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# A prospective study to access the Co-relation between osteoporosis and serum homocysteine level

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**Abstract**
**Introduction:** Osteoporosis is a major health problem which has devastating health consequences through its association with osteoporotic fractures. Prevention of osteoporosis by identifying the risk factors is a major challenge in the field of medical science. Elevated homocysteine level in blood can be a potential risk factor for the development of osteoporosis. We aim to study if a person with high circulating level of homocysteine has a decreased Bone Mineral Density (BMD), thus establishing an association between homocysteine and the risk of developing osteoporosis.
**Method:** Patients between the age group of 40-70 years attending BMD camps between July 2019 and December 2019 were included in the study. All of them underwent BMD test and blood samples were sent to the laboratory for estimation of serum homocysteine levels. The results were collected and analyzed to see if there was any association between serum homocysteine levels and osteoporosis.
**Results:** Out of the 58 males and 20 females with normal BMD, none had elevated serum homocysteine. 21 out of the 58 males and 47 out of the 82 females with osteopenia had elevated serum homocysteine. Of the 27 males with osteoporosis, 25 had elevated serum homocysteine while among the 125 females with osteoporosis, all 125 had elevated serum homocysteine levels.
**Conclusion:** From our study we concluded that people with high circulating level of homocysteine had a decreased Bone Mineral Density (BMD), thus establishing an association between homocysteine and the risk of developing osteoporosis.

**Keywords:** Homocysteine, osteoporosis, BMD, serum homocysteine levels

## Introduction
Osteoporosis is a major health problem characterized by low bone mineraldensity (BMD) and increased risk of fractures [1]. Osteoporotic fractures are associated with increased morbidity and mortality & cause substantial financial loss to the patients and their families [2, 3, 4].
Elevated levels of homocysteine in the blood is associated with an early onset of osteoporosis [5, 6]. An elevated plasma homocysteine level (>15 mmol/l) is prevalent in 30-50% population above 60 years [5, 6]. High homocysteine levels have been associated with an increased risk of fractures, although the factors that contribute to this fracture risk are not fully elucidated.
Homocysteine is an intermediary amino acid formed by the conversion of methionine to cysteine. Elevated serum homocysteine levels show clinical manifestations involving the eyes, blood vessels, nervous system and skeleton including the development of early osteoporotic fractures. Vitamin B12 and folic acid play an important role in homocysteine metabolism [7]. They are cofactors in homocysteine metabolism and their intake can help in reducing serum homocysteine levels [8, 9, 10].
We aim to study if a person with high circulating level of homocysteine has a decreased Bone Mineral Density (BMD), thus establishing an association between homocysteine and the risk of developing osteoporosis.

## Methods
The study population included patients between the age group of 40-70 years attending BMD camps organized by the department of Orthopaedics, PSG institute of medical science and research, coimbatore between July 2019 and December 2019. Both male and female patients were included in the study.

Patients with previous fractures and those on long term steroids were excluded from the study.All of them underwent BMD test by DEXA scan. Blood samples were collected and sent to the laboratory for estimation of serum homocysteine levels.

**The BMD values were interpreted as follows**
Normal: 1 to -1
Osteopenia: -1 to -2.5
Osteoporosis: Below -2.5
The normal serum homocysteine level: 15 mmol/L
The results of both BMD scan and serum homocysteine levels were collected and analyzed to see if there was
any association between serum homocysteine levels and osteoporosis.

## Results

During the study period of 6 months, 370 patients attending the BMD camps fell into our inclusion criteria and wereincluded in our study. Of them 143 were males and 227 were females (Table 1).

**Table 1:** Age Distribution

| Age group (years) | Males | Females |
|---|---|---|
| 40 – 50 | 43 | 61 |
| 51 – 60 | 73 | 112 |
| 61 – 70 | 27 | 54 |
| Total | 143 | 227 |

The average BMD in the age group of 40-50 years was -0.72 in males and -1.6 in females. In the 51-60 years age group it was -1.47 in males and -2.53 in females. The average in 61-70 years age group was -2.61 in males and -3.4 in females (Table 2).

**Table 2:** Average BMD levels

| Age group (years) | Males | Females |
|---|---|---|
| 40 – 50 | -0.72 | -1.6 |
| 51 – 60 | -1.47 | -2.53 |
| 61 – 70 | -2.61 | -3.4 |

In the patients with normal BMD the average serum homocysteine level was 5.4 mmol/L in males and 7.2 mmol/L in females. Osteopenic individuals showed an average serum homocysteine level of 14.1 mmol/L in males and 16.2 mmol/L in females. Those with osteoporosis showed average serum homocysteine level of 38.7 mmol/L in males and 46.1 mmol/L in females (Table 3).

**Table 3:** Average serum homocysteine levels

| BMD | Males (mmol/L) | Females (mmol/L) |
|---|---|---|
| Normal | 5.4 | 7.2 |
| Osteopenia | 14.1 | 16.2 |
| Osteoporosis | 38.7 | 46.1 |

Of the 43 males in the 40-50 years age group, 7 were osteopenic and the rest had normal BMD, while among the 61 females in the same age group, 35 were osteopenic and 6 were osteoporotic. Among the 73 males in the 51-60 years age group, 46 were osteopenic and 5 were osteoporotic, while among the 112 females in the same age group, 47 were osteopenic and 65 were osteoporotic. Out of the 27 males in the 61-70 years age group, 5 were osteopenic and 22 were osteoporotic, while among the 54 females in the same age group all 54 were found to have osteoporosis (Table 4).

**Table 4:** Age and sex wise distribution of BMD results.

| | 40 – 50 years | | 51-60 years | | 61-70 years | |
|---|---|---|---|---|---|---|
| **BMD** | **Male** | **Female** | **Male** | **Female** | **Male** | **Female** |
| Normal | 36 | 20 | 22 | Nil | Nil | Nil |
| Osteopenia | 7 | 35 | 46 | 47 | 5 | Nil |
| Osteoporosis | Nil | 6 | 5 | 65 | 22 | 54 |
| Total | 43 | 61 | 73 | 112 | 27 | 54 |

Out of the 58 males and 20 females with normal BMD, none had elevated serum homocysteine. 21 out of the 58 males and 47 out of the 82 females with osteopenia had elevated serum homocysteine. Of the 27 males with osteoporosis, 25 had elevated serum homocysteine while among the 125 females with osteoporosis, all 125 had elevated serum homocysteine levels (Table 5).

**Table 5:** Relation between BMD and elevated serum homocysteine.

| | Male | | Female | |
|---|---|---|---|---|
| **BMD** | **BMD** | **S. Homocysteine elevated** | **BMD** | **S. Homocysteine Elevated** |
| Normal | 58 | Nil | 20 | Nil |
| Osteopenia | 58 | 21 | 82 | 47 |
| Osteoporosis | 27 | 25 | 125 | 125 |
| Total | 143 | 46 | 227 | 172 |

## Discussion

Osteoporosis is a metabolic bone disease. It is the leading cause of fractures with advancing age leading to pain, hospitalization and increased financial burden to the patient and his family. Even though it is considered as a normalageing process, osteoporosis can be prevented and treated if detected early. Elevated serum homocysteine level or hyperhomocysteinemia is considered to be one of the possible modifiable risk factors of osteoporosis.
Homocysteine is a sulfur containing amino acid that is formed by methionine metabolism. It is metabolized in the body by remethylation or trans-sulfuration pathway (Fig.1).
The normal serum homocysteine level is considered to be below 15mmol/L. A raised serum homocysteine level can bedue to multiple factors – lifestyle, diet, hormonal [11]. Hyperhomocysteinemia is considered to be a potential risk factorfor the development of osteoporosis [12, 13]. Vitamin B12 acts as a co-factor in the remethylation of homocysteine to methylene [14]. Hence vitamin B12 deficiency can lead to elevated serum homocysteine levels.
A study done by van Meurs *et al.* concluded that elevated serum homocysteine levels lead to a 2 fold increase in the incidence of fractures [15]. Another study by Bucciarelli *et al.* showed inverse association of serum homocysteine and BMD in post- menopausal women [16]. Tyagi *et al.* concluded that hyperhomocysteinemia can lead to reduced blood flowin the bones compromising bone quality [17]. A study done by Enneman *et al.* in 2014 showed that elevated serum homocysteine was associated with a decreased BMD [18].
Similarly in our study we found an inverse correlation between serum homocysteine levels and BMD. Out of the 58 malesand 20 females with normal BMD, none had elevated serum homocysteine. 36% males (21 out of 58) and 57% females (47 out of 82) with osteopenia had elevated serum homocysteine levels. However when it came to people with osteoporosis on BMD, 93% males (25 out of 27) and 100% of females (125 out of 125) had elevated serum homocysteine levels. The average serum homocysteine levels in osteoporotic individuals were 38.7 mmol/L in males and46.1 mmol/L in females. Hence we see a definite relation between elevated serum homocysteine level and osteoporosis

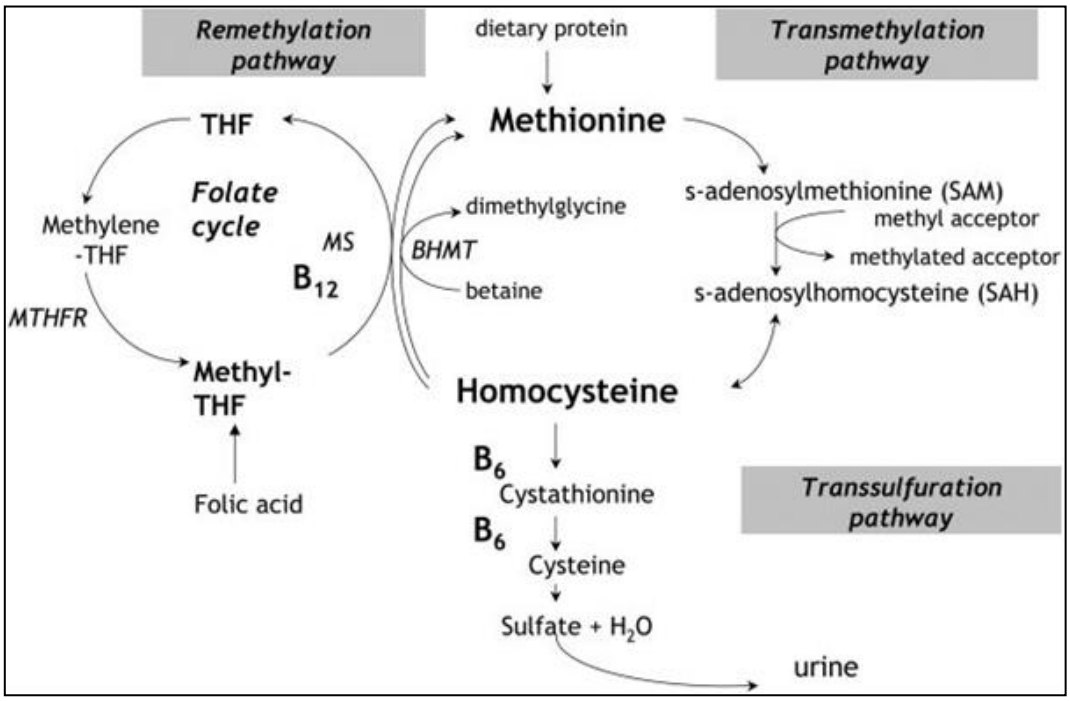


**Fig 1:** Homocysteine metabolism pathway

## Conclusion

Osteoporosis is a major health problem which has devastating health consequences through its associationwith osteoporotic fractures. Prevention of osteoporosis by identifying the risk factors is a major challenge in the field of medicine. Bone metabolism is affected by homocysteine. Elevated homocysteine level in blood isa potential risk factor for the development of osteoporosis.

From our study we concluded that people with high circulating level of homocysteine had a decreased Bone Mineral Density (BMD), thus establishing an association between homocysteine and the risk of developing osteoporosis. Vitamin B12 and folic acid play an important role in homocysteine metabolism [7].

Supplementation with vitamin B12 and folic acid has been shown to normalize plasma homocysteine levels. This could reverse the problem of impaired bone health
and osteoporosis and help in preventing osteoporotic

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