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Prevalence of Vitamin D Deficiency in Newly Diagnosed Multiple Myeloma Patients

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ABSTRACT

Multiple Myeloma (MM) is a plasma cell disorder with skeletal complications. Vitamin D deficiency may contribute to these complications. **Objective:** To check vitamin D levels and determine the prevalence of Vitamin D deficiency in newly diagnosed MM patients. **Methods:** A prospective cross-sectional study was conducted from July 2024 till February 2025 at Liaquat National Hospital, Karachi, including 85 newly diagnosed MM patients. Serum 25-hydroxyvitamin D (25(OH)D) levels were measured. Demographic and laboratory data, including hemoglobin, calcium, creatinine, LDH, uric acid, and serum protein electrophoresis, were collected. Blood samples for vitamin D analysis were collected in red-top tubes. All the data analysis was done by IBM SPSS Version 22.0. **Results:** A total of 85 newly diagnosed MM patients (mean age: 55 ± 8.6 years) were evaluated for vitamin D deficiency. Males comprised 54 (63.5%) patients, while females accounted for 31(36.5%). The mean vitamin D level was 21.79 ± 7.2ng/mL. 56 (65.9%) of the patients had Vitamin D deficiency (<20ng/mL), 22 (25.9%) had insufficiency (20–29ng/mL), and only 7 (8.2%) had sufficient levels (≥30ng/mL). Urban residents had significantly lower vitamin D levels than rural residents (p = 0.03). **Conclusions:** Vitamin D insufficiency was prevalent in newly diagnosed MM patients and may contribute to skeletal complications. Variations in vitamin D levels based on patient residence suggest further investigation into potential contributing factors.

INTRODUCTION

Vitamin D deficiency is a pressing international health challenge, affecting around 14% of the population worldwide. The prevalence varies across regions, with reported deficiency rates of 24%, 37%, and 40% in U.S, Canada and Europe [1]. A meta-analysis conducted by Siddiqee MH revealed that Pakistan has the highest prevalence among South Asian nations at 73%, with Bangladesh and India both at 67%, followed by Nepal at 57%, and Sri Lanka at 48% [2]. Serum Vitamin D3 levels are used to evaluate vitamin D status in clinical practice [3]. Beyond its well-established role in bone metabolism, vitamin D exhibits anti-proliferative effects on various cell types. Previous studies have shown an association between vitamin D deficiency and adverse clinical outcomes in hematological malignancies such as follicular lymphoma, Non-Hodgkin Lymphoma (NHL), and peripheral T-cell lymphoma [4-7]. Similarly low levels of vitamin D have been linked to worse prognoses in Multiple Myeloma (MM) and solid tumors, including colorectal and breast cancers [8, 9]. MM is a malignant hematological disorder primarily affecting the elderly and is characterized by significant skeletal complications. It accounts for approximately 1–2% of all cancers and over 17% of hematological malignancies [10]. While genetic mutations have been implicated, MM is not classified as a hereditary disease. Clinically, it most often presents with bone involvement, including bone pain and pathological fractures. Given that vitamin D plays a critical role in calcium absorption and bone ossification, its deficiency could significantly contribute to the bony manifestations of MM [11, 12]. A study by Graklanov *et al.*,

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involving 148 recently diagnosed MM patients, reported deficiency of vitamin D in 24% of cases [13].

However, no published data exist on the prevalence of vitamin D deficiency in MM patients in Pakistan. Thus, current study aimed to measure vitamin D3 levels and determine the prevalence of vitamin D deficiency in newly diagnosed MM patients in Pakistan.

METHODS

Ilt was a prospective descriptive cross-sectional study and carried out from July 2024 to Feburary 2025 at the Haematology Department of Liaquat National Hospital in Karachi, Pakistan. The study was conducted after obtaining Ethical Review Committee approval from Liaquat National Hospital (Ref App No: 1027-2024-LNH-ERC). All procedures adhered to the ethical guidelines of the 1964 Helsinki Declaration and its amendments. Written informed consents were obtained from the patients before enrollment. 85 patients were included in total and calculated the sample size by using WHO sample size calculator, based on a confidence level of 95% and desired precision of 0.1% and an expected prevalence rate of vitamin D deficiency of 32.5%, as reported in similar studies of hematological malignancies. The following formula was used for the calculation [14].

$$n=\frac{Z^2 \times p(1-p)}{\varepsilon^2}$$

All newly diagnosed were included MM patients presenting to the Hematology OPD at Liaquat National Hospital aged more than 18 years with no history of vitamin D3 replacement in the last one year. All patient were omitted with bone pain due to malignancies other than MM, autoimmune disorders, amyloid-related systemic diseases and patients with age-related bone changes. All newly diagnosed patients of MM presenting in hematology OPD qualify the inclusion criteria were screened for vitamin D deficiency. The samples of blood for vitamin D3 analysis were collected in red-top tubes, centrifuged at 6000 rpm and measured using the Electrochemiluminescence Immunoassay (ECLIA) on the Roche Elecsys E-411 analyzer, following the manufacturer's standardized protocol. Internal and external quality controls were run with each batch to ensure accuracy and reproducibility. Vitamin D levels were categorized based on their concentration; levels below 20ng/mL were considered deficient, those ranging from 21 to 29ng/mL were classified as insufficient, and levels of 30ng/mL or higher were regarded as normal. A structured proforma was used to collect patient information, including demographics and laboratory parameters which were Hemoglobin, vitamin D levels, serum calcium, serum creatinine, LDH, uric acid, serum protein electrophoresis, serum immunofixation, serum immunoquantification, free light chain assay, bone marrow biopsy findings and radiographic findings(X-ray, CT, or MRI reports). All the data analysis was done by SPSS Version 22.

Frequency and percentage were computed for qualitative variables like gender, residence, Vitamin D status, immunofixation, bone marrow findings and radiographic findings. Continuous variables (e.g., age, weight, height, hemoglobin, immunoquantification, free light chain assay, vitamin D levels, LDH, uric acid) were expressed in mean. Data's normality were evaluated by Shapiro-Wilk test. Stratification was performed for age, weight, gender, hemoglobin, creatinine, and calcium to evaluate their effects on the outcome. Fisher's exact test or the Chi-square test (as appropriate) were used for statistical comparisons with a $p \leq 0.05$ was considered significant.

RESULTS

85 patients were included in the study. Male patients comprised 63.5%, while females accounted for 36.5%. The overall mean age was 58.58±9.24 years and the mean weight was 60.14±9.02 kg. 80% of patients were from urban areas, while 20% were from rural areas. The patient's demographics and the key laboratory parameters observed in the study population are shown in Table 1.

Table 1: Frequency Distribution of Different Variables (n=180)

Demographic and Laboratory Variables	Frequency (%)
Age	
Less than 50	16 (18.8)
More than 50	69 (81.2)
Weight	
Less than 60Kg	41 (48.2)
More than 60Kg	44 (51.7)
Sex	
Male	54 (63.5)
Female	31 (36.5)
Hemoglobin	
Less than 10gm/dl	63 (74.1)
More than 10gm/dl	22 (25.8)
Residence	
Urban	68 (80)
Rural	17 (20)
Creatinine	
Less than 2gm/dl	50 (58.8)
More than 2gm/dl	35 (41.2)
Calcium	
Less than 11gm/dl	81 (95.3)
More than 11 gm/dl	4 (4.7)
Free Light Chain	
Kappa	48 (56.5)
Lambda	37 (43.5)
Immunoquantification	
IgA	17 (20)
IgM	12 (14.1)
IgG	56 (65.9)

Among the 85 patients, the distribution of immunoglobulin subtypes was as follows: IgG (65.9%), IgA (20.0%), and IgM (14.1%). Additionally, the light chain distribution showed a

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predominance of kappa chains (56.5%) over lambda chains (43.5%). Imaging findings were documented in 28.2% (n=24), while 71.8% had no radiographic abnormalities. Among those with imaging findings, 66.7% showed osteoclastic activity while 33.3% exhibited bone marrow infiltration. The overall mean of vitamin D3 level was 21.79 ng/mL. Based on predefined criteria 65.9% (n=56) of patients were vitamin D deficient, 25.9% (n=22) of patients had insufficient levels of vitamin D3 and 8.2% had normal vitamin D levels (n=7) (Figure 1).

Figure 1: Vitamin D3

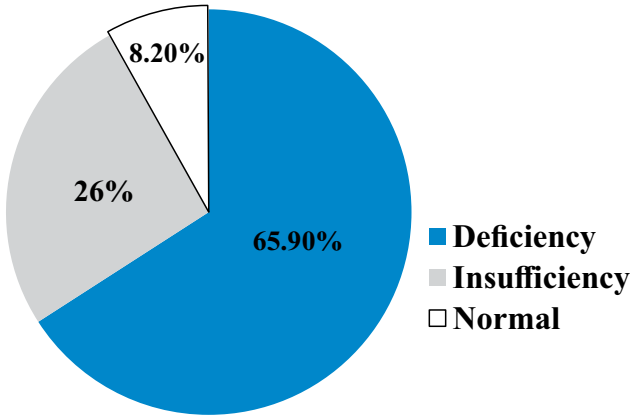

Figure 1: Status of Vitamin D3 in Multiple Myeloma Patients

A notable association of vitamin D levels was seen with place of residence (p = 0.004). However, no meaningful statistical relationship was identified among vitamin D levels and other demographic or laboratory variables. Findings were summarized in table 2.

Table 2: Correlation of Vitamin D Deficiency with Demographic and Laboratory Profile of Multiple Myeloma Patients

Demographic and Laboratory Parameters	Total	Vitamin D Level			p-Value
		Normal Frequency (%)	Insufficient Frequency (%)	Deficient Frequency (%)	
Number	22	6	9	7	
Age					
Less than 50	16	12 (75)	3 (18.8)	1 (6.3)	0.820
More than 50	69	44 (63.8)	19 (27.5)	6 (8.7)	
Weight					
Less than 60kg	41	31 (75.6)	6 (14.6)	4 (9.8)	0.066
More than 60kg	44	25 (56.8)	16 (36.4)	3 (6.8)	
Sex					
Male	54	37 (68.5)	13 (24.1)	4 (7.4)	0.719
Female	31	19 (61.3)	9 (29)	3 (9.7)	
Hemoglobin					
Less than 10gm/dl	63	41 (65.1)	17 (27)	5 (7.9)	0.928
More than 10gm/dl	22	15 (68.2)	5 (22.7)	2 (9.1)	
Residence					
Urban	68	46 (67.6)	20 (29.4)	2 (2.9)	≤ 0.05
Rural	17	10 (58.8)	2 (11.8)	5 (29.4)	
Creatinine					
Less Than 2gm/dl	50	31 (62)	15 (30)	4 (8)	0.608
More Than 2gm/dl	35	25 (71.4)	7 (20)	3 (8.6)	
Calcium					
Less Than 11gm/dl	81	52 (64.2)	22 (27.2)	7 (8.6)	0.699
More Than 11gm/dl	4	4 (100)	0 (0)	0 (0)	
Bony Lytic Lesions	16	14 (87.5)	1 (6.3)	1 (6.3)	1.00
Free Light Chain					
Kappa	48	29 (60.4)	15 (31.3)	4 (8.3)	0.443
Lambda	37	27 (73)	7 (18.9)	3 (8.1)	
Immunoquantification					
IgA	17	9 (52.9)	6 (35.3)	2 (11.8)	0.364
IgM	12	7 (58.3)	3 (25.0)	2 (16.7)	
IgG	56	40 (71.4)	13 (23.3)	3 (5.4)	
BM Plasma Cells %	85	56	27	7	0.118

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DISCUSSION

Patients with Multiple Myeloma (MM) are often found to be vitamin D deficient and the incidence of this condition is impacted by both treatment-related and disease-related variables. Ismail *et al.*, 2023 meta-analysis evaluated the frequency of vitamin D inadequacy and insufficiency in MM patients worldwide. 61% of 430 patients in Europe had the greatest frequency, according to the survey. A comprehensive research conducted in North America revealed that 41% of MM patients had inadequate vitamin D and 20% had deficiency [9].However, data from Asia and Africa remain scarce despite the vast populations of these regions.This study contributed to this dataset, revealing that 69.5% of MM patients were vitamin D deficient and 25.9% had insufficient levels. Notably, there is no association of vitamin D status with age, weight or gender, though the area of residence played a role. This could be attributed to inadequate dietary intake, limited sun exposure, and decreased vitamin D synthesis in older individuals. The findings were consistent with previous study investigating the association between vitamin D insufficiency and hemoglobin and creatinine levels [15]. Additionally, studies have identified a positive interaction between increased C-reactive protein (CRP), low albumin levels and low vitamin D levels [9]. However, this study did not explore these parameters. Similarly, another study showed an association between vitamin D deficiency and increased plasma cell counts in the bone marrow, but this was not observed in the cohort [16]. There is ongoing debate regarding the association between low vitamin D levels and International Staging System (ISS) classification in MM. While studies by Graklanov *et al.*, found no significant correlation, other reports suggest that vitamin D deficiency prevalence increases with higher ISS stages [13]. However, the research did not assess this correlation. Vitamin D insufficiency has also been implicated in musculoskeletal pain and carry an increased risk of bony fractures, which are often overlooked in MM patients due to the nature of the disease [17]. This study failed to find a significant correlation between bone lytic lesions and vitamin D levels, a finding consistent with a study conducted in Japan [18]. Nevertheless, this differs from the findings of Sfeir *et al.*, who documented a notable correlation [14]. Furthermore, inadequate levels of vitamin D has been linked to a higher prevalence of peripheral neuropathy (PN) in MM patients. Prior research suggests that adequate vitamin D supplementation may decrease both the severity and occurence of PN [19, 20]. Vitamin D has been studied for its potential effects on the immune system, cancer progression, and treatment-related side effects [21, 22]. Some studies also propose that patients with MM require significantly higher doses of vitamin D than those currently recommended in clinical guidelines to achieve sufficient levels [20]. Emerging evidence also indicates a potential role of Vitamin D Receptor (VDR) polymorphism in MM pathogenesis and prognosis [4, 23, 24]. Myeloma cells express VDR, and activation of this receptor by vitamin D has demonstrated anti-proliferative effects on malignant cells. However, the precise molecular mechanisms underlying this process remain unclear, highlighting the need for larger-scale studies to further elucidate this association. Future research focusing on levels of vitamin D in MM patients across different Asian populations would provide valuable insights into regional variations in deficiency prevalence and its clinical impact. This study had few limitations. First, the sample size was relatively small due to the limited number of newly diagnosed MM patients presenting at this center during the study period. Secondly, the predominance of urban patients further limited the generalizability of these findings. Additionally, the key risk factors such as sun exposure, sunscreen use, fracture history, and dietary intake of vitamin D were not accounted for, which may have influenced the results.

CONCLUSIONS

This study showed that patients with multiple myeloma have a high prevalence of vitamin D insufficiency, with significant variations observed based on geographic location. Given the substantial influence of vitamin D on bone health, immune function, and overall patient outcomes, it is crucial to monitor vitamin D levels closely in these patients. Supplementation should be considered as part of the systematic management of MM, and further studies is needed to understand its potential role in disease progression and skeletal complications.

Authors Contribution

Conceptualization: RSR
Methodology: SD, SP
Formal analysis: SMA, SP
Writing, review and editing: SMA, NR, SD

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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