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CHARACTERISTICS OF OSTEOPOROSIS PATIENTS WITH GALLSTONE FORMATION IN CHOLELITHIASIS PATIENTS WITH MALIGNANT NEUROLEPTIC SYNDROME

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Abstract

There is a suspected relationship between osteoporosis and gallstone formation in patients with cholelithiasis with neuroleptic malignant syndrome. However, the characteristics of osteoporosis that are related to this problem have not been discussed in previous studies. Knowing the Characteristics of Osteoporosis Patients with Gallstone Formation in Patients Suffering from Cholelithiasis With Malignant Neuroleptic Syndrome. This research is a Systematic Review using the Preferred Reporting Items for Systematic Reviews and Meta-analyses method or commonly called PRISMA, this method is carried out systematically by following the correct research steps or protocols. Sources were taken from the Google Scholar website with journals published in 2005-2022 and then screening was carried out to obtain

the results of 1,910 journal articles. Journal clustering was carried out and the number of Scopus indexed journals obtained was 4 journals Q1, 1 journal Q2, and 1 Q4 journal, so that 6 journals were extracted.

Keywords: Osteoporosis, Gallstones, Cholelithiasis, Malignant Neuroleptics.

INTRODUCTION

Osteoporosis is a bone disease characterized by microarchitectural degradation of bone tissue and loss of bone mass. Osteoporosis (literally means "porous bones") will increase bone fragility and the risk of fractures in sufferers (Clynes et al., 2020). Osteoporosis is characterized by loss of bone mass, degeneration of bone microarchitecture, increased risk of fractures, and the latter consequence is associated with severe morbidity and mortality. The asymptomatic and progressive character of osteoporosis causes the need for early detection of this osteoporosis (Vidal et al., 2019). To anticipate this disease, it is necessary to carry out prevention activities by consuming proper calcium and vitamin D, as well as a healthy lifestyle to maintain bone health. As for the treatment, the drug given will be specific to the character of the fracture and the severity of the patient's disease.

Osteoporosis is a disease that is often experienced by older people, but it is possible for teenagers to experience it. Apart from osteoporosis, gallstones (cholelithiasis) is also a disease that is often experienced by older people. Both osteoporosis and gallstones are common disorders in the elderly worldwide. Both of these disorders are more common in women and can appear during pregnancy and menopause, indicating that sex hormones play an important role in their development. Gallstones can occur without symptoms for years and are often discovered incidentally (when they recur). Likewise with osteoporosis, many people do not realize they have osteoporosis until their bones are broken. With all these parallels, it's not surprising that there is some link between the two diseases. This means that people with osteoporosis are more susceptible to gallbladder disorders, such as gallstones. Cholecystectomy is a popular surgical operation, and patients who have had cholecystectomy are frequently encountered in clinical practice. Gallstones are the most common reason for cholecystectomy, followed by cholecystitis (Lee et al., 2021).

One of the most obvious common causes between the two is inflammation. Studies of osteoporosis conclude that the disease is the result of various metabolic, endocrine, and mechanical factors. However, in recent years, evidence has shown that inflammation has a significant effect on bone formation. This systemic inflammation can inhibit bone formation and overproduce pro-inflammatory mediators such as prostaglandins, cytokines, and nitric oxide. Inflammation often occurs in the biliary tree, including the gallbladder. Excessive and long-term inflammation can damage tissue and cause cholelithiasis. Scars caused by persistent tissue damage can impact the liver and bile, alter enterohepatic circulation and possibly cause gallstones (Klahan et al., 2014); (Lin et al., 2017). According to previous studies, there were as many as 114 cases of gallstones occurring in osteoporosis. The risk of gallstones in osteoporosis results in a likelihood ratio of 1.35 or it means that osteoporosis patients have a higher chance of developing gallstones than the general population (Klahan et al., 2014).

Osteopontin (OPN) is a pro-inflammatory cytokine that is found in various tissues and is involved in various biological processes including bone mineralization, inflammation, and cell survival. It is expressed at high levels in the bone matrix, and can promote autoreactive T cell survival and participate in bone remodeling processes. One study showed that it stimulated adhesion, migration, and bone resorption by osteoclasts. Research shows that osteopontin (OPN) is also a core protein in the formation of cholesterol gallstones (Fodor et al., 2013). Based on these data, osteoporosis patients may have a higher risk of developing gallstones, but the relationship is not clearly known (Chellaiah et al., 2003); (Denhardt & Noda, 1998); (Ichikawa et al., 2009); (Mazzali et al., 2002); (Stromnes & Goverman, 2007).

Based on the study of (Minamisawa et al., 1991), in the case of adult men with alcohol addiction with hematoemesis. The patient experienced a case of rupture of esophageal varices and was then treated with endoscopic injection sclerotherapy. On the 3rd day of treatment, the patient showed alcohol withdrawal syndrome. Then the laboratory results related to the values of CK, LDH, GOT and GPT showed high results, thus strengthening the suspicion of neuroleptic malignant syndrome (NMS).

Knowing the characteristics of osteoporosis sufferers with the formation of gallstones in patients suffering from cholelithiasis with malignant neuroleptic syndrome.

RESEARCH METHODS

This study is a Systematic Review using the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) technique, which is carried out in a systematic and complete manner by following the required research procedures or protocols. A systematic review is a procedure that uses the previously generated review, analysis, evaluation, classification, and categorization of information. The procedure for carrying out a systematic review is quite planned and structured, making this method very different from simply submitting a literature study. This systematic review approach consists of several steps:

1. Arrange Background and Purpose
2. Research problems
3. Literature Search
4. Selection Criteria
5. Training screen
6. Procedure List and Quality Check
7. Data Extraction Strategy and Data Synthesis Strategy

The data used to search for literature is through selection based on cervical cancer criteria, which involves medical research and social health. Furthermore, implementing a literature review related to Osteoporosis, and gallstones. Articles are searched using Google Scholar as a database. A search for research articles relevant to the topic of this research was carried out using the keywords: osteoporosis, osteoporosis characteristics, and gallstone formation, cholelithiasis.

Analysis is the decomposition of a subject into its various parts and the study of the parts themselves and the relationships between the parts to obtain a proper understanding and understanding of the meaning of the whole. While synthesis is a blend (mixture) of various meanings or things so that they form a harmonious

whole. Narrative is the method used in synthesizing this research, this method classifies the extracted data, analyzes the content contained in the research objectives and research results. The analysis used is journal content analysis.

RESULT AND DISCUSSION

A. Research result

This chapter will describe the results and analysis using 3 journals related to osteoporosis and gallstones, 1 journal related to osteoporosis characteristics, 1 journal related to gallstones and osteopontin variables, and 1 journal related to osteoporosis and malginant neuroleptics. .

Journals obtained are screened and extracted into a table to make it easier to explain the contents of the journal. Based on the results of journal clustering, the number of journals indexed by Scopus Q1 was 4 journals, 1 journal Q2, and 1 journal Q4, so that 6 journals were extracted and used as a reference for our systematic review work.

B. Data Analysis

Data information regarding osteoporosis as an independent variable analyzed is presented in tabular form containing the title of the journal, year of publication, the author of the purpose in the journal, sample and criteria, research instruments, between data or research methods and research results in the journal.

Table 1. Journal Analysis

No	Journal Title and Researcher's Name	Objective	Population/ Sample	Instrument	Data Analysis/Research Methods	Results	Journal Clustering
1	Composition and characteristics of trabecular bone in osteoporosis and osteoarthritis (Tamimi et al., 2020)	To analyze trabecular bone architecture, and its crystalline and organic composition in humans, by comparing samples taken from patients with hip fractures (HF) and individuals with hip osteoarthritis (HOA)	31 heart failure patients and 42 HOA cases who underwent joint replacement surgery between 1/1/2013 and 31/12/2013.	Collection of trabecular bone samples	Samples were analyzed using dual-energy X-ray absorptiometry, micro-CT, and high-resolution nuclear magnetic resonance spectroscopy (MAS-NMR) solid-angle magic-spinning.	There is no difference in the structure of the two samples studied	Q2
2	Gallstones in patients with liver cirrhosis: Incidence, etiology, clinical and therapeutical aspects (Acalovschi, 2014)	To present the mechanisms responsible for the development of gallstone disease in patients with cirrhosis of the liver, as well as the clinical and therapeutic	Current data regarding risk factors for gallstones	Analysis of literature review related to risk factors for gallstones	Literature review for existing study-related literature	The prevalence of gallstones increases with age, with a higher ratio of males. Chronic alcoholism, C virus cirrhosis, and non-alcoholic fatty liver disease are the underlying	Q1

		aspects of the gallstones that form.				liver diseases most commonly associated with gallstones. However, closer follow-up of these patients is needed to treat symptoms or complications earlier. For symptomatic stones, laparoscopic cholecystectomy has become the treatment of choice.	
3	Osteoporosis increases subsequent risk of gallstones: a nationwide population-based cohort study in Taiwan (Klahan et al., 2014)	To examine the relationship between osteoporosis and the risk of developing gallstones in Taiwan using a national population-based data set.	1638 patients diagnosed with osteoporosis between 2003 and 2005 identified in the National Health Insurance Research Database	Patient identification based on the International Classification of Diseases, Ninth Revision, Clinical Modification diagnostic criteria	Study group and comparison group to retrospectively examine the relationship between osteoporosis and gallstones.	Over a 5-year period, 114 and 311 cases of gallstones occurred in the osteoporosis and control groups, respectively. The risk of gallstones in osteoporosis and the comparison group resulted in a	Q4

						hazard ratio of 1.35 (95% confidence interval: 1.07 - 1.69; $p < 0.01$)	
4	Physical activity and decreased risk of clinical gallstone disease among post-menopausal women (Storti et al., 2005)	Effect of physical activity to prevent gallstones	182 postmenopausal women	Statistical analysis was performed for both population studies using Statistical Analysis Software, version 8.2 (SAS Institute Inc; Cary, North Carolina).	The activity/gallstone relationship was examined in postmenopausal women from the Study of Osteoporotic Fractures (SOF; 1986–1988), a prospective study of fracture risk factors in 8010 women (mean age = 71.1 years, SD = 4.9)	Physical activity is inversely related to the development of gallstone disease in postmenopausal women regardless of their body mass index where they tend to be more susceptible to developing osteoporosis.	Q1
5	Increased risk of osteoporosis in patients with primary biliary cirrhosis (Liao et al., 2018)	Evaluating osteoporosis risk in patients with primary biliary cirrhosis (PBC) using a national population-based data set.	2,493 PBC patients who were 18 years of age or older and had been diagnosed with PBC according to	The risk of developing osteoporosis was estimated using a Cox proportional hazard regression	Cohort study	Osteoporosis was diagnosed in 150 (6.02%) patients in the PBC group and 539 (5.41%) patients in the non-PBC group. The risk of osteoporosis was	Q1

			the International Classification of Disease (ICD-9-CM) code 571.6, during 2000-2010. consisted of 9,972 randomly selected, trend-matched (based on age, sex, , and index date), without PBC.	model.		found to be 3.333 times greater in the PBC group than in the non-PBC group when measured 6 years after PBC diagnosis. In addition, the risk of osteoporosis was significantly higher in PBC patients on steroids (aHR: 6.899 vs 3.333). Non-cirrhotic patients are prone to osteoporosis at a younger age compared to the cirrhotic group.	
6	Inflammation in bone physiology and pathology (Adamopoulos, 2018)	Knowing the understanding of the physiological and pathological mechanisms that cause changes will enable the utilization of inflammatory	Literature related to bone physiology and pathology	Bone physiology and pathology analysis based on Juvenile Amputee Overgrowth	Literature review	The results show that inflammatory signals can stimulate transcription factors that regulate osteoblast differentiation from their	Q1

		signals in bone regeneration. Looks at the role of inflammation in bone resorption and bone formation, which gives rise to various pathologies and analyzes the great potential of exploiting these inflammatory signals to achieve bone regeneration.				precursors.	

C. Characteristics of Osteoporosis Patients in Patients Suffering from Cholelithiasis based on age & gender

Osteoporosis is a bone disease caused by microarchitectural degradation of bone tissue and bone mass. The characteristics of this disease are the fragility of the bones and the risk of fractures which are generally asymptomatic. People with osteoporosis are more susceptible to gallbladder disorders and the formation of gallstones. In osteoporosis patients with gallstone formation, they will experience inflammation, in which this aspect influences bone formation factors. Where inflammation will inhibit bone formation and overproduction of pro-inflammatory mediators such as prostaglandins, cytokines, and nitric oxide which are characteristic of osteoporosis sufferers. Inflammation often occurs in the biliary tree. Inflammation over a long period of time then causes Cholelithiasis (Clynes et al., 2020). Inflammation that occurs in people with osteoporosis will progressively increase with age. This goes hand in hand with the occurrence of cholelithiasis, in which pro-inflammatory mediators, namely prostaglandins, decrease and cause bone density to decrease, at the same time the biliary system which carries out the physiological circulation of bile is disrupted resulting in the formation of gallstones (Vidal et al., 2019).

Sustained inflammation then causes tissue damage and causes cholelithiasis. This damage then triggers the formation of gallstones. In the case of gallstones, patients will experience systemic inflammation that can inhibit bone formation and overproduce pro-inflammatory mediators such as prostaglandins, cytokines, and nitric oxide. According to previous studies, there were 114 cases of gallstones occurring in elderly adult women (> 45 years) suffering from osteoporosis. Gender plays a major role in the occurrence of cholelithiasis which is closely related to osteoporosis, one of which is women, because in women the condition of nitric oxide in the body which plays a role in the process of bone development is hampered more quickly due to the influence of female hormones, one of which is LH which causes disruption of the biliary system and gallstones form. However, because these two diseases are both triggered by inflammation, studies regarding which factors trigger each other are still lacking to be explained in detail both in terms of age and gender (Vidal et al., 2019).

D. Characteristics of Osteoporosis Patients with Gallstone Formation in Patients Suffering from Cholelithiasis with Neuroleptic Malignant Syndrome based on duration of taking medication & type of drug

Gallstones can form if the body has produced too much bilirubin due to a liver condition or if the body's liver produces too much cholesterol. Pigment gallstones are the most common form, with cholesterol stones accounting for around 15% of cases of SNM. In people with cholelithiasis, inflammation will appear and if it continues to occur it will form gallstones. Where according to the exposure above it will lead to the formation of pigment gallstones (a greater probability than cholesterol stones) (Coruch, et al. 2017). In the case of patients with gallstones, patients will experience systemic inflammation which can inhibit bone formation and overproduce pro-inflammatory mediators such as prostaglandins, cytokines, and nitric oxide. So it can be said that indirectly the characteristic of osteoporosis sufferers with the formation of gallstones in patients with neuroleptic malignant syndrome is that the patient will experience

inflammation which inhibits the process of bone formation. Inflammation of the bone microenvironment results in changes that lead to excessive bone loss and bone formation.

One of the incidences of osteoporosis related to drug withdrawal syndrome is in patients with a history of schizophrenia and receiving antipsychotic drugs, one example of which is risperidone. Risperidone is able to erode bone thickness and strength or in other words bone loss. US. Valproate, codeine, etc (Vidal. et al. 2019). The duration of treatment related to these conditions depends on the patient's discontinuation of treatment without advice from the relevant doctor (Adamopoulus, 2018). It was found in the results of the study, a number of 80 people in NHS Europe who were both male and female took antipsychotic treatment for a minimum of 4 months and a maximum of about 1 year and 3 months which could cause SNM due to their non-compliance with not taking medication. The drug that most often causes NMS due to the effect of decreasing dopamine activity is valproate acid by 60%, the rest is risperidone (Coruch, 2017).

CONCLUSION

Based on the results of the study, the incidence of osteoporosis associated with the formation of gallstones / cholelithiasis and drug withdrawal syndrome / SNM, one of which is in patients treated with risperidone, as valproate, in psychotic patients who are able to erode bone thickness and strength or in other words bone loss. US. Valproate, codeine, etc. The duration of treatment related to these conditions depends on stopping the patient's treatment without advice from the doctor concerned. It was found in the results of the study, a number of 80 people in NHS Europe who were both male and female took antipsychotic treatment for a minimum of 4 months and a maximum of about 1 year and 3 months which could cause SNM due to their non-compliance with not taking medication. The drug that most often causes NMS due to the effect of decreasing dopamine activity is valproate acid by 60%, the rest is risperidone.

Inflammation that occurs in people with osteoporosis will progressively increase with age. This goes hand in hand with the occurrence of cholelithiasis, where pro-inflammatory mediators, namely prostaglandins, decrease and cause bone density to decrease, along with that the biliary system which carries out the physiological circulation of bile is disrupted so that gallstones form. Sustained inflammation then causes tissue damage and causes cholelithiasis. This damage then triggers the formation of gallstones. In the case of gallstones, patients will experience systemic inflammation which can inhibit bone formation and overproduce pro-inflammatory mediators such as prostaglandins, cytokines, and nitric oxide. According to previous studies, there were 114 cases of gallstones occurring in elderly adult women (> 45 years) suffering from osteoporosis. Gender plays a major role in the occurrence of cholelithiasis which is closely related to osteoporosis, one of which is women.

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