

Prevalent vitamin D deficiency and impact of vitamin D on acute GVHD in HCT

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QUESTION

- **Should we supplement patients with vitamin D during hematopoietic cell transplant (HCT)?**
 - Vitamin D is an essential mineral with function range from mediating bone hemostasis to immune modulation
 - Vitamin D production requires the skin, liver and kidney to convert it to its active form
 - HCT patient's are at increased risk of vitamin D deficiency due to multiple variables such as:
 - use of immunosuppressive medications
 - corticosteroids
 - altered gastrointestinal absorption
 - lack of sun exposure
 - allogeneic myeloablative treatments

INTRODUCTION

- The impact and prevalence of vitamin D deficiency after hematopoietic cell transplant (HCT) is not well known
- Symptoms are vague and subtle such as muscle weakness and pain
- Deficiency of vitamin D can impair bone health and compromise immune status
- Graft Versus Host Disease (GVHD) is a life threatening reaction of donor immune cells against host tissues which can occur as acute and/or chronic after HCT
- Vitamin D deficiency may increase the risk of acute GVHD due to the loss of known immunomodulatory effects
- Questions still remain on the potential buffering of acute GVHD by vitamin D supplementation

DANA FARBER STUDY

[Glotzbecker B.](#) Apr 2013BMT 48(4):593-7

Low levels of 25-hydroxyvitamin D before allogeneic hematopoietic SCT correlate with the development of chronic GVHD

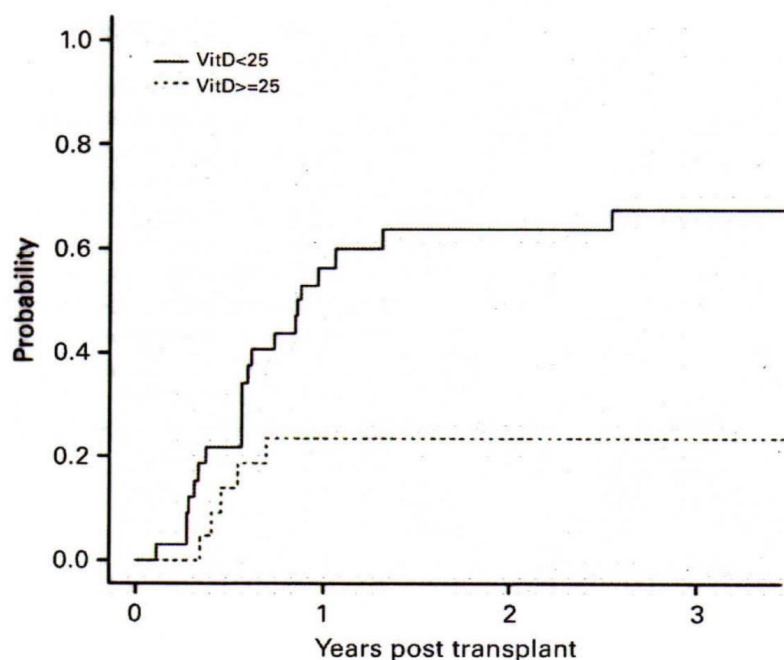
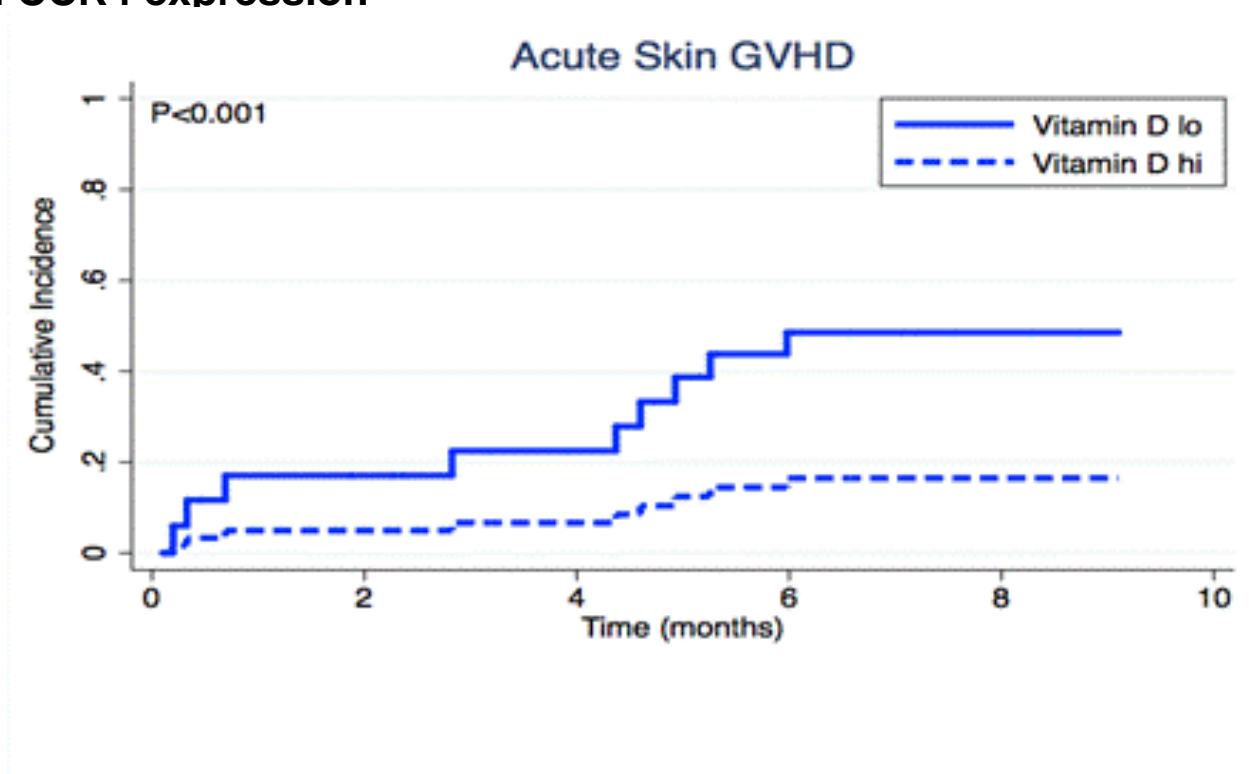


Figure 1. CI of cGVHD with death/relapse as a competing risk. The CI of chronic GVHD (cGVHD) at 2 years in patients with 25-OH vitamin D < 25ng/mL was 63.8%, compared with 23.8% in patients with vitamin D levels equal to 25 ng/mL ($P = 0.009$).

Vitamin D Deficiency Predicts Acute Cutaneous Graft-Versus-Host Disease in Reduced-Intensity Allogeneic Hematopoietic Stem Cell Transplantation

- Vitamin D may confer a protective effect against acute skin GVHD via reduction in CCR4 expression



CURRENT RESEARCH GAPS

- Current research shows vitamin D deficiency has been associated with chronic Graft Versus Host Disease (cGHVD), and insufficient vitamin D levels have been shown in patients who have undergone hematopoietic cell transplant (HCT)
- We have limited data on vitamin D deficiency and acute GVHD

HYPOTHESIS

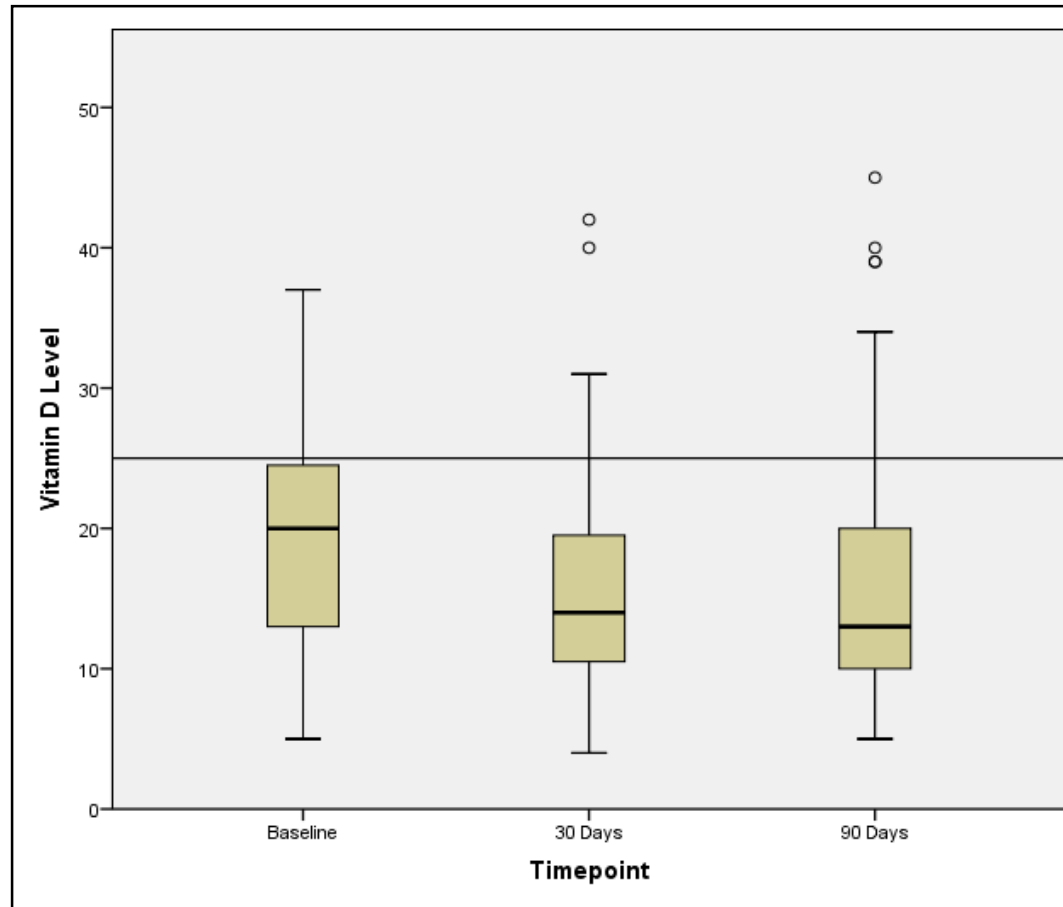
Vitamin D deficiency is prevalent in the HCT population

Vitamin D deficiency increases the risk of acute GVHD

METHODS

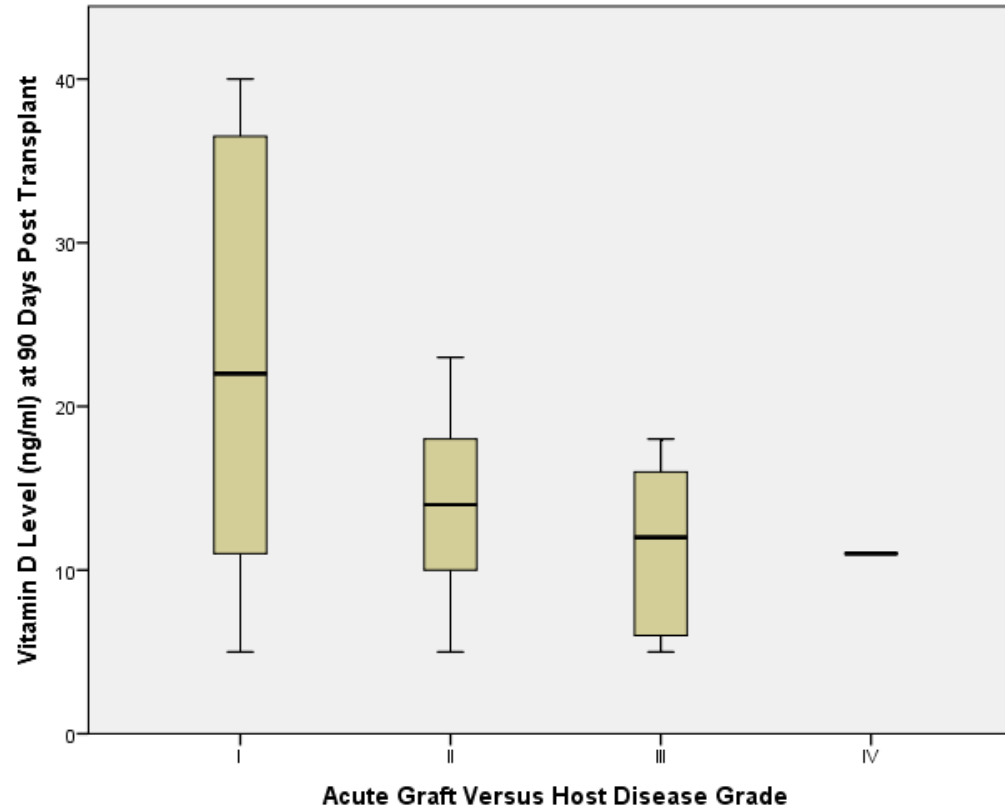
- Retrospective, pilot study
- Timeline:
 - first quarter- complete data gathering
 - second quarter- finalizing data
 - third quarter- analysis
 - fourth quarter- compile and report results
- Stem Cell Therapeutics Lab provide vitamin D levels from n=50 consecutive, allogeneic myeloablative HCT patients
- Each patient with at least one baseline vitamin D level and levels at +30 days, + 60 days, and +90 post transplant
- Incidences of acute graft vs host disease
- Clinical data was obtained from the BMT registry, EPIC and subjects' clinical record
- Vitamin D levels were dichotomized at 25ng/ mL

VITAMIN D LEVELS AT BASELINE, 30 DAYS, AND 90 DAYS POST TRANSPLANT



77% of samples (116/150) were below threshold for vitamin D (<25 ng/ml). 74% were vitamin D deficient pre-HCT (20 ± 8 ng/ml). **Significantly decreased by day +30 (16 ± 8 ng/ml, $p=.048$)** and remained constant at day +90 (16 ± 10 ng/ml). Only 6% had normal Vit. D levels at all the 3 time points. None of these patients (3/3) had GVHD

DISTRIBUTION OF 90 DAY POST-TRANSPLANT VITAMIN D LEVELS BY GVHD I-IV



GVHD was present in 46%. No significant relationship to vitamin D and aGVHD ($p=.9$), but all 15 subjects with grade II-IV had vitamin D deficiency (median 12 ± 6 ng/ml, range 5-23ng/ml, $p=.08$)

RESULTS OF PILOT STUDY

- Majority pt. samples (77%) were below threshold for vitamin D (<25 ng/ml)
 - Only 3/50 (6%) had normal vitamin D levels at all the 3 time points
- A significant decline in vitamin D levels at day 30 post-HCT
 - 73% had vitamin D deficiency at baseline (20 ± 8 ng/ml)
 - significantly decreasing at 30 days (16 ± 8 ng/ml, $p=.048$)
 - remained constant at 90 days (16 ± 10 ng/ml)
- All subjects with acute GVHD (grade II-IV) had vitamin D deficiency
 - All 15 subjects with grade II-IV GVHD at 90 days had vitamin D deficiency (median 12 ± 6 ng/ml, range 5-23ng/ml, $p=.08$)

CONCLUSION

- This study identifies prevalent vitamin D deficiency within this cohort. As a pilot study, we are unable to determine an association with acute GVHD
- Given our findings as well as other recent research, it compelled our Blood and Marrow Transplant (BMT) program to adopt a standard of care for monitoring and supplementing vitamin D

IMPLEMENTATION OF VITAMIN D SUPPLEMENTATION

- Systematic check of vitamin D levels on all BMT patients
 - Pre transplant level (within a 7 day range)
 - + 30 days post transplant
 - + 60 days post transplant
 - + 90 days post transplant
 - + 1 year and annually post transplant
- Supplementation of vitamin D to maintain levels \Rightarrow 25 ng/ml
- < 25 ng/ml supplement weekly 50,000 IU D2 ergocalciferol weekly (prescription) to take with dinner (high fat meal to enhance absorption)
- ≥ 25 ng/ml supplement with daily 1,000 IU D3 cholecalciferol over the counter (certified product)

COMMUNICATION: BMT VITAMIN D STANDARD OF PRACTICE FOLLOW UP

- Faculty meeting communication and updates
- Inpatient/outpatient inservices (RNs, APPs, Fellows)
- RN Coordinator meetings
- Newsletters
- Inclusion in BMT MD guidelines
- Incorporation into RN/Group message boards in patient charts
- EPIC charting templates (APPs, RNs, RDs, Fellows)
- Communication at multidisciplinary rounds
- Inclusion in pre-transplant letter to referring MD

GOALS FOR MOVING FORWARD

- Increase “compliance” for early and monthly level checking
- Increase “compliance” for supplementation timing and accuracy
- Optimize intake of Vitamin D- starting early pre transplant
 - initiating as soon as possible post level result
 - minimizing missed doses
- Gather new data for a powered study with goal of N=300
- Analyze data

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