RESEARCH ARTICLE

Association of Vitamin D levels in Multiple Myeloma Iraqi Patient with ABO Blood groups

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ABSTRACT

Multiple myeloma (MM) is designated as the neoplastic proliferation of a plasma cell clone that leads to monoclonal antibody production. The skin that is subjected to UV radiation normally reproduces vitamin D. Generally, vitamin D's key functions are related to minerals absorption such as calcium and bone health. An enhanced probability of having rickets or osteomalacia is present in children and adults with vitamin D insufficiency. Besides, recent findings from observational studies suggest that vitamin D levels are inversely linked to the risk of Coronary heart disease, diabetes.

Keywords: ABO blood groups, Multiple Myeloma, Vitamin D3.

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INTRODUCTION

One percent among all tumors and about 10% of all haematologic carcinomas were accounted as multiple myeloma (MM).[1-5] 20,000 suspected cases of myeloma cancer have been identified each year in the Americas.[6] In males, multiple myeloma is significantly more prevalent than females and is almost as predominant in African Americans as related to Caucasians.[7] A patient's median age at the duration of the diagnosis is approximately 65 years.[8]

Unlike some bone-metastasizing tumors, there is no new bone formation of osteolytic bone lesions in multiple myeloma.[9] The major cause of morbidity is bone disease and can be identified by usual skeletal radiographs, magnetic resonance imaging (MRI), or positron emission tomography/computed tomographic scans Polyethylene Terephthalate (PET), computed tomography (CT).[10] Anaemia, hypercalcaemia, renal dysfunction, and an elevated risk of infections are other significant clinical symptoms. At the time of initial diagnosis, approximately 1 to 2% of patients have an extra-medullary disease (EMD), whereas 8 %t develop EMD subsequently during the trajectory of the disease.[11]

From an asymptomatic pre-malignant stage called monoclonal gammopathy of undetermined significance (MGUS), mostly all patients with multiple myeloma develop.[12,13] MGUS appears in over 3% of the individuals over 50 years of age and develops at 1% per year to multiple myeloma or associated tumor.[14] Since MGUS is symptomless, more than 50% of people diagnosed detected with MGUS had the disorder before clinical diagnosis for more than 10 years. Intermediate asymptomatic yet more advanced pre-malignant stage, referred to as smouldering multiple myeloma (SMM) may be clinically detected in some patients.[15] For the first 5 years after diagnosis, SMM progresses to multiple myelomas at a rate of approximately 10% per year, 3% per year for the next 5 years, and 1.5% per year thereafter. This rate of development is affected by the underlying cytogenetic form of cancer, and therefore the probability of development from SMM to multiple myeloma is significantly higher in patients.[16]

Vitamin D3

Vitamin D deficiency is now widely acknowledged as a global health concern that affects musculoskeletal health and has a wide variety of acute and chronic diseases and has been identified chiefly as having many health implications.[17] Increased risk of type 1 diabetes mellitus, cardiovascular disease, some cancers, cognitive impairment, depression, pregnancy complications, autoimmunity, allergies, and even

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frailty have been correlated with low vitamin D status.[18] vitamin D, metabolizing occur during sunlight exposure, converts 7-dehydrocholesterol (7-DHC) to pre-vitamin D3 in the skin. In all the layers of human skin, the 7-DHC is present.[19] The epidermis contains approximately 65% of 7-DHC, and more than 95% of the pre-vitamin D3 formed is in a viable epidermis and cannot be removed from the skin when cleaned.[20] Either photoconversion to lumisterol, tachysterol, and 7-DHC or heat-induced membrane-enhanced isomerization to vitamin D3 can also be performed when pre-vitamin D3 has been synthesized inside the skin.[19] Skin pigmentation, sunscreen usage, a time during the day, climate, and environmental pollution negatively influence the dermal vitamin D3 formation.[21]

Higher serum levels of 25(OH) D were associated with a decreased occurrence of several cancer types in observational studies. Local conversion of 25(OH) D to 1, 25(OH) 2D in normal cells in the colon, breast, and prostate has been suggested to assist prevent malignancy by stimulating cellular maturation, inducing apoptosis, and stop angiogenesis while improving the coding of genes including P21 and P27 to control the cancer progression.[22] The effect of vitamin D on the regulated CYP3A4 gene is detoxification of lithocholic acid bile acid through its protein product.[23] It is estimated that lithocholic acid compromises the DNA of intestinal cells, which can trigger the colon's carcinogenesis. Activating 1, 25(OH) 2D to create a detoxifying enzyme that clarifies a preventive role in enhancing the level of vitamin D toward colorectal cancer.[24] As vitamin D regulates several physiological processes, including immune regulation, oxidative stress resistance, and other hormone regulation, that's not shocking that low vitamin D levels have been linked with an increased incidence of various diseases and fatalities from cancers.[25] While the significance of non-coding RNAs emerged, in many cancer cell lines, patient tissues, and serums, a tendency of 1, 25 (OH) 2D to control microRNAs (miRNAs) was discovered.[26]

It has been found that there are substantial differences in miRNAs between control groups and patient groups in recent studies that evaluate the role of vitamin D. Significant specific miRNA variations were correlated with sera levels of 25(OH) D in prior studies, the findings suggested that increasing vitamin D3 intake will regulate specific miRNA(s) levels in patient groups.[26]

Aims of the Study

- The current study aimed to evaluate the levels of vitamin D3 in some Iraqi patients with multiple myeloma over a disease duration varying from about one year to more than three years, at the Medical City of Baghdad, Teaching Hospital, Cancer Unit.
- Notation the ABO blood groups frequency in this cross-section study of multiple myeloma patients.

MATERIALS AND METHODS

This study was administered to some Baghdad's patients who attended the outpatient clinic of the cancer centre at the medical city of Baghdad from the first of June, 2019 till 1st November 2019, whom Oncologist consultant diagnosed. One hundred and ten myeloma patients with both genders within the age range of 30–79 year were enclosed during this short study.

Tools of the Study

Face-to-face patient interviews provided data collections through the use of:

A. A questionnaire composed of comprehensive socio-demographic data (gender, age, family history of patients, signs, symptoms, duration of disease and therapy used).

B. Biochemical and Serological tests

- Detection of M-band (Monoclonal immunoglobulin) using serum protein electrophoresis by an automated system, Electrophoresis Gel paper, SAS-1 serum analysis, SP-24, Helena, Biosciences Europe, England.
- Vitamin D3 level is estimated by using a fully automated system BECKMAN ACCESS 2, USA.
- In which blood type is established using the antigen-antibody reaction between antigens on RBC and antisera, Haemagglutination test is known as the 'gold standard ' for ABO blood-antigen.

Statistical Analysis

The statistical analysis was carried out using the social sciences statistical package (SPSS), version 23, and (Excel 2010). Using numbers and percentages, there were qualitative results. A mean and standard deviation were used to present quantitative data. We used statistical tests as follows:

A. Test of Chi-square: in categorical variables.

B. ANOVA-test: for normal quantitative variables.

The statistical importance of $p < 0.05$ was achieved.

RESULTS AND DISCUSSION

Table 1. Represented frequency distribution (count and percentage) of categorical variables (n 110) for the age range per year, gender distribution, duration of disease, blood group distribution of ABO and medications used in this study. Chi-square tests were carried out. p-value is significant at the level of 0.05 (2-tailed). Statistically, the consequences were significant - differences between all these categorical variables except for ABO blood group distribution in this study were statistically non-significant differences. Age-frequency percentage range per year from 60 to 69 years was 43.6%, from 50 to 59 years was 32.7%, and gender distribution 64, 58.2 % male vs 46, 41.8 % female with the male-to-female ratio is 1.4. These findings apply to previous studies on age, gender distribution, and male-to-female ratios, which show that only 18% of patients under 50 years of age and only 3% of patients are under 40 years of age.[4] As reported in the previous studies, the male vs female percentage was (60 vs 40%, respectively), and the ratio of male to females was 1.5.[27] In Table 1 and Figure 1, the percentage distribution for the ABO blood group was 30% for the A blood group and 27% for the O blood group, 25% for the B blood group, and 18% for the AB blood group, respectively. These findings are consistent with previous studies on the association between the ABO blood group and Nasopharyngeal Carcinoma.[1]

Table 1: Frequency Distribution of the categorical variables (n 110)

Class: Age/Year	*Count*	*Percentage*	*Chi-Square for goodness of Fit p-value*
30–39	3	2.7	Chi^2 value = 67.909 p-value <.00001** degrees of freedom (df) = 4
40–49	7	6.4	
50–59	36	32.7	
*60–69	48	43.6	
70–79	16	14.5	
Class: Gender distribution	*Count*	*Percentage*	*p-value*
Male	64	58.2	Chi^2 value = 2.945 p-value =.08612 degrees of freedom (df) = 1
Female	46	41.8	
*Male/Female ratio = 1.4			
Class: Duration of disease	*Count*	*Percentage*	*p-value*
Newly diagnose	22	20.0	Chi^2 value = 41.127 p-value <.00001** degrees of freedom (df) = 3
< Year	34	30.9	
*1–3 Year	50	45.5	
> 3 Year	4	3.6	
Class: ABO Blood group	*Count*	*Percentage*	*p-value*
A	33	30	Chi^2 value = 3.382 P-Value =.33642 degrees of freedom (df) = 3
O	30	27.3	
B	27	24.5	
AB	20	18.2	
Class: Treatment	*Count*	*Percentage*	*p-value*
*Velcado, Zometa	35	31.8	Chi^2 value = 35.745 p-value <.00001 ** degrees of freedom (df) = 5
Lenalid 10 mg	29	26.4	
pomalidomide, decadron, Zometa	15	13.6	
Newly diagnosed without treatment	14	12.7	
Lenalid 10mg, velcado, dexa, Zometa	13	11.8	
velcado, decadron, Revlimid	4	3.6	
Total	110	100.0	

**p-value is highly significant at the 0.01 level (2-tailed).
*p-value is significant at the 0.05 level (2-tailed).
The result is not significant at p > 0.05.

Ultimately, (Velcade, Zometa, and Lenalide 10 mg) drugs (32 percent and 26 percent), respectively, are the most common frequency percentage of the drug category used in Table 1 and Figure 2. These findings are in line with previous studies in the latest class of anti-cancer drugs known as proteasome inhibitors, the first of its type being Velcade®. The cells are all proteasome. Removing unwanted, extra, or damaged proteins acts like a garbage disposal system in a cell; slowing down proteasome activity can also delay the degradation of essential proteins that help cells combat cancer.[28] On the opposite hand,

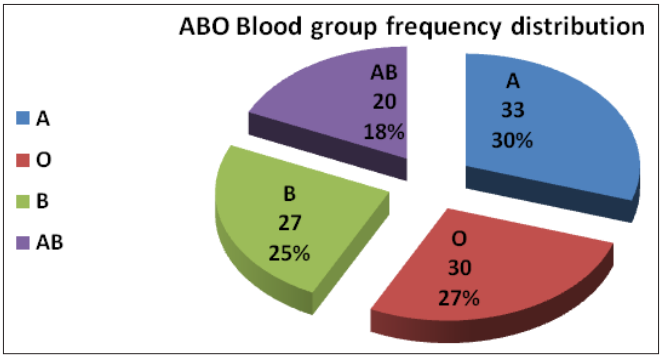

Figure 1: Frequency distribution of the ABO blood group in this study (count and percentage).

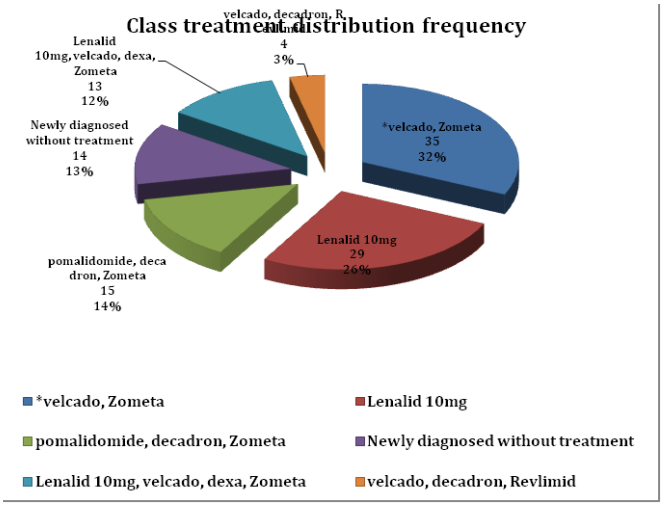

Figure 2: Frequency of distribution (count and percentage) of the medication group in this study.

bisphosphonates (BPs) are highly bone-affinity pyrophosphate analogs and, therefore, the ability to inhibit osteoclast (OC) features. Supported this argument, BPs are utilized in the clinic as antiresorptive agents for treating high bone turnover diseases. Paget's disease and bone disease are extensively employed in cancer-associated osteoporosis, among which BPs, pamidronate (Pam) and zoledronic acid (ZA) are most ordinarily wont to treat myeloma-associated bone disease.[29] While Lenalidomide could also be recommended together with dexamethasone in both previously untreated and multiple myeloma-treated patients.[30]

Table 2: The descriptive statistical data (minimum, maximum, mean ± Standard Deviation (SD), variance and confidence level (95.0%)) of the continual variables (n 110) with one-way repeated measures ANOVA calculator significance level: 0.05, degrees of freedom (df) = 7, F-ratio value is 733.3 and thus the p-value is <.00001 (statistically highly significant). The age annually was 31 minimum (79 maximum) and so the mean ± Standard Deviations were (60.0 ± 9.4) with the variance of 89.0 and a good confidence interval with level 95% is 1.78. These results concerning about the age in myeloma Iraqi patients were coinciding with the previous studies.[8]

Findings of the serum protein electrophoresis throughout this study, the usual pattern of myeloma patients with elevated

Table 2. Summary of Data (n 110)

One-way repeated measures ANOVA calculator
significance level: 0.05

	Descriptive statistic						One-way repeated
Variables	*Minimum*	*Maximum*	*Mean*	*± SD*	*Variance*	*Confidence level (95.0%)*	
Age/ Year	31.0	79.0	60.0	9.4	89.0	1.78	
*Total protein: (N 64–83 g/L)	48.0	130.0	75.1	18.5	341.4	3.49	Measures ANOVA Calculator Significance level: 0.05
*Albumin: (35–50 g/L)	18.2	44.8	32.9	6.7	44.8	1.26	
Alpha-1 globulin: (N 1–3 g/L)	1.7	5.6	3.4	1.1	1.1	0.20	degrees of freedom (df) = 7
Alpha-2 globulin: (N 6–10 g/L)	3.6	13.0	8.8	2.2	4.6	0.41	F-ratio value is 733.3
Beta globulin: (N 7–2 g/L)	4.4	12.0	8.1	1.9	3.7	0.36	The p-value is <.00001**
*Gamma globulin: (N 7–16 g/L)	7.6	88.0	21.0	13.0	169.5	2.46	
*Vitamin D3 25-Hydroxyvitamin D: (N 30–50 ng/mL)	4.0	53.0	16.0	13.2	173.9	2.49	

**p≤0.01 (2-tailed) is highly-significant.
S.D standard deviation, N normal reference, a good confidence interval is 1.960, with a 95% level.* Increasing levels of confidence raise the variance, widening the confidence interval. Lowering the level of confidence reduces the variance, narrowing the confidence interval.

serum total protein levels (g/l) was 48.0 minimum (130.0 maximum), mean ± Standard Deviations (75.1 ± 18.5) with high variance (341.4) and high confidence level (3.49), serum albumin levels (g/l) were at least 18.2 (44.8 maximum), mean ± Standard deviations (32.9 ± 6.7) were at low variance (44.8) and low confidence levels (1.26) and relating to serum gamma globulin levels (g/ l) was 7.6 minimum (88.0 maximum), mean ± standard deviations were (21.0 ± 13.0) with high variance (169.5) and high confidence level (2.46). These observations are linked to previous studies on the diagnostic test of symptomatic multiple myeloma (MM) including clonal bone marrow plasma cells (BMPCs), often > 10%, or plasmacytoma, M-protein serum and/or urine, and associated organ or tissue impairment. [31]

Finally, the relevant point is the level of vitamin D3 (ng/mL) in this evaluation, which reveals low significant levels represented as 4.0 minimum (53.0 maximum), mean ± SD (16.0 ± 13.2) with high variance (173.9) and high confidence level (2.49). Such a study is harmonious with the influence of a low level of vitamin D3 on the prognosis of multiple myeloma's patients.[32]

CONCLUSION

In the current study

1 The mean age/year of multiple myeloma patients was 60 years of age with a high proportion 43.6% of age ranging from 60 to 69 years of age, the male-to-female ratio was 1.4 with the ABO blood groups type A were high prevalence percentage among this study group was 30% and 45.5 % represented as the high-frequency distribution of the malady period about one to three years.
2. About vitamin D levels were substantially low, with a minimum of 4.0 ng/mL (maximum of 53.0 ng/mL) and an overall mean of 16.0 ng/mL. Thus, vitamin D deficiency level (about 20 ng/mL) is associated with an increased prevalence of various cancer types, like myeloma, and a worse response to therapy. Osteomalacia may be triggered through vitamin D deficiency and generalized musculoskeletal pain, extreme fatigue, with a greater risk of injuries can emerge in such cases.

RECOMMENDATIONS

Vitamin D levels usually decline during chemotherapy, but this decline is not associated with poor remediation in itself. Therefore, healthcare professionals recommend a need to take nutritional supplements containing a high ratio of vitamin D during the period of illness, since vitamin D supplementation can improve vitamin D levels in the blood, enhancing therapeutic response substantially. Vitamin D is cell membrane antioxidants with an anti-cancer impact. Omega-3, selenium, vitamin D and vitamin E are the safest and cheapest nutrients for malignancies.

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