

Differences of N-Mid Osteocalcin and Magnesium Levels in Severe and Not Severe Osteoarthritis

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Abstract: Background: Osteoarthritis (OA) is a degenerative joint disease, characterized by erosion of articular cartilage. OA is the most common form of arthritis and a major cause of pain and disability. Recently, the potential use of biomarkers for the diagnosis and monitoring of osteoarthritis has been widely used. Various biomarkers, such as C- or N-propeptide of type II procollagen; N-propeptide from type I and type III collagen; collagen type II neoepitope; C-telopeptide from type I and type II (CTX-II) collagen; Matrix metalloproteinases, C-reactive protein, N-MID Osteocalcin and magnesium have previously been explored for use in the diagnosis of OA. Methods: This research is an observational study with cross sectional data collection method. This study took blood samples from patients with severe OA and non-severe OA who came to the Orthopedic Surgery and Traumatology Polyclinic as many as 35 patients. Samples were checked only once for N-MID Osteocalcin and Magnesium. The research was conducted after obtaining ethical approval and informed consent. Result and Discussion: There were 30 female subjects (85.7%). The mean age of the subjects was 64.17 years with the youngest age being 48 years and the oldest being 80 years. Using the Independent T test showed that there was no significant difference in magnesium levels based on the severity of osteoarthritis ($p = 0.226$). Using the Independent T test showed that there was no significant difference in N-Mid Osteocalcin levels based on the severity of osteoarthritis ($p = 0.212$). Conclusions and suggestions: There was no significant difference in the levels of N-Mid Osteocalcin and Magnesium based on the severity of osteoarthritis. Further research is needed to involve subjects with more varied characteristics in osteoarthritis patients.

Keywords: Osteoarthritis, N-Mid Osteocalcin, Magnesium.

1. Introduction

Osteoarthritis (OA) is a degenerative joint disease, which occurs mainly in the elderly and is characterized by erosion of the articular cartilage, hypertrophy of the bone at the margins (osteophytes), subchondral sclerosis, and biochemical and morphological changes of the synovial membrane and joint capsule. Risk factors for OA include genetics, female gender, trauma, advanced age, and obesity. The incidence of hand, hip and knee OA increases with age, and women have a higher susceptibility than men, especially those aged 50 years and over. Knee OA is the most common site of OA.¹

Because there are limitations to the use of radiography, recently, the potential use of biomarkers for the diagnosis and monitoring of osteoarthritis has been widely used. Various biomarkers, such as C- or N-propeptide of type II procollagen; N-propeptide from type I and type III collagen; collagen type II neoepitopes; C-telopeptide from type I and type II (CTX-II) collagen; matrix metalloproteinase, C-reactive protein, magnesium and N-MID Osteocalcin, have previously been explored for their use in the diagnosis of OA.¹

N-MID Osteocalcin is the largest non-collagenous protein of bone. Osteocalcin has a high affinity for calcium and exhibits a γ -carboxyglutamic acid (Gla) \square calcium dependent alpha helical conformation, in which the residue binds and enhances the uptake of hydroxyapatite in the bone matrix, in this way bone mineralization occurs. OC, a bone-specific protein synthesized by osteoblasts in bone.²

Magnesium is one of the six essential minerals contained in the human body. Magnesium helps build bones. This substance contributes to the development of bone structure and Magnesium is involved in bone formation and affects the activity of osteoblasts and osteoclasts. Magnesium also affects the concentrations of both parathyroid hormone and the active form of vitamin D, which is a major regulator of bone homeostasis.³

2. Research Purposes

This study aims to analyze the differences in the levels of N-MID Osteocalcin and magnesium in patients with severe and non-severe OA.

3. Research Methods

This research is an observational study with cross-sectional data collection method. This research was conducted at the Department of Clinical Pathology, USU Medical Faculty/H. Adam Malik Hospital, Medan in collaboration with the Department of Orthopedic Surgery and Traumatology, USU Medical Faculty/H. Adam Malik Hospital and Setia Budi Hospital Medan in the selection of osteoarthritis patients starting from August 2021 until February 2022. The study sample was patients with severe osteoarthritis who had been diagnosed by the Department of Orthopedic Surgery and Traumatology at H. Adam Malik Hospital Medan and Setia Budi Hospital Medan.

The inclusion criteria in this study were patients with

osteoarthritis who had been diagnosed according to the American College of Rheumatology (ACR) Criteria for Classification of OA. All patients who have been diagnosed with primary OA. Willing to participate in the study. The exclusion criteria in this study was Rheumatoid Arthritis. Gout Arthritis, Osteoporosis and Patients receiving magnesium supplements

The N-MID examination of Osteocalcin and magnesium was carried out at the Department of Clinical Pathology, USU Medical Faculty / H. Adam Malik Hospital, Medan using the Cobas e 411 automatic analyzer with the Elisa method and Architect with the enzymatic method.

4. Statistical Analysis

Data analysis was performed using SPSS (Statistical Package for Social Sciences, Chicago, IL, USA) software for Windows. The description of the characteristics of the research subjects is presented in tabulated form and described. Differences in N-MID levels of Osteocalcin and magnesium in patients with severe OA using the T test if the data are normally distributed. If the data is not normally distributed, the Mann Whitney test is used. All statistical tests with p value < 0.05 were considered significant.

5. Result

This study was followed by 35 patients with osteoarthritis who went to the Polyclinic of the Department of Orthopedic Surgery and Traumatology H. Adam Malik Hospital Medan and the Polyclinic of Orthopedic Surgery and Traumatology Setia Budi Hospital Medan. All patients included in this study met the inclusion criteria. There were 30 female subjects (85.7%). The mean age of the subjects was 64.17 years with the youngest age being 48 years and the oldest being 80 years. The average BMI of the subjects was 27.36 kg/cm². Based on the categorization of BMI values, there were 26 people (74.3%) including obesity. A total of 19 subjects (54.3%) were housewives. The largest ethnic group is the Batak tribe with 22 people (62.9%). All subjects had complaints of knee pain. The most history of disease was hypertension, amounting to 18 people (51.4%). Of the 30 female subjects, almost entirely as many as 28 people (93.3%) had experienced menopause. Based on the calculation of the score shows as many as 22 people (62.9%) with a severe degree of severity.

Table 1: Characteristics of Research Subjects

Characteristics of Research Subjects	n = 35
SEX, n (%)	
Male	5 (14,3)
Female	30 (85,7)
AGE, YEARS	
Mean (SD)	64,17 (8,21)
Median (Min – Max)	64 (48 – 80)
Body Mass Index, kg/cm ²	
Mean (SD)	27,36 (3,201)
Median (Min – Max)	27,88 (21,33 – 33,24)
Nutrition Status, n (%)	

Normal	3 (8,6)
Overweight	6 (17,1)
Obesitas	26 (74,3)
Menopause, n (%)	
No	2 (6,7)
Yes	28 (93,3)
Pekerjaan, n (%)	
Government employees	3 (8,6)
Trader	7 (20)
Farmer	6 (17,1)
House wife	19 (54,3)
ethnic, n (%)	
Batak	22 (62,9)
Chinese	4 (11,4)
Jawa	9 (25,7)
Comorbid, n (%)	
DM	3 (8,6)
Hipertensi	18 (51,4)
Hiperkolesterolemia	1 (2,9)
No	13 (37,1)
Severity, n (%)	
Mild	13 (37,1)
Severe	22 (62,9)

Table 2 shows magnesium levels in patients with osteoarthritis based on the severity of osteoarthritis. Magnesium levels based on the severity of osteoarthritis did not appear much different. In osteoarthritis patients with moderate severity, the mean magnesium was 2.05 mg/dL (SD ± 0.3 mg/dL) and in severe grades the mean was 1.93 mg/dL (SD ± 0.17 mg/dL). Using the Independent T test showed that there was no significant difference in magnesium levels based on the severity of osteoarthritis (p = 0.226).

Table 2: Differences in Magnesium Levels by Severity of Osteoarthritis

Severity Levels	n	Magnesium, mg/dL		p*
		Mean (SD)	Median (min-Max)	
Mild		2,05 (0,3)	2,02 (1,56-2,6)	0,226
Severe		1,93 (0,17)	1,92 (1,65-2,23)	

*T Independent

Table 3 shows the levels of N-Mid Osteocalcin in patients with osteoarthritis based on the severity of osteoarthritis. Osteoarthritis patients with moderate severity showed an N-Mid Osteocalcin average of 22.33 ng/mL (SD ± 6.29 ng/mL) and in severe grades it was 26.48 ng/mL (SD ± 12.97 ng/mL). Using the Independent T test showed that there was no significant difference in N-Mid Osteocalcin levels based on the severity of osteoarthritis (p = 0.212).

Table 3: Differences in N-Mid Osteocalcin Levels based on the Severity of Osteoarthritis

Severity Levels	n	N-Mid Osteocalcin, ng/mL		p*
		Mean (SD)	Median (Min-Max)	
Mild		22,33 (6,29)	23,8 (13,86-34,09)	0,212
Severe		26,48 (12,97)	25,01 (10,1-55,17)	

*T Independent

6. Discussion

Our study was followed by 35 people. There were 30 female subjects (85.7%). The mean age of the subjects was 64.17 years with the youngest age being 48 years and the oldest being 80 years. The average BMI of the subjects was 27.36 kg/cm². Based on the categorization of BMI values, there were 26 people (74.3%) including obesity.

Study results from research conducted by Tschon et al 2021. Researchers studied the relationship between age, gender, BMI, physical activity and history of trauma with quality of life in clinically diagnosed osteoarthritis patients at the Orthopedic and Traumatology Outpatient Clinic between January 2015 to December 2016. Methods: This study is a hospital-based cross-sectional study. analytical studies. The research sample was Osteoarthritis patients who were clinically diagnosed at the Orthopedic and Traumatology Outpatient Polyclinic in a US hospital from January 2015 to December 2016. Results: There were 43 patients who could be reached at the Orthopedic and Traumatology Outpatient Clinic between January 2015 to December 2016. The mean age is 54.35 ± 5.32 years and the sex of the most subjects is female (72.1%). The mean BMI of the subjects was 26.20 ± 3.75 and most of them were overweight (60.5%). Most of the subjects never had a history of trauma (76.7%) and also had inactive physical activity (65.1%).⁴

The next factor that can cause knee OA is excessive body weight or obesity which is also related to the incidence of osteoarthritis, this happens because of life style that the age factor cannot determine a person will experience a normal body mass index (BMI), fat, and obese. Many factors affect body mass index (BMI) including dietary factors, smoking habits, and daily activities. Although at a young age, he has a poor diet such as frequently consuming fatty foods, junk food, and having daily activities whose duration is less than 60 minutes, he rarely does other activities. So it can happen that a person has an excessive body mass index (BMI) due to his poor lifestyle which causes obesity, will increase the load received by the surface of the bone joints, especially the joints that function as body supports such as the knee and hip joints so that in ultimately can cause mechanical or biological damage to joint cartilage, which results in the formation of inflammatory cascades as well as enzymatic destruction.⁵

The largest distribution of knee OA patients based on research is the female gender. Women have a greater risk of suffering from knee OA, especially in women over 50 years of age. This happens due to hormones in women who have menopause, which causes the hormone estrogen to drop which causes a decrease in bone and joint density. Other risk factors, such as mechanical factors such as joint injury.⁵

Menopause can be interpreted as a physiological condition of women who have entered a period of aging which is characterized by decreased levels of the ovarian estrogen hormone which plays a very important role in sexual reproduction, often interferes with women's activities and even threatens domestic happiness. A decrease in estrogen can

cause osteoarthritis and osteoporosis because a decrease in estrogen causes a decrease in the collagen matrix so that cartilage becomes damaged and causes pain. Decreased estrogen hormone can cause damage to the collagen matrix and cartilage itself is damaged so that it can cause osteoarthritis which causes joint pain complaints. Joint pain that occurs affects postmenopausal women to carry out activities of daily living.⁶

Hypertension is also closely related to OA. OA patients with hypertension are often found with obesity and metabolic syndrome. Obesity causes mechanical stress and produces adipokine pro-inflammatory compounds that affect chondrocytes, synoviocytes, and cartilage causing oxidative stress. Fatty acids and excessive blood fat levels will stimulate chondrocytes and synoviocytes to produce pro-inflammatory compounds. Increased serum cholesterol also increases the incidence of OA. Hypertension causes atherosclerosis which can cause arterial occlusion and cause stasis of blood flow in the subchondral vessels, a subchondral ischemia occurs so that the exchange of nutrients and gases is disrupted into the articular cartilage which is a potential initiator of degradative changes in cartilage.⁷

The study was conducted by Kluzek et al in 2016. In this cohort study, a total of 120 cases of knee osteoarthritis patients, including gender or age > 40 years were enrolled. Cases were selected according to the diagnostic criteria of the American College of Rheumatology. For clinical severity, the VAS and the Lequesne Index were used. To assess the radiological severity of the disease, K-L grading was used and bilateral knee X-rays were performed to see the radiological changes of the disease. The results of the study showed: There is a significant correlation between hypertension and clinical severity of OA.⁸

Magnesium levels based on the severity of osteoarthritis did not appear much different. In osteoarthritis patients with moderate severity, the mean magnesium was 2.05 mg/dL (SD ± 0.3 mg/dL) and in severe grades the mean was 1.93 mg/dL (SD ± 0.17 mg/dL). Using the Independent T test showed that there was no significant difference in magnesium levels based on the severity of osteoarthritis ($p = 0.226$).

In line with the research conducted by Nicoletta et al., 2020. They conducted a cross-sectional study of 326 patients with knee OA and all study subjects were examined for magnesium and calculated the severity of OA using the Kellgren-Lawrence classification. The results of their study showed all knee OA patients with grade > 2 according to the Kellgren-Lawrence classification, with a mean magnesium 9.23 ± 0.395 . Using the Independent T test showed that there was no significant difference in magnesium levels based on the severity of osteoarthritis between study subjects and healthy control subjects. ($p = 0.339$).⁹

Osteoarthritis patients with moderate severity showed an N-Mid Osteocalcin average of 22.33 ng/mL (SD ± 6.29 ng/mL) and in severe grades it was 26.48 ng/mL (SD ± 12.97 ng/mL). Using the Independent T test showed that there was no

significant difference in N-Mid Osteocalcin levels based on the severity of osteoarthritis ($p = 0.212$).

In line with the research conducted by Nagy et al, 2020. They conducted a cross-sectional study of 69 patients with knee OA and all study subjects were examined for N-MID Osteocalcin and calculated the severity of OA using the Kellgren-Lawrence classification. The results of their study showed 38 knee OA patients with grade 2 and 31 knee OA patients with grades 3 and 4 according to the Kellgren-Lawrence classification, with the mean OC of 38 knee OA patients with grade 2 being 8.15 ± 4.71 . And 31 knee OA patients with grades 3 and 4 according to the Kellgren-Lawrence classification, with a mean OC of 8.92 ± 4.68 Using the Independent T test showed that there was no significant difference in magnesium levels based on the severity of osteoarthritis between study subjects and healthy control subjects ($p = 0.502$).¹⁰

7. Conclusion

From the characteristics of the subjects in patients with severe and non-severe OA, it was found that based on gender, female was more than male as much as 85.7%, based on age there was a mean age of 64 years, based on risk factors for the disease, hypertension was 51.4%. The average magnesium level in patients with severe OA is 1.93 mg/dL, and the average level of magnesium is 2.05 mg/dL. The average N-MID Osteocalcin level in patients with severe OA was 26.48 ng/mL and the average N-Mid Osteocalcin was 22.33 ng/mL. Using the Independent T test showed that there was no significant difference in magnesium levels based on the severity of osteoarthritis ($p = 0.226$). And by using the Independent T test showed that there was no difference in levels of Significant N-Mid Osteocalcin based on the severity of osteoarthritis ($p = 0.212$).

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