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The Alteration of Serum Magnesium Levels in Postmenopausal Bangladeshi Women

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Abstract

Magnesium as an essential element for various physiological functions in the human body especially in cardiovascular and skeletal system. Menopause can effect on magnesium homeostasis in women's body. A cross-sectional, comparative study was conducted in the Department of Biochemistry, Mymensingh Medical College, Bangladesh, between July 2022 and June 2023, to compare serum magnesium levels and prevalence of magnesium deficiency between pre- and post-menopausal women. A total of 110 women attending the outpatient departments of Mymensingh Medical College Hospital, being either pre-menopausal or post-menopausal, were included in this study through convenience sampling, based on selection criteria (i.e., 55 pre-menopausal women were in group-I and 55 post-menopausal women were in group-II). Demographic data, clinical history and dietary intake information was collected from the participants through face-to-face interview using a structured questionnaire. Dietary intake of magnesium was estimated based on the simplified food-frequency questionnaire (FFQ) modified from common Bangladeshi foods (such as pulses, nuts and green vegetables). Height and weight were obtained using a standardized procedure for calculating BMI. Then, venous blood samples (5 mL) were drawn from all participants in the morning after an overnight fasting. The samples were centrifuged and the serum was then kept at −20°C until analysis. Serum magnesium was determined by xylidyl-blue colorimetric method with an automatic biochemistry analyzer. The mean age was found higher in group-II compared to group-I (52.80±3.56 years vs. 33.76±3.55 years; p<0.001). Similarly, BMI was also found higher in group-II (26.54±1.93 kg/m² vs. 23.62±1.27 kg/m²; p<0.001). In contrast, serum magnesium was found significantly lower in group-II (2.22±0.56 mg/dL vs. 2.39±0.22 mg/dL; p<0.05). Moreover, a sharp decline was observed in serum magnesium levels with longer duration of menopause (p<0.05) as compared among postmenopausal women having menopause for <5 years, 5–10 years and >10 years. Magnesium deficiency needs to be screened, monitored and treated in postmenopausal women in follow-up visits.

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Introduction

Magnesium, an indispensable intracellular cation essential for over 300 enzymatic reactions including nucleic acid synthesis, neuromuscular conduction, cellular energy metabolism, membrane stability and bone mineralization. Sufficient magnesium status is associated with the maintenance of normal skeletal structure, parathyroid hormone regulation and calcium–phosphate balance. As a result, there is an important role of serum magnesium disruption in the context of chronic disease burden, especially if we consider women in menopausal stage and hormonal changes that lead to increased bone loss and metabolic dysfunction.[1] During menopause, the decline in circulating estrogen is linked to disturbances in mineral metabolism and increased urinary magnesium excretion, reduced intestinal

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absorption and progressive bone loss secondary to a negative balance of calcium.[2] Magnesium conservation has been reported to be impaired microscopically both at renal tubules and intestines due to estrogen deficiency which could lead to enhanced bone resorbing cells activity like secondary hyperparathyroidism and accelerated rate of skeletal turnover. These alterations increase susceptibility of postmenopausal women to magnesium insufficiency that can also potentially contribute to increased risk for osteoporosis, hypertension, insulin resistance and systemic inflammation.[3] The added overlay of the compounding effect of nutrient insufficiency is especially important in low-and middle- income countries (LMIC) where dietary magnesium intake typically does not meet recommendations, given reduced consumption of leafy vegetables, nuts, whole grains.[4] Throughout the world, deficiency of magnesium is common in elderly women. Epidemiologic studies have revealed that 20–40% of adults, especially women older than 50 years consume magnesium less than the estimated average requirement.[5] More than 60% of postmenopausal women in the USA are believed to have deficient magnesium intake; this is even greater in urban low-income populations.[6] Near identical trends have been observed in South and Southeast Asia where indigenous diets are typically low in magnesium containing foods, whereas high phytate content present in main cereal staples further reduces mineral bioavailability.[7] Magnesium deficiency is associated with various cardiometabolic diseases. Low blood magnesium levels are correlated with endothelial dysfunction, increased vascular resistance and high BP, corresponding proof that magnesium deficiency may be implicated in hypertension development of postmenopausal women[8] In addition, an inverse correlate of serum magnesium with those markers of metabolic syndrome (fasting glucose, triglycerides and insulin resistance) has been demonstrated among mid-life and older women.[9] Reduced serum magnesium also relates to reduced bone mineral density (BMD), which is also relevant in postmenopausal osteoporosis.[10] While there has been considerable investigation of magnesium and metabolic outcomes in Western populations, less is known among South Asians. Bangladesh is characterized by low dietary diversity, high levels of micronutrient deficiency and a very high lifetime risk of metabolic disease in women. However, routine biochemical analysis of magnesium is not routinely incorporated into work-up of perimenopausal or postmenopausal women in limited-resource health care settings. As a result, possible electrolyte derangements might remain undetected until it is too late for prevention. Hence, we proposed this study to compare serum magnesium levels and prevalence of magnesium deficiency between pre- and post-menopausal women in Bangladesh.

Methods

A cross-sectional, comparative study was carried out in the Department of Biochemistry, Mymensingh Medical College, Bangladesh, from July 2022 to June 2023. A total of 110 women attending the outpatient departments of Mymensingh Medical College Hospital, being either pre-menopausal or post-menopausal, were included in this study through convenience sampling, based on selection criteria. Serum magnesium was determined by colorimetric method with Magon sulfonate using the test kit. Inclusion criteria were: pre-menopausal women (40–50 years) with regular menstrual cycles for group-I and post-menopausal women (45–65 years) with amenorrhoea ≥12 months.

Exclusion criteria were: known case of diabetes mellitus, cardiovascular disease, chronic renal or liver disease or malabsorption disorders, on magnesium supplementation within the preceeding 3 months, on hormone replacement therapy (HRT), pregnant or lactating women, significant acute illness (e.g., infection) and history of hospitalization within the past 1 month. Finally, we had 55 premenopausal women were in group-I, while the other 55 postmenopausal women were in group-II. Following recruitment, demographic data, clinical history and dietary intake information was collected from the participants through face-to-face interview using a structured questionnaire. Dietary intake of magnesium was estimated based on the simplified food-frequency questionnaire (FFQ) modified from common Bangladeshi foods (such as pulses, nuts and green vegetables). Height and weight were obtained using a standardized procedure for calculating BMI. Then, venous blood samples (5 mL) were drawn from all participants in the morning after an overnight fasting. The samples were centrifuged and the serum was then kept at −20°C until analysis. Serum magnesium was determined by xylidyl-blue colorimetric method with an automatic biochemistry analyzer.

After collection, data was scrutinized, compiled and coded. IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. Descriptive statistics were presented as mean±SD (standard deviation) for continuous variables. Unpaired Student's t-test was used to compare variables between pre-menopausal and post-menopausal groups. Statistical significance was set at <0.05.

Ethical clearance for this study was obtained from the Institutional Review Board (IRB) of Mymensingh Medical College, Mymensingh, Bangladesh (MMC/IRB/2023/542).

Results

We included 110 women (55 pre-menopausal as group-I and 55 post-menopausal as group-II). The mean age in group-I was 33.76±3.55 years and 52.80±3.56 in group-II. The difference was statistically significant (p<0.001). Regarding the body mass index (BMI), group-II had a higher BMI compared to group-I (26.54±1.93 kg/m² vs. 23.62±1.27 kg/m²). The difference was also statistically significant (p<0.001). The mean serum magnesium levels were 2.39±0.22 mg/dL and 2.22±0.56 mg/dL in group-I and group-II respectively, with a statistically significant difference (p<0.05) (Table-I). Moreover, a sharp decline was observed in serum magnesium levels with longer duration of menopause (p<0.05) as compared among postmenopausal women having menopause for <5 years, 5–10 years and >10 years (Fig. 1).

Table-I: Comparison of age, BMI and serum magnesium level between premenopausal (group-I) and postmenopausal women (group-II)

Variables	Premenopausal (Group-I) n=55 Mean±SD	Postmenopausal (Group-II) n=55 Mean±SD	p-value
Age (in years)	33.76±3.55	52.80±3.56	<0.001[S]
BMI (kg/m²)	23.62±1.27	26.54±1.93	<0.001[S]
Serum magnesium (mg/dL)	2.39±0.22	2.22±0.56	<0.05[S]

Unpaired Student's t-test was applied to reach p-value; S=significant.

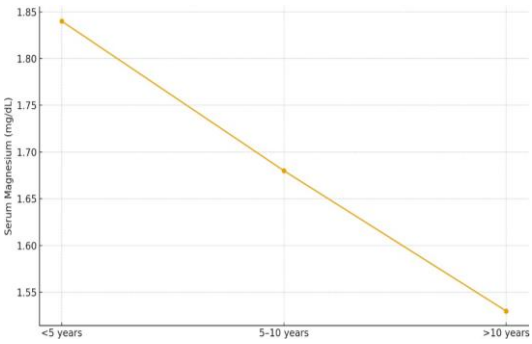

Fig. 1: Serum magnesium levels by duration of menopause.

Discussion

The difference between the pre-menopausal and post-menopausal women in clinical, as well as biochemical parameters was a clear-cut dissociation of magnesium status associated with menopause. The mean age in premenopausal group was 33.76±3.55 years, while for postmenopausal 52.80±3.56 years ($p<0.001$), as expected. Although it cannot be changed, menopausal age provides information on physiological and metabolic modifications.[11] Older age is associated with decreased oestrogen production, reduced intestinal uptake of minerals, and profound effects on renal handling all factors that could potentially lower post-menopausal women's magnesium and calcium levels.[12] Comparing BMI between two groups, postmenopausal group had higher body mass index (26.54±1.93 kg/m²) compared to premenopausal group (23.62±1.27 kg/m²) ($p<0.001$). This is consistent with previous studies, where weight gain was also identified as usual during the menopausal transition due to decreased basal metabolic rate and hormonal changes.[1,12-16] Body mass index (BMI) is clinically relevant, as it increases inflammation, endothelial dysfunction and insulin resistance which could potentially modulate magnesium utilization leading to magnesium deficit. Serum magnesium levels were significantly lower in the postmenopausal group (2.22±0.56 mg/dL) as compared to premenopausal group (2.39±0.22 mg/dL) ($p<0.05$). The higher BMI and the lower magnesium levels in postmenopausal group can provide some physiological background for the low magnesium observed.[12-16] While the absolute numerical difference of serum magnesium levels may be modest, there are significantly and generally wider variations in postmenopausal patients, indicating a biologically meaningful reduction (declining serum magnesium levels as found with longer duration of menopause i.e., menopause for <5 years, 5–10 years and >10 years). This is consistent with the proposed role of oestrogen deficiency in inducing renal magnesium wasting and reduced intestinal absorption.[13,17-20] Lower magnesium may also play a role in the increased frequency of hypertension in postmenopausal women, as it is a natural calcium antagonist and vasodilator. Lower values may thus be a risk factor for increased vascular tone and blood pressure.[1,5,9] Serum magnesium positively correlated with serum calcium. This implies that patients with greater magnesium levels can better preserve homeostatic calcium balance. This association is physiologically plausible because magnesium is required for parathyroid hormone (PTH) production and activity. In states of magnesium deficiency, the release of PTH is dysfunctional and secondary hypocalcemia may develop despite adequate dietary intake of calcium. Thus, the described association is supportive for the notion of a joined regulation of calcium and magnesium metabolism or an effect of altered homeostasis of either ion on that of the other.[19,20] Women with a more recent onset of menopause exhibited higher magnesium levels, in contrast to those who became menopausal years ago

and had experienced more severe lowering. This trend may reflect a persistent long-term effect of estrogen deprivation on magnesium metabolism. Over time, continued reduction in hormonal production results in progressive increase in renal excretion of magnesium and decrease in absorption efficiency, until biochemically measurable deficiency develops.[19] Postmenopausal patients are older with more BMI and much lower levels of serum magnesium. Such diametrically opposite tendency in anthropometric and biochemical indicators suggests a complex phenomenon influenced by endocrine deviations, metabolic modifications and dietary habits related to ageing of women.[17,19,20] Moreover, the association of magnesium with calcium emphasizes the importance evaluating them in combination for certain clinical conditions.[18] In summary, the comparison of all findings suggests that magnesium deficiency is more frequent, more varying and more clinically relevant in postmenopausal women. As the serum magnesium level and calcium are associated with bone metabolism and involve blood pressure regulation, those results point to regular monitoring of serum magnesium in menopausal care.

Conclusion

Postmenopausal women have significantly lower serum magnesium levels with presence of high prevalence of magnesium deficiency than that of premenopausal women. Our results indicate that assessment of magnesium status in postmenopausal women is clinically relevant and surely benefit overweight or hypertensive women as well. Dietary counselling or magnesium supplementation may also be of consideration for interventions.

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