HCV PCR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Negative</td>
<td>16</td>
<td>94.1</td>
<td>68</td>
</tr>
<tr>
<td>- Positive</td>
<td>1</td>
<td>5.9</td>
<td>12</td>
</tr>
</tbody>
</table>
Parameter | Vitamin D < 30 ng/ml | Vitamin D ≥ 30 ng/ml | P value
---|---|---|---
| No | % | No | % |
| 17 | 100 | 80 | 100 |

<table>
<thead>
<tr>
<th>HBVsAG</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Negative</td>
<td>15</td>
<td>88.2</td>
</tr>
<tr>
<td>- Positive</td>
<td>2</td>
<td>11.8</td>
</tr>
</tbody>
</table>

No supplement was given during the study observation period; otherwise the impact of vitamin D status would not have been judged. As the patients were not symptomatizing before or after transplant during follow up visits, vitamin D was not re-analyzed. However, patients are given routine Ca and Mg supplementation.

Hepatitis B positive patients receive lamivudine 300 mg once daily pre- and post-transplant until the patient is referred to a hepatologist. Hepatitis C positive patients are transplanted and referred to a hepatologist post-transplant. For CMV positive patients, the eligibility level is < 200 copies for both patient and donor. If either (or both) exceeds this limit, gancyclovir is administered in a dose of 6mg/kg every 12 hours for one week, then once daily until PCR is negative; the patient is transplanted once the eligibility level is achieved.

No significant difference was encountered between both groups with regards to age, gender, or diagnosis. Both groups received comparable myeloablative conditioning regimens. GVHD prophylaxis consisted of CSA and MTX in 94 patients while 3 patients received MMF and MTX. The only significant difference was a higher percentage of HBVsAg + ve cases among patients with vitamin D level < 30 ng/ml (p = 0.023).

Donors had an age range of 9–58 with a median of 28 years. Donor–recipient gender matching was present in 57 cases (58.8%) while mismatching was present in 40 cases (41.2%). Table [2] presents the gender mismatch in context of vitamin D level.

<table>
<thead>
<tr>
<th>Gender: Donor to patient</th>
<th>Total</th>
<th>Vit D &lt; 30 ng/ml</th>
<th>Vit D ≥ 30 ng/ml</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
</tr>
<tr>
<td>Male to female</td>
<td>25</td>
<td>25.8</td>
<td>3</td>
<td>17.6</td>
</tr>
<tr>
<td>Male to male</td>
<td>46</td>
<td>47.4</td>
<td>9</td>
<td>52.9</td>
</tr>
<tr>
<td>Female to female</td>
<td>11</td>
<td>11.3</td>
<td>2</td>
<td>11.8</td>
</tr>
<tr>
<td>Female to male</td>
<td>15</td>
<td>15.5</td>
<td>3</td>
<td>17.6</td>
</tr>
</tbody>
</table>
Association between vitamin D level and occurrence of acute GVHD

After HSCT, 33 patients [34%] developed grades II–IV acute GVHD; 23 (23.7%) had acute GVHD skin, 19 (19.6%) had acute GVHD gastro-intestinal tract and 7 patients (7%) had acute GVHD liver. Serum vitamin D levels were comparable between patients with or without acute GVHD (38.596 ± 9.41 vs. 38.247 ± 10.45ng/ml, p = 0.873). Also, there was no association between vitamin D level and occurrence of acute GVHD when the patients were categorized based on vitamin D level: 4/17 (23.5%) patients with vitamin D level < 30 ng/mL developed acute GVHD as compared to 29/80 (36.3%) with vitamin D level ≥ 30 ng/mL (p = 0.315).

Risk factors for the development of grades II-IV acute GVHD

We evaluated donor age, patient diagnosis, recipient sero-positivity for cytomegalovirus, the use of a female donor for a male recipient, CD 34 count and the conditioning regimens as risk factors for the development of grades II-IV acute GVHD. Only the use of a female donor for a male recipient was associated with increased risk of grades II-IV acute GVHD: 13/25 (52%) vs. 20/72 (27.8%) respectively (p = 0.028).

Association between vitamin D level and occurrence of chronic GVHD

Twenty-nine patients (29.9%) developed chronic GVHD; 10 (10.3%) had limited disease and 19 (19.6%) had extensive chronic GVHD. Vitamin D level was comparable between patients with and without chronic GVHD (37.5603 ± 8.74 vs. 38.7091 ± 10.73ng/ml, p = 0.61). There was no difference, either, in the frequency of chronic GVHD between patients with vitamin D level < 30 ng/mL (4/17, 23.5%) and those with vitamin D level ≥ 30 ng/mL (25/80, 31.3%) (P value = 0.315)

Risk factors for the development of chronic GVHD

We evaluated patient age, patient diagnosis, prior acute GVHD, recipient sero-positivity for cytomegalovirus, the use of a female donor for a male recipient, CD 34 count and the conditioning regimens as risk factors for the development of chronic GVHD. None of these factors was associated with an increased risk of Chronic GVHD.

Impact of vit. D level on neutrophil and platelet engraftment

Neutrophil engraftment was faster with high vitamin D level ≥ 30ng/ml (13.16 ± 2.89) vs. 14.46 ± 1.76 for patients with vitamin D level < 30ng/ml. Though this was statistically insignificant (p = 0.13), yet there was borderline negative correlation between vitamin D level and time to neutrophil engraftment (r= -2.88, p = 0.04, Fig. 1).
On the other hand, platelet engraftment was not affected by vitamin D level.

**Impact of vitamin D level on chest infection:**

Chest infection was reported in 6/17 (35.29%) and 23/80 (28.75%) in patients with vitamin D level < and \( \geq \) 30 ngm/ml respectively (p = 0.59). Vitamin D level was 36.3748 ng/ml in patients with vs. 39.2147 ng/ml in patients without chest infection (p = 0.21).

**Impact of vitamin D level on survival:**

The mean PFS for all patients was 15.5 months [Fig. 2a] and mean OS was 17 months [Fig. 2b]. There was no impact of vitamin D level on either PFS or OS (Fig. 3a and b).

**stem cell transplantation from an identical sibling**

**Discussion**

In this study, we evaluated the relation between 1,25(OH)2D3 [vitamin D] level in the serum and the outcome of HSCT including the risk of development of GVHD.

Because there is no consensus for optimal vitamin D levels, the cutoff was different among the studies which addressed the impact of vitamin D level on the outcome of allogeneic HSCT [8].

We adopted the guidelines from the Endocrine Society which defined 3 levels: deficiency for values of \( \leq \) 20 ng/mL; insufficiency for values between 20.1 and 29.9 ng/mL and normal state [vitamin D sufficiency] for values of \( \geq \) 30 ng/mL [10]. However, another study adopted the level of 25 ng/ml [8] and a third adopted the level of 30 ng/ml [11] as a cutoff to discriminate between vitamin D deficient and sufficient state. It was also reported that patients who are vitamin D sufficient prior to transplant tend to stay so up to 180 days post transplant [12].

In our study, only two patients had a level < 20 ng/ml and hence the patients were divided into two cohorts based on a vitamin D level: < 30 ng/mL (17 patients) or \( \geq \) 30 ng/mL (80 patients). Both groups were comparable with regards to age, gender, diagnoses, conditioning regimen and GVHD prophylaxis. With regards to viral screening, they were comparable as regards CMV and HCV status. However, the group with vitamin D level < 30 ng/ml had a higher frequency of HBV surface antigen (2/17 vs. 1/80 patients, p = 0.023). Significant as it is the number is just two cases in the first group and one in the second which requires caution in interpretation.

In our study, grades II-IV acute GVHD occurred in 34% of patients. This is comparable to the 31% value previously reported by our group [13] and others [14] but lower than the 51% reported by Kanda et al. [15].

Vitamin D has well known immunomodulatory functions [8, 16]; recent reports indicate that it may play a protective role against GVHD after HSCT and recommendations for early post-transplant vitamin D supplementation have been suggested [17, 18, 19].
Our results demonstrated that there were no significant differences in serum vitamin D levels between patients with or without acute GVHD. This is in agreement with previous studies involving adult and pediatric patients and adopting different vitamin D cutoff levels, 25 and 30 ng/ml [8, 11, 20, 21, 22]. Paradoxically, studying 123 children post allogeneic HSCT, Hansson et al, [12] reported a higher frequency of grade II-IV acute GVHD in vitamin D sufficient group (47% versus 30%, P = 0.05). However, their cutoff value for vitamin D was rather high at 50 ng/ml; we could not test the impact of this level as only 6 of our patients exceeded this value. It has to be taken in consideration that most recommendations for what is called vitamin D sufficient level are derived from studies related to bone health; the situation for HSCT may be different [23]. Specific guideline on vitamin D monitoring and treatment, in HSCT setting, is currently unavailable [24].

Previous reports indicate high frequency of vitamin D deficiency, up to 70–89% in adult patients prior to HSCT [25, 26]. Lack of this phenomenon in our patients may be attributed to the sunny weather of Egypt; most of our patients are from rural areas where exposure to sun is part of the norma

In this study 29 patients (29.9%) developed chronic GVHD; 10 (10.3%) had limited disease and 19 (19.6%) had extensive chronic GVHD.

Chronic GVHD occurs in approximately 33% of HLA identical sibling recipients and 50–70% of recipients of unrelated or mismatched-related marrow grafts [27]. Limited and extensive chronic GVHD varied in different reports with 6% and 71% in one study [28] and 16% and 34% of patients in another [15].

Our results demonstrated that there were no significant differences in serum vitamin D levels between patients with or without chronic GVHD. Neither was there an association between vitamin D level and occurrence of chronic GVHD when patients were divided into two cohorts based on a vitamin D level < 30 ng/mL or ≥ 30 ng/mL (P value = 0.315). This is consistent with previous studies both in children and adults [11, 12, 20, 21].

In contrast, Glotzbecker et al [8] reported increased frequency of chronic GVHD in patients with vitamin D level < 25ng/ml (63.8%, vs. 23.8%, p = 0.009) that was extensive in 54.5% versus 14.3% (P = 0.005); significance was retained in multivariate analysis (hazard ratio = 5.26, P = 0.02). However, vitamin D level was much lower in their cohort (7.8–45.7, median 21.9 ng/mL) and they followed up their patients for 2 years.

Similarly, Von Bahr et al, [29], reported vitamin D level before HSCT as a significant independent risk factor for development of chronic GVHD in multivariate analysis; median value of vitamin D in their patients was 42 nmol/L (equivalent to 42 ng/ml) which is higher than the previous study. Similar results were reported in children [30].

The discrepancy may be partly explained by the variability in the adopted vitamin D level cutoff values. This raises the need for standardization of criteria of vitamin D sufficiency, insufficiency, or deficiency in context of HSCT setting which may be different from those adopted for bone health measures.
Also, there are no clinical guidelines focusing on vitamin D status and its optimal levels required for prevention of post-transplant complications [31].

In the current study, vitamin D level ≥ 30 ng/ml was associated with shorter time to neutrophil engraftment. Though the difference was insignificant, yet there was a borderline inverse correlation between vitamin D level and time to neutrophil engraftment in individual patients. This is in line with the significantly faster neutrophil recovery reported in children with vitamin D level ≥ 50 ng/ml [12]. In contrast no difference was detected in time to neutrophil engraftment between vitamin D sufficient and deficient children as evaluated before HSCT [18].

In the current study vitamin D level had no impact on infectious complications post HSCT. This result is consistent with the findings of Beebe et al [11] who stated that overall infection risk was not significantly related with pre-HSCT vitamin D level. On the other hand, significant association between vitamin D insufficiency and CMV infection was reported [25]. As almost all our patients are CMV positive, such an association cannot be tested. However, the frequency of HBV surface antigen was higher among our patients with vitamin D level < 30ng/ml.

In the current study, there was no impact of vitamin D level on PFS or OS. Comparable results were previously reported with different vitamin D cutoff levels of 20 ng/ml [20], 25 ng/ml [8] and 30 ng/ml [11]. In contrast, vitamin D level > 50 ng/ml was significantly associated with better overall survival among children with malignancies (87% versus 50%, P = 0.01) [12]. Also, Bhandari et al [22] reported 28% decreased risk of death in children for every 10-ng/mL increase in vit D level (P = 0.01). This was encountered for all-cause mortality but not with individual comorbidities.

**Conclusions**

The current study failed to demonstrate an impact of pre-transplant vitamin D level on chronic GVHD reported in some studies. Neither had we encountered an impact on acute GVHD or survival. This might be attributed to the low prevalence of vitamin D deficiency in our population on account of our almost always sunny weather. The marked variability in the level of vitamin D that is considered sufficient interferes with objective comparison between studies; a consensus on what is considered sufficient, insufficient, or deficient is highly needed. Also, the marked variability in the pre-transplant vitamin D level in different study cohorts markedly affects its potential impact on transplantation outcome. In some areas of the world with very sunny weather, like Egypt, vitamin D deficiency may not be a problem for transplanted patients while in other areas with prevalent vitamin D deficiency a supplementation program has to be adopted.

**Abbreviations**

HSCT
Hematopoietic stem cell transplantation
Declarations

Ethics approval and consent to participate: The study was approved by the South Egypt Cancer Institute Review Board: SECI-IRB IORG000563. Approval No 155 and a written informed consent was obtained from all patients before transplantation

Consent for publication: Not applicable

Availability of data and material: All data generated or analyzed during this study are included in this published article

Competing interests: The authors declare that they have no competing interests.

Funding: This work was supported by South Egypt Cancer Institute, Assuit University, Egypt.

Authors’ contributions

AM made the study design and the final revision of the manuscript, ER performed the vit D assay and was a major contributor in writing the manuscript. AZ, AZ, AI, AR, RA and MA: analyzed and interpreted the patient data regarding the hematological disease and the transplant. All authors read and approved the final manuscript. All authors have agreed to be personally accountable for the author’s own contributions and ensured that questions related to the accuracy and integrity of the work, were appropriately investigated, and resolved.

Acknowledgements: Not applicable

References


24. Hong S, Ferraro CS, Hamilton BK, Majhail NS. To D or not to D: vitamin D in hematopoietic cell transplantation. Bone Marrow Transplant. 2020;55:2060–70.


**Figures**

![Figure 1](image_url)
Correlation between vitamin D level and neutrophil engraftment in 97 patients who received hematopoietic stem cell transplantation from an identical sibling ($r= -2.88$, $p=0.04$).

Figure 2

(a): Progression free survival for 97 patients who received hematopoietic stem cell transplantation from an identical sibling

(2b): Overall survival for 97 patients who received hematopoietic stem cell transplantation from an identical sibling
Figure 3

(3a): Association between vitamin D level and progression free survival in 97 patients who received hematopoietic stem cell transplantation from an identical sibling (p=0.778)

(3b): Association between vitamin D level and overall survival in 97 patients who received hematopoietic stem cell transplantation from an identical sibling (p=0.998)