

Review article

Vitamin B status and its impact in post-menopausal women: A reviewStefy Samuel¹, Kalaivani Manokaran¹, Kusumakshi Nayak¹, Gayathri M. Rao², Saritha Kamath U.¹¹Department of Medical Laboratory Technology, Manipal College of Health Professions, Manipal Academy of Higher Education (MAHE), Manipal, 576104, Karnataka, India²Department of Biochemistry, Kasturba Medical College, Mangalore, Manipal Academy of Higher Education (MAHE), Manipal, Karnataka, India

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Corresponding author: **Saritha Kamath U.** Email: saritha.kamath@manipal.edu**ABSTRACT**

Menopause is an age-related naturally occurring phenomenon in women. Women generally attain menopause between the 40-58 years of age, during which they undergo several physiological changes that have an impact on their daily activities. The deficiency of B vitamins occurs mainly due to the dietary pattern, absorption and blood loss which may leads to health problems such as cognitive decline, osteoporosis, physical and mental imbalance. This review evaluated the published evidence on the vitamin B status and its impact in post-menopausal women. Selected data sources were searched for relevant literature (2010-2020) and included as per the set criteria using Prisma guidelines. The NIH quality questionnaire tool was used to rate the articles. Finally eleven articles were included for full length review having reports on the impact of B vitamins on bone loss, cognitive decline and physical activity. Existing evidences show that there is no association between B vitamins and bone loss. Very few studies are available which concluded association of B vitamin with cognitive decline and physical health. More studies are required to address this research gap.

Keywords: Vitamin B complex; post-menopausal women; water-soluble vitamin.**INTRODUCTION**

Menopause, is a time of transition in a woman's life. Between the ages of 40 and 58 years, and an average of 51 years, as hormone levels drop, one may experience a series of physiological changes, such as hot flashes, sleeplessness, night sweats, vaginal dryness, and fluctuating moods. Though these symptoms are not experienced by all, many people may find they cause inconvenience and discomfort. Sufficient amount of B vitamins may help overcome some of these changes during menopause (1, 2).

Vitamin B complex derivatives/co-enzymes, are requirements for many of the metabolic/enzymatic reactions, energy production, methylation, immune function, DNA repair (3), and in the maintenance and normal functioning of the nervous system. B vitamins are essential water-soluble vitamin found in many foods, but none of which are synthesized in sufficient amounts in humans, plays a great role in global health and wellbeing. Even after several fortification programmes, many countries still face the deficiency of vitamin B during menopause, and that could be due to inadequate intake, malabsorption, and medicines interacting with the metabolism of members of the vitamin B complex.

Deficiency of B complex vitamin mainly includes thiamine (B1), pyridoxal (B6), folate (B9), cobalamin (B12), which can cause changes in the one-carbon metabolism network. They are also co-factors for the

energy-producing metabolic pathways of carbohydrates, fats, and proteins. In ageing populations, B vitamins deficiency has been linked to cardiovascular disorders, cognitive dysfunction, osteoporosis, and methylation disorders. It can also increase the risk of developing degenerative diseases, cognitive impairment, cardiovascular disease, and osteoporosis (4, 5). Along with Vitamin D, B vitamins also plays a major role in the bone health of an individual (6). Vitamin B6 (pyridoxal), B9 (folate), and B12 (cobalamin) act as cofactors in homocysteine metabolism. Hence deficiency of these vitamins increase the serum level of homocysteine (7, 8). Hyper-homocysteinemia is one of the major risk factors for cognitive impairment, cardiovascular disease, bone loss, the common/ frequent outcome in post-menopausal status (9, 10).

In postmenopausal women, osteoporosis is one of the complications due to decline in Estrogen level (11). Increased homocysteine and decreased B vitamins are the independent risk factors for bone loss (12). Low bone mineral density (BMD) and increased fracture risk are associated with decreased vitamin B12 status, which is mainly assessed by plasma levels (13). The increased risk for fractures in women could be due to the deficiency of B vitamin and D vitamin, this risk is mainly seen in the hip, wrist, and spine. However, there is no link between vitamin B12 and folic acid with the risk of hip fractures (14).

A large -scale randomized control trial study revealed that a high dose of vitamin B6 is associated with an

increase in hip fractures (15). The deficiency of B vitamins are related to depressive disorder and is one of the characteristics of menopause. Administration of folic acid along with antidepressant are found to be more effective (16-18). It has been also reported that vitamin B status to be associated with Alzheimer's disease and dementia, which may accelerate cognitive decline if it is left untreated and may lead to irreversible neurological damage (19- 21).

B vitamin status has a large impact on health. The deficiency of these vitamins occur mainly due to dietary pattern and decreased absorption (22). Menopause is the period where women experience problems such as bone loss, cardiovascular problems, impairment in cognition, dementia etc. (23). Hence, it is important to know the status of these vitamins and their impact on postmenopausal status to improve their quality of life. With this aim, we conducted this narrative review systematically.

MATERIAL AND METHODS

Search methods for the identification of the studies

The articles were searched in Single Window of Health Science library includes PubMed, Scopus, Web of Science, Google scholar, available in Health Science Library of Manipal Academy of Higher Education during the study period February 2021 to March 2021. Articles published between 2010 - 2020 were included during the review process. Keywords used for the search strategy included, B vitamin OR water-soluble vitamin OR B vitamin Complex OR

vitamin B1 OR Thiamine OR vitamin B6 OR pyridoxine OR pyridoxal OR pyridoxamine OR vitamin B9 OR Folate OR vitamin B12 OR cobalamin OR cyanocobalamin OR methyl-cobalamin AND Post-menopausal women OR Middle-aged women OR women. Articles on B vitamin status and its impact on physical health/ mental health among post-menopausal women were included.

Study selection, data extraction and risk of bias

The titles of the articles were collected from the databases using pre-selected key words by two authors and saved in excel sheets. Duplicates were removed from these with the use of the software Rayyan. Title and abstract screening were done by two authors based on the inclusion and exclusion criteria and any discrepancies were sorted by the third author. The selected articles for full text were assessed for eligibility with the help of data extraction form. The quality rating using the NIH quality questionnaire tool by two authors independently. The study design of evidences selected and included for this review was cross sectional study, cohort study. The articles which included post-menopausal women aged 40 years and above as participants with relevant description of link between B vitamin status and its impact on mental/ physical health were included for full length review. The selected full length articles were subjected to quality rating based on NIH quality assessment tool by two reviewers independently.

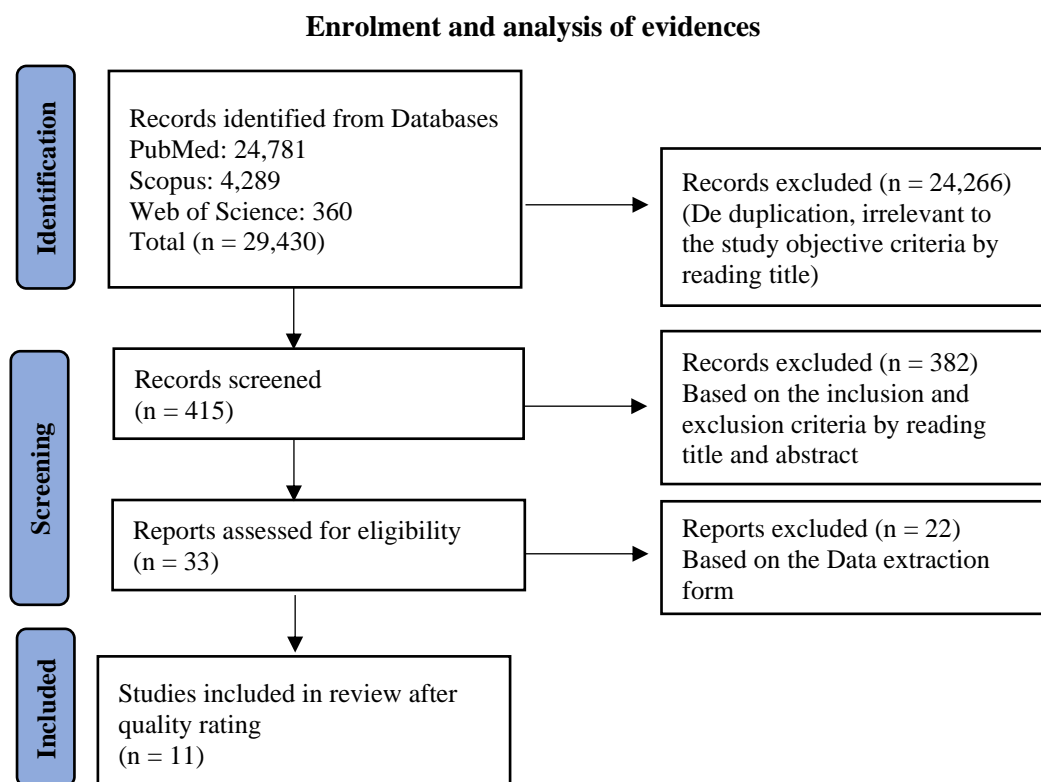


Fig. 1: Systematic review of flow diagram

RESULTS

Out of 11 published articles included in our study, 3 were from Morocco, 3 from Japan, 1 article each from London, Italy, Brazil, Turkey, and the Netherlands, among these 8 were cross-sectional studies and 3 cohort studies. Out of 11 studies, six aimed to investigate B vitamin status and bone health, three studies aimed to investigate B vitamin status and physical health, and the last two aimed to investigate B vitamin status and cognition/ memory. The sample size ranged from 70 to 1,352. The participants included were within the age range of 40 to 91 years. Two studies were with both genders and, were retrieved as per our inclusion criteria.

B vitamin and bone health

A cross-sectional cohort study conducted by Maataoui *et al.*, on healthy post-menopausal women from Morocco found that low levels of vitamin B12, vitamin B9, and high levels of homocysteine are not associated with a bone fracture (24). A study by Maghraoui *et al.*, (25) also examined the influence of homocysteine, vitamin B12 and folate on the prevalence of asymptomatic vertebral fractures in post-menopausal women from Morocco, and reported these factors to be independent and not related to the osteoporotic status.

A cross-sectional cohort study published by Kakehashi *et al.*, on asymptomatic post-menopausal women from Brazil indicated that serum vitamin B12 is not related to bone mineral density (26). A cross-sectional cohort study published by De Martinis *et al.*, on post-menopausal women from Italy found that elevated serum homocysteine, decreased folate, and vitamin B12 were found in decreased bone mineral density group when compared with normal bone mineral density (27).

A cohort study published by Kuroda *et al.*, on post-menopausal women from Japan found that vitamin deficiency additively increases the risk of fracture (28). A cross-sectional study published by Ouzzif *et al.*, on post-menopausal women from Morocco concluded that vitamin B12 and homocysteine (HCY) are the independent risk factors for osteoporosis. Their findings suggested that supplementation of vitamin B12 for menopausal women may prevent osteoporosis (29).

Vitamin B and physical health

A cohort study published by Tumura *et al.*, on post-menopausal women from Japan found that no correlation between depressive symptoms and vitamin B12 level (30). A cross-sectional study published by Ao *et al.*, on the elderly population from Japan found that there was no significant association between serum folate concentration and gait speed nor between serum B12 and physical performance among women.

Serum folate level is positively contributed to handgrip and limb muscle strength (31). A cohort study published by VanSchoor, *et al.*, on post-menopausal women from the Netherlands found that elevated homocysteine to be associated with poorer physical performance while, there is no association between B12 and physical performance (32).

B vitamin and cognitive function

A cross-sectional study published by Sengul *et al.*, on post-menopausal women from Turkey found that no correlation between depressive symptoms and vitamin B12 and vitamin B9 level (33). A cross-sectional study published by Nalder *et al.*, on older women from London found that they are more prone to vitamin B12 deficiency and there is a correlation between vitamin B12 status and deficit in attention and memory (34).

DISCUSSION

The associations between the cognitive decline, physical health, and bone health of menopausal women with other B vitamins have been extensively studied in the most diverse populations, as shown in Table 1. We included 11 studies in this review. Six studies reviewed the role of vitamin B on bone health, three studies about the role of B vitamin on physical health and two articles based on the role of B vitamin on the cognitive function of postmenopausal women.

During this systematic review, most of this evidence was from the developing and developed countries which showed varied populations from Morocco, Japan, London, Italy, Brazil, Turkey, and the Netherlands. Participants involved in the reviewed study had different age varying from 40 to 91 years. A lesser range of 45 to 55 years maybe is required to include a uniform population and better result. Vitamin level included in these studies is B9 and B12, not much on other B vitamins. Methyl malonic acid is the early indicator to know about functional deficiency of vitamin B12 and we found only one study which included this parameter.

Vitamin B status and its impact on bone health

Osteoporosis is a major health problem in the elderly. Many therapeutic solutions are available to prevent fractures due to osteoporosis. Nutritional intervention and training physical activities were found to be effective. Among various nutritional factors, vitamins play an important role in this regard. Due to improper care taken during the menopausal period, menopausal women are more prone to nutritional deficiency. homocysteine is one of the factors which leads to impaired bone metabolism and fracture. Deficiency of vitamin B9 and vitamin B12 leads to an elevated level of homocysteine.

Table 1: Study characteristics of included articles

Ref No:	First Author	Year	Study Design/ Country	Subject/ Age	Health Impact	Result	Conclusion	NIH Score
Role of B Vitamin on bone health								
(27)	Massimo De Martinis	2020	Cross-sectional study, Italy	252 Postmenopausal women 50 - 65 years	BMD(Osteopenia, osteoporosis, inflammation)	Compared HCY with vitamin B9, B12, BMD was significant	Elevated serum HCY, decreased vitamin B9 and B12 were associated with osteopenia, osteoporosis and increased bone loss, inflammation when compared to normal	5/14
(28)	T. Kuroda	2019	Cohort study, Japan	889 postmenopausal women age 68.3 \pm 9.5 years	Risk of fractures	Compared risk of fracture with vitamin D, osteocalcin and HCY was significant	Vitamin deficiency additively increases the risk of fracture	6/14
(24)	Aissam El Maataoui	2017	Cross-sectional study, Morocco	122 healthy postmenopausal women, age: above 45 years	BMD and vertebral fracture	Compared vertebral fracture with HCY, Vitamin B9, B12, was not significant	Low levels of vitamin B12, vitamin B9 and high level of HCY are not associated with bone fracture	5/14
(25)	Abdellah El Maghraoui	2012	Cross-sectional study, Morocco	188 postmenopausal women, age: 41 to 91 years	Vertebral fracture	Compared vertebral fracture risk with HCY, vitamin B9, B12, was not significant	Vitamin B9, B12 and high level of HCY not associated with osteoporotic fracture	5/14
(26)	Adriana Maria Kakehasi	2012	Cross-sectional study, Brazil	70 asymptomatic postmenopausal women, mean age: 62.5 \pm 7 years	BMD, Wrist fractures, Vertebral fracture, Hip fracture	Compared BMD with vitamin B12 was not significant	Serum vitamin B12 was not associated with bone mineral density	5/14
(29)	Zhor Ouzzif	2010	Cross-sectional study, Morocco	188 healthy volunteer postmenopausal women, age > 45 years	Bone Mineral Density	Compared BMD with vitamin B9, Vitamin B12, HCY was significant	Vitamin B12 and HCY are the independent risk factors for osteoporosis.	5/14
Role of B vitamin on physical health								
(30)	Takashi Tamura	2020	Cohort study, Japan	1046 men and 1033 women, age: 56.0 \pm 8.9 years	Physical health	Compared hypertension with plasma levels of HCY, vitamin B9 and B12 was significant with HCY and B12	Low serum B12 is positively associated with hypertension and HCY was positively linked with hypertension	6/14
(31)	Misora Ao	2019	Cross-sectional study, Japan	86 residents 83.5 years on average with no gender difference	Physical health	Compared physical health with HCY, vitamin B9, B12 and was significant with B9	Serum B9 level is positively contributed to handgrip and limb muscle strength.	5/14
(32)	NM van Schoor	2012	Cohort study, Netherlands	1352 elderly aged 65 years and above	Physical health	Compared physical health with HCY, vitamin B12 and was significant with HCY	Elevated HCY is associated with lower physical performance were as there was no association between B12 and physical performance	6/14
Role of B Vitamin on cognitive function								
(34)	L. Nalder	2020	Cross-sectional study, London	1347 community-dwelling men and women aged 60-85 years	Cognitive performance	Compared cognitive function with vitamin B9, B12, HCY, MMA was significant with B12	They are more prone to vitamin B12 deficiency. A correlation seen between vitamin B12 status and deficit in attention/memory.	5/14
(33)	Ozlem Sengul	2014	Cross-sectional study, Turkey	95 postmenopausal women, 45 to 59 years	Cognitive function (Depressive symptoms)	Compared Depressive symptoms with Serum B9, B12	There was no correlation between depressive symptoms and vitamin B12 and vitamin B9 level.	5/14

Based on the findings of the six articles studied, they have included osteopenia, osteoporosis, inflammation, vertebra fractures, wrist fractures, hip fractures, and BMD to study bone health. Post-menopausal women aged 41 years and above usually are affected. The parameters used in these studies were associated mainly with HCY, folate, vitamin B12 and vitamin B9. A recent study from Morocco found that there is no association between B vitamin status and bone fractures (24), two studies from Morocco and Italy found that there is a positive relationship between B vitamin status and BMD (25,27,29). One study from Brazil found that no association between vitamin B12 and BMD (26), a study from Japan found that additively increases the effects of vitamin deficiency and are associated with bone fracture (28). Vitamin deficiency additively causes the risk of fractures and only B vitamin deficiency may not be the reason for osteoporotic fractures in post-menopausal women.

B vitamin status and its impact on physical health

Among the studies included in this systematic review, three were about B vitamins and its impact on physical health which included hypertension, physical performance, handgrip, and limb muscle strength. The parameters mainly used for these studies were HCY, folate and vitamin B12. Both decreased vitamin B12 and elevated HCY positively associated and linked with hypertension (30). According to Misora Ao *et al.* (31) the serum folate levels contribute to the handgrip and limb muscle strength. The elevated HCY levels are linked with the lower physical performance in post-menopausal women whereas vitamin B12 has no association (32).

Vitamin B status and its impact on cognitive function

Based on the role of B vitamin on cognitive function of postmenopausal women, Şengül *et al.*, and Nalder *et al.*, came to two different conclusions (33, 34). According to Sengul *et al.*, there is no major relationship between the menopausal period and depressive symptoms (33). There can be several factors affecting depression mainly the intake of nutrients can play a role. The parameters used for the study on cognitive function were folate, MMA, vitamin B12, and HCY. Alzheimer's disease (AD) and dementia are associated with increased levels of HCY, MMA, decreased levels of folic acid levels and vitamin B12 (35). Very less research is conducted on the area of cognitive function and B vitamin deficiency. Throwing more light on this area is required to help women to prevent this deficiency and assisting in leading a healthy life.

CONCLUSION

B vitamins play a great role in the well-being of an individual, deficiency of any of the B vitamin can impact on health, especially among postmenopausal

women. Most of the included studies found that there is no association between B vitamin status and bone health in postmenopausal period, additive effect of the vitamin may be the reason for bone loss among postmenopausal women. A very few evidence reports the association of B vitamin status with physical performance and cognitive function. Further research is needed in B vitamin status and cognitive function.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

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