(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume3, Issue 6, Page No: 693-700
November-December 2020

To Study Association between Vit D Deficiency and Mastalgia among Patients Visiting Outpatient Department: A Prospective Study

Dr Natasha Thakur, Dr Mohd Yousuf Dar, Dr Sajad Hussain Bhat
Department of genaral and minimal invasive surgery SKIMS soura soura srinagar J&K india
Department of hospital administration SKIMS soura srinagar J&K india

***Corresponding Author:**
Dr Sajad Hussain Bhat
Department of hospital administration SKIMS soura soura srinagar J&K india

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

ABSTRACT

Mastalgia is a very common complaint among young females and it is a frequent problem among patients visiting OPD.

Aim: The aim of this study was to investigate if vitamin D deficiency has any link to breast pain and whether supplementation can deliver symptomatic improvement.

Methods: A prospective study was conducted in department of general and minimal access surgery at sher -i-kashmir institute of medical science Soura, Jammu and Kashmir. All participants were recruited from the out patient department. Patients who had presented with breast pain had a full history and clinical examination. Imaging and other clinical investigations were performed to exclude other potential causes of breast pain. Vit D levels were measured before and after supplementation and impact of vit D supplementation on mastalgia was noted.

Results: A total of 100 patients participated in our study. All participants were female, mean age at recruitment was 33 years (±8.89). In case of cyclical mastalgia there was improvement in mastalgia by supplementation of vitamin D but it was not statistically significant($p>.05$). While in case of acyclical mastalgia there was improvement in symptoms which is statistically significant($p<0.05$).

Conclusion: Vit D supplementation has a significant role on improvement in acyclical mastalgia.

Keywords: Mastalgia, vitamin D

INTRODUCTION

Mastalgia is a very frequent symptom in the female population and can be a source of anxiety due to fear of cancer among women and in severe cases, it may even affect quality of life or disturb partnership[1,2]. Mastalgia can be classified as true mastalgia or referred , mostly from the chest wall. True mastalgia can be cyclic and exacerbate with menstrual cycles, or be non-cyclic and constant. Etiology of mastalgia is uncertain; various factors such as hormonal or dietary issues have been implicated [3,4]. Because of the unknown origin of mastalgia treatment guidelines are not clearly defined. Various therapies have been suggested from old times till now, from reassurance to oral nonsteroidal analgesics, to hormone therapy. Among vitamins, vitamins A, B6 and E have been prescribed for true mastalgia; the latter is widely used and is still recommended in treatment of this disorder.[5,6,7] vitamin D has been shown to play an important role in the development and function of the mammary gland. Little is known about the effects of vitamin D deficiency on non-cyclical breast pain and how supplementation could potentially improve symptoms. Our study aims to determine the correlation between deficiency of vitamin D and

mastalgia, and if its supplementation could give pain relief.

Objective: The aim of this study was to investigate if vitamin D deficiency has any link to breast pain and whether supplementation can deliver symptomatic improvement.

Materials and methods: This is a prospective observational study conducted in department of general and minimal access surgery at sher -i-kashmir institute of medical science soura, jammu and kashmir for a period of one year from 1st jan 2018 to 31st aug 2018. All participants were recruited from the out patients department. Patients who had presented with breast pain had a full history and clinical examination. Imaging and other clinical investigations were performed to exclude other potential causes of breast pain. Patients over 18 years old with breast pain were approached, provided information and a blood test to investigate vitamin D levels was performed. The cut off selected for defining deficiency was a serum level of vitamin D 25(OH) <50 nmol/L. [8]. Blood samples were tested via a biochemical assay. All patients with low vitamin D were sent an information sheet detailing our findings and recommendations for vitamin D supplementation. A follow up questionnaire was then sent to those who had low vitamin D blood levels 2 months following the initial appointment in order to follow uptake of recommended treatment and clinical response. The questionnaire asked the patient to rate the improvement, if any, in pain (Pain Score 1-10). The responses were categorized as Poor (pain score >5), Average (pain score 4-5), Good (pain score 2–3) and Excellent (pain score =1). We classified the groups into those who experienced symptomatic improvement (pain score ≤ 5), and those who did not have symptomatic improvement (pain score >5. All analysis was performed using SPSS version 16.0.

Results: A total of 100 patients participated in our study. All participants were female, mean age at recruitment was 33 years (±8.89) (table 1, 2) . 68% females were married and 32 %females were unmarried.

Table 1: Age of patients

Number	Minimum	Maximum	Mean	Std deviation
100	17	60	33	8.891

Table 2: Gender of staff

Number	Female	Male
100	100	0

Most females had unilateral (67%) while as (33%) had bilateral breast pain (Table 3) .

Table 3: Unilateral vs bilateral breast pain

Unilateral	Bilateral	Total
67	33	100

Only 31% of patients had cyclical mastalgia whereas 69% of females had non cyclical mastalgia . Baseline serum vitamin D level at recruitment was 27.17 nmol/L (±20.2) while as Serum vitamin D levels after vitamin D supplimentation was 68.99((±18.615)(table 4).

Volume 3, Issue 6; November-December 2020; Page No 693-700

Table 4: Vit D Levels Before and After Supplementation

	Mean	Number	Std deviation	Std error mean
Vitamin level before medication	27.17	100	20.205	2.021
Vitamin level after medication	68.99	100	18.615	1.862

In case of cyclical mastalgia there was improvement in mastalgia by supplimentation of vitamin D but it was not statistically significant(p>.05). While in case of acyclical mastalgia there was improvement in symptoms which was statistically significant(p<0.05).

DISCUSSION: Mastalgia is one of the most common breast disorders experienced by women. Although increased awareness and overestimation of breast cancer risk [10] may prompt more women to seek medical attention for breast symptoms, mastalgia generally is underreported. In a survey of working women in South Wales, 45% described mild breast pain, and 21% described severe breast pain, but fewer than half of the women with severe pain had reported this symptom to a physician.[9] The evaluation of breast pain varies according to its assignment within the 3 broad classifications of cyclic mastalgia, noncyclic mastalgia, and extramammary (nonbreast) pain.[5,9,10-16] Cyclic mastalgia, by definition, occurs in premenopausal women and connotes breast pain that is clearly related to the menstrual cycle. Noncyclic mastalgia is defined as constant or intermittent breast pain that is not associated with the menstrual cycle. Extramammary pain from various sources may present with symptoms of breast pain. Cyclic mastalgia accounts for approximately two thirds of breast pain in specialty clinics, whereas noncyclic mastalgia accounts for the remaining one third[.17] The distinctions are important because the evaluation and the likelihood of response to intervention vary among the different types of breast pain.[14,18] Mastalgia is a common and enigmatic condition; the cause and optimal treatment are still inadequately defined. Mastalgia may be severe enough to interfere with usual daily activities, and its effect on quality of life often is underestimated[19] Outcome can be successful in most patients with reassurance, nonpharmacological measures, and in some instances, one of several effective medications. [10,13,18]-

In Cyclic Mastalgia minor breast discomfort and swelling within the few days before onset of menses is considered a normal physiological occurrence. In order of decreasing frequency, premenstrual breast symptoms reported by women are tenderness, swelling, pain, and lumpiness.9 Women who experience more severe and prolonged pain are considered to have cyclic mastalgia. Research criteria for the diagnosis of cyclic mastalgia are (1) pain severity greater than 4.0 cm measured on a 10.0-cm visual analog scale and (2) pain duration of at least 7 days per month.[19] This information is most accurate when obtained from a patient's prospective breast pain record[.18,20] Applying this threshold in a clinic-based study in the United States, approximately 11% of premenopausal women could be diagnosed as having cyclic mastalgia. However, an additional 9% of premenopausal women experienced breast pain of severity greater than 4.0 cm on the visual analog scale for 5 to 6 days per month.[19] Cyclic breast pain usually starts during the luteal phase of the menstrual cycle and increases in intensity until onset of menses, when it dissipates. Some pain may be present to a lesser degree during the entire cycle with premenstrual intensification of symptoms. The pain typically involves the upper outer breast area and radiates to the upper arm and axilla. Most cyclic mastalgia is diffuse and bilateral but may be more severe in one breast. Patients often describe the pain as "dull," "heavy," or "aching." The consequences of cyclic mastalgia are not trivial. Cyclic mastalgia typically presents during the third or fourth decade of life.[17] The symptoms tend to

Volume 3, Issue 6; November-December 2020; Page No 693-700

persist with a relapsing course. Remission often occurs with hormonal events such as pregnancy or menopause. Only 14% of women with cyclic mastalgia experience spontaneous resolution; however, 42% experience resolution at menopause.[16]

Noncyclic mastalgia involves constant or intermittent pain that is not associated with the menstrual cycle. Less common than cyclic mastalgia, it accounts for approximately 31% of women seen in mastalgia clinics.[21] but in our study most of females have noncyclical mastalgia69% .Noncyclic mastalgia tends to be unilateral and localized within a quadrant of the breast; however, diffusely distributed pain and radiation to the axilla also occur.[5] Typically, noncyclic mastalgia presents at a later age; most women are in the fourth or fifth decade of life at diagnosis[.5,10,13,17] Many women are postmenopausal at onset of symptoms.

Noncyclic breast pain may result from pregnancy, mastitis, trauma, thrombophlebitis, macrocysts, benign tumors, or cancer; however, only a minority of breast pain is explained by these conditions. Most noncyclic breast pain arises for unknown reasons, yet it is believed more likely to have an anatomical, rather than hormonal, cause. An exception may be breast pain that is associated with medication use . Approximately 16% and 32% of women report breast pain as an adverse effect of estrogen and combined hormonal therapies, respectively.[21] Unilateral, noncyclic breast pain may result from exogenous estrogen exposure. Extramammary pain due to various conditions may present as breast pain. The differential diagnosis for mastalgia is extensive (Table 4); however, the causes most commonly encountered in the evaluation of breast pain are costochondritis and other chest wall syndromes[9,10,22]. Distinguishing between pain localized to the breast or chest wall or radiating from elsewhere is usually straightforward, although diagnosis of patients with inconsistent findings or more than 1 source of pain is more challenging. Chest wall syndromes comprise a group of conditions causing musculoskeletal chest pain, including costochondritis, Tietze syndrome, slipping and clicking ribs, and arthritis, which may be nontraumatic and insidious at onset[23-26]. The absence of a clear precipitating event increases the patient's concern regarding a sinister or malignant cause.89 Breast pain prompts many women to seek medical attention because of concerns about cancer[10,20,28,29,30-32] .The risk of subsequent occult malignancy after normal findings on clinical and mammographic evaluation for breast pain is estimated to be only 0.5%, making reassurance in this setting appropriate.[13,33,34] In clinical practice, 78% to 85% of symptomatic women are reassured after normal findings on evaluation and do not want specific intervention to alleviate the breast pain.[13.32]. Approximately 10% to 22% experience more severe pain and elect treatment to improve or relieve symptoms.[9,11,14,20,30]. There is overlap between the initial therapeutic approaches for patients with cyclic and noncyclic mastalgia; however, response to intervention varies[.32] Hormonally active medications are more effective for patients with cyclic mastalgia and are indicated only for patients with severe, prolonged symptoms.[9,10,11,13,16]. Numerous difficulties arise when reviewing the effectiveness of therapies for breast pain because the pain is subjective, cyclic, or fluctuating in severity and is occasionally self limited. These characteristics make assessment of response to an intervention challenging. , the definition of a therapeutic response differs between studies, and there is a placebo effect of at least 20% (range, 10%-40%)[9].

Vitamins.—Several vitamins have been evaluated as potential treatments for breast pain, including vitamins B1,B6, and E.[35-38] Of these, vitamin E is used most commonly for breast pain. Early studies with small numbers of patients suggested a potential beneficial effect of vitamin E (α-tocopherol) in fibrocystic breast disease.[38] Proposed mechanisms include its potential to alter steroidal hormone production (dehydroepiandrosterone or progesterone), to correct abnormal serum cholesterol–lipoprotein distribution, and to function as an antioxidant.132-136 Subsequently, a few small randomized, double-blind, placebo-controlled studies have shown no differences in breast pain using dosages of 150 to 600 IU of vitamin E per day.134,135 Additionally, mean serum concentrations of estradiol, progesterone, testosterone, and dehydroepiandrosterone did not differ between vitamin E- and placebo treated women.136 Many practitioners continue to recommend vitamin E for breast pain, although

Volume 3, Issue 6; November-December 2020; Page No 693-700

uncertain of whether the relatively low doses and short duration of treatment in these trials exclude a beneficial effect. Small studies of vitamins B1 and B6 showed no benefit compared with placebo for the treatment of cyclic breast pain.[36,37] At this time, evidence is insufficient to support routine use of vitamins for breast pain.[35,39]

Vitamin D has a significant role in bone, joint and muscle metabolism [40], is critical to calcium and phosphorus homeostasis and has been implicated in cancer, metabolic syndromes, heart failure, infection and immune disorders [41-44]. There are two main sources of non-prescriptive vitamin D: Diet and sun exposure. For dermal synthesis of vitamin D to occur exposure to ultraviolet B radiation is necessary. Other factors such as diet, occlusive clothing, age and pregnancy can also compound this risk Several mechanisms have been proposed for developing musculoskeletal pain in vitamin D deficient states. One proposed explanation is an interruption of calcium deposition in collagen matrices of bone, which results in malformation of pathologically soft bone that continues to expand and exerts pressure on periosteal surfaces and subsequently on sensory pain receptors [45]. Other mechanisms that have been suggested include a reduction in nerve conduction velocity resulting in muscular atrophy and myopathy [46,47] and hyperparathyroidism by way of proteolysis of muscle leading to fatigue and muscle, bony and joint pain, however the mechanism for vitamin D deficiency in non-cyclical breast pain is unclear. Recent studies have shown that vitamin D receptors are available in almost all cells [48] and current theories around the pathogenesis of this heightened pain response implicates an exaggerated immune possibly as a reaction to infection and sensitisation of pain signalling pathways [49,50-52]. This would reflect how vitamin D deficiency is linked to a number of multi-organ disease states and could be the underlying mechanism by which vitamin D deficiency results in breast tissue tenderness... The lowest serum level of vitamin D 25(OH) necessary for promotion of optimal bone health is considered to be approximately 12-30 nmol/L, as this is the level required to prevent increases in parathyroid hormone (4). However, this standard may be insufficient to achieve improvement in pain and may not represent the therapeutic threshold we should be targeting treatment. Our results show that that those with a severe vitamin D deficiency (<15 nmol/L) have the most demonstrable improvement in pain from high dose vitamin d supplementation but improvement came after few months when compared with those with mild deficiency (<35-50 nmol/L), suggesting that low dose supplementation is not enough to elevate vitamin D levels sufficiently to yield therapeutic results in those with severe deficiency and high dose supplementation is recommended for them. This reflects the findings of a systematic review study looking into the optimum target vitamin D levels for multiple end points, including reduced myopathy. Bischoff found that a post treatment serum level of at least 30 nmol/L produces the most detectable adventitious outcomes and demonstrates continuing improvement with higher concentrations, though not as pronounced [53]. This is also in line with several other studies that have noted a threshold of demarcation whereby improvement in musculoskeletal pain was achieved with serum vitamin D level of 30-66 ng/ml (75-165 nmol/L) [5-8], and conversely, post-treatment serum vitamin D levels of <30 ng/ml (75 nmol/L) did not achieve a significant improvement in musculoskeletal pain. However the serum vitamin D targets suggested by these studies are considerably higher than what was found in our study. One possible explanation is that all of these studies were conducted on patients undergoing AI treatment for breast cancer. These patients are at higher risk of vitamin D deficiency due to reduced oestrogen levels and subsequent diminished joint vitamin D receptors, which leads to development of myopathy and joint pain, and increased metabolic requirements as vitamin D plays a crucial role in the detoxification of aromatase inhibitors by the liver [54]. Therefore, a therapeutic threshold can still be observed, but is likely to be observed at much higher level. In light of this, perhaps we should not only be supplementing simply to improve serum vitamin D, but calibrating our treatment towards achieving a therapeutic threshold and clinical reduction in pain. we suggest that for non cyclical mastalgia vitamin d is an add on to hormonal therapy while in noncyclical mastalgia vitamin d supplementation should be considered as primary modality of treatment. our is one of pioneering studies with small sample size we suggest more studies with large sample size should be considerd and accordindly results interpretted.

Volume 3, Issue 6; November-December 2020; Page No 693-700

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Volume 3, Issue 6; November-December 2020; Page No 693-700

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Volume 3, Issue 6; November-December 2020; Page No 693-700

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Volume 3, Issue 6; November-December 2020; Page No 693-700