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## Osteoarticular complications in diabetes - literature review

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**ABSTRACT** 

Due to the increasing number of patients suffering from diabetes mellitus scientists raise

awareness of different symptoms that patients might present.

The disease results from a defect in insulin secretion or action. Chronic hyperglycemia in

diabetes causes damage and dysfunction of organs, especially the eyes, kidneys, nerves, heart

and blood vessels. Diabetes can occur at any age and always requires treatment.

A common non-specific symptom of untreated DM may be osteoarticular complications.

Typical symptoms of diabetes include polyuria, increased thirst, dehydration, weakness and

drowsiness. Complications of the disease include eyes, kidneys, nerves, microangiopathies,

diabetic foot syndrome, bones, joints, skin. In all patients, the most important thing is to

control glycemia from the beginning of the disease.

The following article is an overview of the current knowledge on the correlation of diabetes

with osteoarticular complications, its pathomechanism and metabolic control. The article was

based on publications available in the Pubmed and Google Scholar databases.

Keywords: diabetes, diabetes-related complications, education, diabetic knowledge.

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Diabetes is one of the most common metabolic diseases worldwide. It is a global problem of modern medicine, which is why it is called the epidemic of the 21st century by the WHO (World Health Organization) [1]. Despite the dynamic development of diabetes, the use of new therapeutic therapies, experience and development of medical knowledge, the main problem remains the chronic complications of this disease. Diabetes is a group of chronic metabolic diseases characterized by elevated blood glucose levels (hyperglycemia) resulting from impaired insulin secretion by the pancreas or a defect in its action in the body. There are many types of this disease, taking into account its etiopathogenesis. Classic symptoms include polyuria (polyuria), increased thirst (polydipsia), drowsiness, and weakness. There are also less specific symptoms - infections of the urogenital system, purulent skin lesions. Diagnosis of diabetes is based on the detection of increased glycemic values that meet the criteria for diagnosing diabetes, and then on determining its type (cause) in accordance with the current WHO classification of the World Health Organization [2]. Chronic hyperglycemia leads to micro- and macrovascular disorders, resulting in damage to the circulatory system, kidneys and eyes. Complications also affect the musculoskeletal system, being a source of pain and disability. This disease not only worsens the quality of life, but also shortens the survival time compared to the population of people without diabetes. The authors of The Emerging Risk Factors Collaboration sought the answer to this question. They analyzed data from 820,700 patients from 97 prospective studies in which 123,205 people died. After adjusting the data for sex, age and BMI, they found that the overall risk of death (hazard ratio [HR] = 1.80; CI 1.71–1.90) in patients with diabetes was 80% higher in compared to people without the disease [3]

The following article is an analysis of current medical knowledge regarding the occurrence of complications in the osteoarticular system based on available publications.

The mechanism of the adverse effects of hyperglycemia on the body, including the musculoskeletal system

The metabolic effects of hyperglycemia result from the toxic effects of chronically elevated blood glucose levels. Initially proliferating pancreatic  $\beta$  cells become depleted and degranulated with prolonged duration of elevated blood glucose levels - the phenomenon of glucotoxicity. [4] Increased glycemia results in the activation of many metabolic pathways in cells in which glucose transport is independent of insulin. These include, among others: increased production of protein glycosylation end products (AGEs), production of free radicals, activation of the polyol pathway and activation of protein kinase C [5].

The mentioned non-enzymatic glycosylation of type IV collagen results in an increase in the number of cross-links in the collagen molecule, making it resistant to the action of collagenase. The result is the deposition of abnormal proteins in soft tissues and reduced tissue perfusion, which together lead to hypoxia of the nerves and blood vessels [6]. The described mechanisms usually manifest themselves after a long period of the disease, but in a few cases they may be its first symptom. Periarticular, joint and muscle changes are often neglected and unnoticed, which is why clinicians' awareness in this area is very important.

# Selected osteoarticular complications in the course of diabetes

Chronic complications of diabetes include damage to the peripheral and autonomic nervous systems. Diabetic neuropathy affects approximately 50% of patients, and one of the most common syndromes is peripheral and sensory polyneuropathy. They manifest themselves by abnormal perception of touch, burning in the hands and feet, night pain and areas of loss of sensation (the so-called "glove or sock syndrome") [7]. As a result of vascular microangiopathy and hypoxia, diabetic foot syndrome develops, which occurs in 0.5–2% of patients with type 1 diabetes and in 12–18% of patients with type 2 diabetes [8, 9]. Longlasting, but above all very difficult, healing wounds increase the likelihood of infection of surrounding tissues, muscles and joints. Severe pain, redness, increased joint warmth, and fever may suggest the diagnosis of bacterial arthritis. In such situations, laboratory blood tests and synovial fluid examination along with culture should be performed to establish the correct diagnosis. [10]

In long-term patients with poor metabolic control of glycemia, neuromuscular reflexes weaken after some time, and constantly repeated micro- and macro-injuries lead to ligament degeneration and bone fractures. Improper functioning of the autonomic system leads to dilation of blood vessels, which increases bone resorption by increasing blood flow. Charcot's joint is then formed, characterized by swelling, instability of the ankle joint, and crackling sensations when the joint is moved. [11] Due to ischemic and neuropathic changes, ulcers appear on the skin, which are very difficult to treat.

Generalized idiopathic skeletal hyperostosis - Forestier's disease, also known in clinics as diffuse idiopathic skeletal hyperostosis (DISH), most often occurs in the 6th decade of life in patients with type 2 diabetes and obesity. The etiopathogenesis highlights the relationship between hyperglycemia, hyperinsulinemia, insulin resistance and insulin-like growth factors, through which growth hormone intensifies calcification processes. The described degenerative and productive changes mainly concern the thoracic spine and include the formation of pseudoosteophytes on the edges of the vertebral bodies, creating bone bridges.

[12] The changes may be asymptomatic, but they are often responsible for pain and stiffness of the spine. Treatment involves symptomatic therapy - non-steroidal anti-inflammatory drugs (NSAIDs) and physiotherapy. [13]

Chronic hyperglycemia leads to calcium and phosphate metabolism disorders. Progressive impaired osteoblast function, increased bone resorption, and deficiency of active vitamin D metabolites due to nephropathy lead to complications such as osteopenia, generalized and local osteoporosis, and secondary hyperparathyroidism. [14] Osteoporosis prevention involves the use of calcium and vitamin D preparations, but above all, achieving proper glycemia. [15]

The long-term course of the disease, abnormal metabolic control of diabetes, collagen glycation and connective tissue fibrosis lead to limited mobility of the wrist, metacarpophalangeal and interphalangeal joints, causing stiffness and hand contracture. This syndrome is called cheiroarthropathy. [16]. Physiotherapy and kinesitherapy are recommended for treatment

Duputryen's contracture is the result of damage to collagen fibers, resulting in fibrosis, thickening and gradual shortening of the palmar aponeurosis. Contracture occurs in the metacarpophalangeal and proximal interphalangeal joints. [17]

In diabetic patients, vascular microangiopathy and hypoxia result in wounds that are difficult to heal. This increases the likelihood of infection of tissues, joints and sepsis. [18] Severe pain, redness, increased joint warmth, and fever may suggest the diagnosis of bacterial arthritis. In such situations, laboratory blood tests and synovial fluid examination along with culture should be performed to establish the correct diagnosis. [19]

Obesity is a risk factor for both diabetes and osteoarthritis. In patients with diabetes, degenerative and productive changes are observed much more often than in the general population, affecting both large and small joints. The development of degenerative disease occurs due to impaired synthesis of proteoglycans and glycosaminoglycans, macrocirculation disorders and excessive load on the joints. [20]

### Conclusions

The incidence of diabetes worldwide is constantly increasing. It is expected that approximately 440 million people will be affected by diabetes in 2030. This disease causes deterioration of the quality of life and shortening of survival time. According to epidemiological studies, it is one of the most common social diseases. [21] The negative effects of diabetes cause disability and reduce the quality of life of diabetic patients. Health education plays a very important role in preventing disease complications. [22] Continued

knowledge of the pathogenetic mechanisms of diabetes complications makes us optimistic that even more effective preventive measures against diabetes complications will be developed in the near future. At the moment, early detection of the disease and proper metabolic control remain the only method of stopping the development and progression of micro- and macroangiopathy.

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#### **Conflict of interest statement**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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#### **Authors contribution:**

Conceptualization: Kinga Przyborowska, Michał Łata; methodology: Justyna Kwiecień, Katarzyna Wiejak, Mateusz Rukat; formal analysis: Beata Getka, Kinga Przyborowska, Justyna Kwiecień; investigation: Kinga Przyborowska; writing-rough preparation: Kinga Przyborowska, Michał Łata, Justyna Kwiecień, Katarzyna Wiejak; writing-review and editing: Beata Getka, Justyna Kwiecień, Mateusz Rukat; visualization: Kinga Przyborowska, Beata Getka

All authors have read and agreed with the final, of the manuscript.

#### **Board statement:**

Not applicable - this review included an analysis of the available literature.

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