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Association of vitamin D deficiency with risk in multiple myeloma: A real-world cohort analysis.

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Background: Multiple myeloma (MM) is a plasma cell malignancy characterized by immune dysfunction and end-organ damage. Emerging preclinical evidence suggests vitamin D is implicated in MM biology through effects on plasma cell differentiation and immune regulation. Vitamin D deficiency is common among patients with MM, yet its prognostic significance remains unclear. Clarifying its role may inform risk stratification and supportive management in MM. **Methods:** We conducted a retrospective cohort study using the multicenter TriNetX research network. Adults aged ≥20 years diagnosed with MM between 2011 and 2024 were included. Vitamin D status was defined using serum 25-hydroxyvitamin D levels, with deficiency defined as ≤30 ng/mL and normal levels defined as 31–80 ng/mL. Patients were stratified into two groups based on vitamin D status at the time of MM diagnosis. Propensity score matching (1:1) was performed to balance age, sex, race, baseline laboratory values, and clinically relevant comorbidities between groups. Kaplan–Meier survival analyses and Cox proportional hazards models were performed for outcome analyses. **Results:** A total of 36,273 patients with MM were included, of whom 42% (n = 15,262) had vitamin D deficiency. After propensity score matching, 14,023 vitamin D–deficient patients were well balanced with 14,006 non-deficient patients across baseline characteristics. In the matched cohort, the mean age was 64 years, 49% were female, and 64% were White. At five years, vitamin D deficiency was associated with a significantly higher risk of mortality (hazard ratio [HR] 1.63, 95% CI 1.54–1.72), with lower five-year overall survival (OS) compared with non-deficient patients (71.1% vs 80.8%, $p<0.05$). Vitamin D deficiency was also associated with increased risks of pneumonia (risk ratio [RR] 1.11), bacteremia (RR 1.22), and critical care admission (RR 1.30) (all $p<0.05$). Additionally, deficient patients had higher risks of acute kidney injury (AKI) (RR 1.19) and venous thromboembolism (RR 1.18) (both $p<0.05$). Notably, the risk of MM relapse was modestly increased among vitamin D-deficient patients (RR 1.07, 95% CI 1.01–1.13). No significant associations were observed between vitamin D deficiency and amyloidosis or pathologic fractures. In multivariable Cox regression, vitamin D deficiency remained independently associated with worse five-year OS (adjusted HR 1.60, 95% CI 1.52–1.67). **Conclusions:** This study highlights the negative impact of vitamin D deficiency in patients with MM. It identifies a high-risk subgroup of patients characterized by worse five-year OS, higher rates of serious infections, AKI, critical care utilization, and an increased risk of MM relapse. These findings suggest vitamin D deficiency as a clinically relevant prognostic marker in MM. Prospective studies are warranted to determine whether vitamin D level optimization can improve MM outcomes. Research Sponsor: None.