Prevalence of joint diseases in postmenopausal women

By

Hanan K. Alkadhim Babylon University,College of Medicine

Jameel T. Mehsen Babylon University,College of Medicine

Mohannad Ali Hasan Babylon University,College of Medicine

Abstract

Arthritis have become the most prevalent bone and joint disease in postmenopausal women all over the world. The present study aims to establish the relationship between hormonal changes that occur during and after menopause and the onset of bone degenerative diseases. The relationship betwen obesity and arthritis have also been established by analyzing the BMI of selected patients and type of arthritis present. The analysis of data from 150 postmenopausal women showed that osteoarthritis (OA) was the most common form of arthritis in postmenopausal women and affected around 38.6% of the samples, followed by rheumatoid arthritis (RA) which was found in 2% and gout was observed in 1.3% of women. In relation to obesity and joint diseases, it was found that 66.7% (1 out of 3 patients; P Value >0.05) and 12.1% (7 out of 21; P Value < 0.001) of RA and OA patients were obese and they have a BMI of greater than 25, respectively. The duration of menopausal event or the sex hormonal deficiency period showed a proportional and statistically significant relationship (P value < 0.001), with the prevalence of joint disease, with OA being the most prevalent, and was present in 67.5% of women who have post menopause duration of more than 10 years. The prevalence of RA and gout was not affected by the time period of menopause and BMI and showed statistically insignificant results (P value >0.05).

التعليق **[m1]:** The introduction is fine but too long. You need to shorten it to less than 1000 words

Introduction

Menopause is the physiological event that occurs in the female body and lead to the halting or ending of the process of menstruation, which had started at the time of puberty. This termination of menstruation cycle lead to the loss of development of ovarian follicle [1]. Women all over the world undergo this process and it has been proposed that the exact age of onset of menopause is genetically determined and is not affected by age at menarche (puberty), race, socioeconomic status, or number of ovulations cycles over the life time [2].

Menopause is linked with physiological and functional changes in the pituitary and hypothalamic hormones that play important role in the menstrual cycle regulation, but primarily menopause is a failure of ovarian function. As there is a complete loss of ovarian follicles, the ovary becomes unbale to respond to various pituitary hormones, including follicle-stimulating hormone (FSH) and luteinizing hormone (LH). This ultimately leads to the termination of production of sex

hormones in the ovary, including estrogen and progesterone [3]. Among the various hormones that are produced by during normal ovarian function, estrogen has been characterized as the vital hormone for the regulation of bone and joints health [4].

An interesting relationship exists between estrogen hormone and bone metabolism in the body. It has been found that estrogen plays a crucial role in the growth and maturation of bone. It also regulates the rate of bone turnover in adult bones. In men and women, estrogen is essential during bone growth as it provides the necessary closure of epiphyseal (cartilage) growth plates. In young skeleton, also, estrogen is considered very crucial for the normal bone growth as its deficiency can lead to increased osteoclast formation which cause an increase in the resorption of bone [5].

The onset of menopause leads to estrogen deficiency that have deleterious effects on the bone heath. Estrogen deficiency lead to spongy and cortical bone loss. There is an uncontrollable increase in the bone resorption in spongy bones that lead to general bone loss as well as destruction of overall bone architecture. In cortical bones, estrogen deficiency initially causes an enhanced endocortical resorption and later lead to decreased bone mass and reduction in bone strength [6].

التعليق [m2]: delete

The presence of certain levels of estrogen in the body regulate the differentiation of osteoclasts in the body and keep their number under check. These cells carry out the remodeling and degradation of bones. This effect is mediated through some cytokines, and interleukin 1 and 6 (IL-1 and IL-6) are the most active candidates. Thus, when there is a decrease in estrogen level in the body due to menopausal events, the entire metabolic process of bone resorption and remodeling is affected and may act as precursors for various bone and joint disorders, including arthritis [6,7].

Arthritis is a general term that signifies joint pain or joint disease. It is very common, afflicts both sexes and at any age, however, it is more common among women and occurs more frequently in old age. The symptoms of arthritis include joint pain, joint swelling, stiffness and decreased range of motion. The symptoms may be mild or severe, but they cause permanent damage to joint and hence need careful evaluation and treatment. Among a hundred different types of arthritis, the most common ones include gout, osteoarthritis and rheumatoid arthritis [6].

التعليق [m3]: delete

Rheumatoid arthritis (RA) is an autoimmune disorder that affects the joints. And is more common in women as compared to men. The most common joints involved are of the hands and wrists with the same joints typically involved on both sides of the body [7]. Many researchers have found close link between menopausal event and onset of various kinds of arthritis. For instance, according to the findings of Islander et al. there is a high rate of RA prevalence in women who pass through menopause and experience a marked decline in production of ovarian sex hormone [8]. The association between onset of rheumatoid arthritis and menopause is the sex hormones, which have been characterized as vital modulators of the autoimmune diseases [9]. The hormonal decrease, especially estrogen and progesterone, lead to the production of various

pro-inflammatory mediators and lead to inflammation and pain in joints and loss of bone, which is the characteristic feature of RA [4].

The decline in estrogen levels in the body on the onset of menopause makes the bone prone to inflammation and bone loss. This bone loss is attributed to a complex interaction of cytokines and hormones that play important role in the remodeling process of bone. As it is known that RA is an autoimmune disorder, it is found that the deficiency of estrogen also effects the immune system [10]. It triggers the immune response against self-tissues and increase the activation of T cells, along with an increase in interlukin-7 (IL-7) and IFN-γ. The production of inflammatory modulators along with an increase in production of osteoclasts (cells that break down and dissolve bone tissues) lead to drastic bone loss and inflammation of the joints and serve as precursors of RA [11]. Estrogen also induce oxidative stress in the body as it downregulates the antioxidant pathways and level of ROS is increased. The increase in oxidative stress worsens the inflammatory process and lead to pain and swelling in the joints [10].

Osteoarthritis (OA) is most common type of joint disease [5] and is characterized by wear and tear of the cartilage. It commonly affects the weight-bearing joints like hips, knees, cervical (upper) and lumbosacral (lower) spine and feet [6]. It is a gradually progressing disease and lead to irreversible damage to the bone and cartilage that lead to complete failure of joint [12]. OA is not only a joint cartilage disorder but also causes other adverse effects on the skeletal and muscle system. For instance, it causes thickening of bone, formation of osteophyte and inflammation of synovial membrane, that is the connective tissue present in the joints. There is an increasing evidence that sex hormone, especially estrogen have a crucial play in the maintenance of homeostasis of joint and articular tissues. The presence of certain estrogen receptors (ERs) present in the joint tissues also suggest the definitive association between osteoarthritis and loss of ovarian function due to menopause [13].

Gout is a form of arthritis characterized by persistent increased amounts of uric acid in the blood. It tends to effect smaller joints, particularly the big toe, but can occur in any joint [14]. There has been emerging evidence that although gout is more prevalence in men as compared to women. However, the incidence of gout in women has been postulated to be linked with sex hormones and their imbalance in older population of female. Menopause have been found to independently cause high levels of uric acid in the body, which subsequently increase the risk of gout [15]. And hormone therapy in postmenopausal women lead to a decrease in the serum urate level in women, which further supports the role of estrogen in pathogenesis of osteoarthrosis. The estrogen levels have been found to directly influence the uric acid level in the body, as estrogen along with progesterone, play important in the excretion of uric acid form the body via kidneys. The absence of estrogen in the postmenopausal period can lead to accumulation and high serum level of urate in the body that can lead to gout [14].

Certain other factors such as sex, age, life style, duration of menopause period and obesity (BMI index) have a definitive role in the triggering and prevalence of joint diseases. For instance,

obesity and aging are the two main risk factors for development of osteoarthritis and rheumatoid arthritis [16] [17]. OA of knee has been found to be strongly linked with increased metabolic activity and inflammatory environments found in obesity [18]. the cytokines present in the adipose tissue, including adiponectin, and leptin influence the pathogenesis of osteoarthritis and rheumatoid arthritis through direct degradation of articular cartilage and upregulating the local inflammatory processes. Similarly, the main risk factors of gout in women have been found to include increasing age, hypertension, obesity, alcohol consumption, use of diuretic incident gout among women [19].

The arthropathies have been studied for centuries but only a handful of studies have examined sex differences in prevalence and epidemiology. In women, the joint diseases develop characteristically after menopause which led the researchers to explore a connection between the two. Different recent comparative studies have shown how women become more likely to develop the inflammatory bone and joint diseases with age and hormonal changes.

The present study aims to analyze the prevalence of rheumatoid arthritis, osteoarthritis and gout in postmenopausal women. The selected patients were also evaluated for the underlying risk factors for the respective joint disorder, including BMI and duration of menopause to establish the role of sex hormones and obesity in the triggering of disease in postmenopausal women.

Methods

150 postmenopausal women age (50-59 years……) were recruited from (private clinic in the period from January 2017 to September 2018 ……..). The patients were evaluated for the presence of OA, RA or gout and diagnosed on clinical, radiological and laboratory bases. For each participant medical history, weight, height, body mass index and duration of menopause were recorded. Statistical analysis was performed using SPSS.

التعليق [m4]: You need to write main results as continuous text too not just tables

Results

Sample Collection and Screening

- 150 postmenopausal women were screened for osteoarthritis (OA), rheumatoid arthritis (RA) and gout.
- Joint disease was related to body mass index (BMI) and duration of menopause

Table 1. No of OA in postmenopausal women.

No. of OA	Total
58 (38.6%)	150

No. of RA	Total
3 (2%)	150

No. of GOUT	Total
2 (1.3%)	150

Table 2. Relation of joints disease to Body Mass Index (BMI)

	BMI		
	<25	>25	P Value
OA	51 (87.9%)	7 (12.1%)	<0.001
RA	1 (33.3%)	2 (66.7%)	>0.05
GOUT	0 (0%)	2 (100)	>0.05

Table 3. Relation of joints disease to Body Mass Index (BMI)

Duration of menopause (years)	0-5	6-10	>10	P Value
OA	8 (13.7%)	12 (20.6%)	38 (65.7%)	<0.001
RA	2 (66.7%)	1 (33.3%)	0 (0%)	>0.05
Gout	2 (100%)	0 (0%)	0 (0%)	>0.05

Discussion

التعليق [m5]: You need to add more information about the percentage of OA, RA and gout in postmenopausal women in other studies

The prevalence of bone and joint diseases in postmenopausal women has been an area of interest since many decades. The present study involves the analysis of 150 samples from women who have aged beyond menopause who were screened for the presence of type of arthritis. The present study also aims to establish the relationship between hormonal changes that occur during and after menopause and the onset of bone degenerative diseases. The screening test showed that OA was the most prevalent in postmenopausal women, as 58 women out of 150 were positive for OA, making 38.6% of the study sample (Table 1). There were also samples that were found positive for RA and gout, however, their prevalence was quite low, being 2% and 1.3%,

respectively. These findings are inconsistent with the findings of Lawrence et al. who reported that osteoarthritis is the most common type of arthritis in women [7]. It has also been reported that certain structural and functional changes occur on the articular structures which start at early menopause and persist post-menopause. These changes lead to an increase in the prevalence of OA in the latter population. According to Roman-Blas et al. both experimental and observational evidence support a relevant role for estrogens in the homeostasis of joint tissues and the health. Estrogens influence the metabolism of bones at many crucial levels and are part of several complex molecular mechanisms. The regulatory effects of estrogens at joints are either significantly decreased or completely lost as a result of postmenopausal ovarian dysfunction [4].

The relationship between obesity and type of arthritis was stablished by analyzing the BMI of patients and type of arthritis present in them. The overweight individuals were characterized to have BMI between 25-30, while individuals with BMI above 30 were considered obese. In relation to obesity and type of joint diseases, it was found that 66.7% (1 out of 3 patients; P Value >0.05) and 12.1% (7 out of 21; P Value < 0.001) of RA and OA patients were obese and they have a BMI of greater than 25, respectively (Table 2). It has been previously reported that aging and obesity are the primary risk factors for development of OA [12]. There is a strong tendency that there is gain of weight with age as the metabolism of body is altered and become less efficient. Evidence also support the role of menopause as a trigger of obesity. As obesity and metabolic disorders have been found to be three times more prevalent in postmenopausal life of women as compared to before menopause [20]. Therefore, obesity and menopause being interrelated play significant role in aggravating joint diseases, especially OA.

In the present study, a statistically non-significant relationship was found between obesity and other two joint diseases, RA and gout (Table 2). The reason for this might be the small sample size overall, and for RA and gout. However, 2 out of 3 (66.7%), RA patients were found to be obese, and had a BMI of greater than 25, while both (100%) of the gout patients were also obese. These findings, if reciprocated to larger scale suggest a definitive role of obesity in the triggering and pathogenesis of RA and gout. Similar findings have been reported by Dar et al., who suggested that obesity has a significant association with RA. According to the findings of Zhu et al. the increasing prevalence of gout in the United States is attributed to the obesity epidemic [21].

The duration of menopausal event is an important determinant of postmenopausal physiological changes in the body. The relationship between the postmenopausal period, distributed in three groups of 0-5 years, 6-10 years and more than 10 years, and the prevalence of gout, OA and RA was analyzed. The number of post menopause years or the sex hormonal deficiency, period showed a proportional with incidence of osteoarthritis. OA was found to be present in 67.5% of women who have post menopause duration of more than 10 years. It was found that a statistically significant relationship (P value < 0.001) exist between OA and the duration of menopause in women (Table 3). This can be explained by the findings of Gokhale et al., who explained the significant role of estrogen in maintenance of healthy bone metabolism and

estrogen deficiency may lead to deterioration of bone and joint tissues. This deterioration is directly proportional to duration of estrogen deficiency and with the passage of time can lead to an increase in the development of bone and joint disorders [22]. The incidence of RA and gout was higher in the earlier stage of menopause, and there was a statistically non-significant relationship between increase in post menopause years and prevalence of RA and gout (P value >0.05).

Thus, this study suggests that a definitive association is present between postmenopausal physiological changes and joint disorders, and the primary role is played by the underlying hormonal imbalance that is initiated by menopause. High rate of obesity in postmenopausal women and increase in duration of menopause event, further increase the incidence of joint disease and can be marked as risk factors for osteoarthritis, rheumatoid arthritis and gout. Further research is required in this area in order to understand the predispose factors of joint and bone disorders in postmenopausal women and provide insight to hormone therapy so that women can cope better with the physiological effects of menopause and can protect their bone and joints.

التعليق [m6]: Add conclusion

REFERENCES

التعليق [m7]: Use references without brackets

[1]. Sherwin B. Menopause: Myths and realities. Psychological aspects of women's health care. In: Stotland NL, Stewart DE, editors. The Interface Between Psychiatry and Obstetrics and Gynecology. Arlington: American Psychiatric Publishing; 2001. pp. 241–59.

[2]. Spinelli MG. Depression and hormone therapy. Clin Obstet Gynecol. 2004;47:428–36. [PubMed]

[3]. Väänänen HK, Härkönen PL. Estrogen and bone metabolism. Maturitas. 1996;23:S65-S9.

[4]. Roman-Blas JA, Castañeda S, Largo R, Herrero-Beaumont G. Osteoarthritis associated with estrogen deficiency. Arthritis research & therapy. 2009;11(5):241.

[5]. Cauley JA. Estrogen and bone health in men and women. Steroids. 2015;99:11-5.

[6]. Sacks JJ, Luo YH, Helmick CG. Prevalence of specific types of arthritis and other rheumatic conditions in the ambulatory health care system in the United States, 2001–2005. Arthritis care & research. 2010;62(4):460-4.

[7]. Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: Part II. Arthritis & Rheumatism. 2008;58(1):26-35.

[8]. Islander U, Jochems C, Lagerquist MK, Forsblad-d'Elia H, Carlsten H. Estrogens in rheumatoid arthritis; the immune system and bone. Molecular and cellular endocrinology. 2011;335(1):14-29.

[9]. Gabriel SE. The epidemiology of rheumatoid arthritis. Rheumatic Disease Clinics of North America. 2001;27(2):269-81

[10]. Khan D, Ansar Ahmed S. The immune system is a natural target for estrogen action: opposing effects of estrogen in two prototypical autoimmune diseases. Frontiers in immunology. 2016;6:635.

[11]. Weitzmann MN, Pacifici R. Estrogen deficiency and bone loss: an inflammatory tale. The Journal of clinical investigation. 2006;116(5):1186-94.

[12]. Brandt K, Radin E, Dieppe P, Van De Putte L. Yet more evidence that osteoarthritis is not a cartilage disease. BMJ Publishing Group Ltd; 2006

[13]. Braidman IP, Hainey L, Batra G, Selby PL, Saunders PT, Hoyland JA. Localization of estrogen receptor β protein expression in adult human bone. Journal of bone and mineral research. 2001;16(2):214-20.

[14]. Roddy E, Zhang W, Doherty M. The changing epidemiology of gout. Nature Reviews Rheumatology. 2007;3(8):443.

[15]. Hak AE, Choi HK. Menopause, postmenopausal hormone use and serum uric acid levels in US women–the Third National Health and Nutrition Examination Survey. Arthritis research & therapy. 2008;10(5):R116.

[16]. Rezende MUd, Campos GCd, Pailo AF. Current concepts in osteoarthritis. Acta ortopedica brasileira. 2013;21(2):120-2.

[17]. Dar L, Tiosano S, Watad A, Bragazzi NL, Zisman D, Comaneshter D, et al. Are obesity and rheumatoid arthritis interrelated? International journal of clinical practice. 2018;72(1):e13045.

[18]. Sowers MR, Karvonen-Gutierrez CA. The evolving role of obesity in knee osteoarthritis. Current opinion in rheumatology. 2010;22(5):533.

[19]. Bhole V, de Vera M, Rahman MM, Krishnan E, Choi H. Epidemiology of gout in women: Fifty- two–year followup of a prospective cohort. Arthritis & Rheumatism. 2010;62(4):1069-76.

[20]. Kwaśniewska M, Pikala M, Kaczmarczyk-Chałas K, Piwonńska A, Tykarski A, Kozakiewicz K, Pająk A, Zdrojewski T, Drygas W. Smoking status, the menopausal transition, and metabolic syndrome in women.Menopause. 2012 Feb; 19(2):194-201.

[21]. Zhu Y, Pandya BJ, Choi HK Arthritis Rheum. Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007-2008.. 2011 Oct; 63(10):3136-41

[22] Gokhale JA, Frenkel SR, Dicesare PE. Estrogen and osteoarthritis. Am J Orthop (Belle Mead NJ). 2004 Feb; 33(2):71-80