

Summary in English

Objective: Patients with RA are at greater risk of developing diabetes due to genetic factors, limited physical activity, active inflammation, potential diabetogenic influence of drugs and classic risk factors such as unhealthy diet, obesity, aging, lipid disorders and arterial hypertension. The aim of the study was to determine the incidence and course of individual types of diabetes, including autoimmune diabetes LADA, in patients with RA hospitalized in the Department of Rheumatology of the Institute of Rheumatology in Warsaw. Further work tasks were: assessment of insulin resistance based on: fasting insulin, HOMA-IR index, QUICKI index, McAuley index and CRP as well as the evaluation of beta cell function by HOMA-B index. An attempt was made to determine the relative and absolute predictive value and mechanisms of action of the major risk factors for developing diabetes in patients with RA. We analyzed musculoskeletal conditions in patients with RA and diabetes, taking into account the pathologies associated with diabetes.

Material and Methods: The work was divided into two main parts. In the first part of the study, designed to determine the prevalence of diabetes in patients with RA, we made a retrospective analysis of medical records of patients hospitalized in the Department of Rheumatology in 2006-2008. There were 48 cases of Type 2 diabetes detected in the group of 400 patients with rheumatoid arthritis. Into the second part of the work, carried out in 2010-2011, we enrolled 51 people with rheumatoid arthritis and concomitant diabetes and 64 non-diabetic patients with rheumatoid arthritis as a control group. The analysis of the interview data was targeted to determine the risk factors for diabetes, course and treatment of RA. We obtained data from the physical examination, including the full internal examination, weight and height, assessing the number of tender and swollen joints, changes in the musculoskeletal system in the course of diabetes. We summarize the results of laboratory tests, including the routine tests carried out on the purposes of the in-hospital diagnosis and treatment, and additional tests for concentration of glycated hemoglobin A1c (only in persons with diagnosed diabetes), insulin (in patients not treated with insulin), 25 (OH) D and titers of anti-GAD antibodies.

Results: The first, epidemiological part of the study showed that the incidence of Type 2 diabetes in patients with rheumatoid arthritis treated at the Department of Rheumatology was 12%.

During the second part of the work aimed at analyzing risk factors for diabetes, after designations of anti-GAD autoantibodies, we identified 13.2% of patients with autoimmune diabetes LADA in the group of with initial diagnosis of Type 2 diabetes mellitus. Analysis of insulin resistance based on HOMA-IR, QUICKI and McAuley indices showed that more than 40% of patients with RA appeared to have insulin resistance, and patients with type 2 diabetes

and patients in the control group did not differ significantly in terms of its frequency ($p > 0.05$). In the group with Type 2 diabetes significant majority of patients had impaired insulin secretion assessed by HOMA-B values lower than 100% ($p < 0.026$). People with diabetes have shown a significantly higher BMI values than those in the control group ($p < 0.034$). There were definite more overweight or obese patients in the group with type 2 diabetes ($p < 0.048$). Further assessment of the most important risk factors typical for the general population on the incidence of diabetes in patients with RA, and the separation of risk factors for RA-patients, including an analysis of the relationship between susceptibility to diabetes and factors such as duration, activity and treatment of RA, corticosteroids treatment, vitamin D deficiency, showed no relationship with the development of type 2 diabetes. Increased BMI has been proved as the only factor that had a significant impact on the incidence of type 2 diabetes. The value of OR calculated for this factor confirmed that the increase in BMI of 1 kg / m², was associated with 13% higher probability of developing type 2 diabetes ($p < 0.04$). Analysis of metabolic markers in Type 2 diabetes has shown that most patients in this group were treated incorrectly. HbA1c $< 6.5\%$ achieved only 30.0% patients, and recommended total cholesterol level < 175 mg / dl and LDL < 100 mg / dl, 27.6% 17.4% patients respectively. Assessment of musculoskeletal pathologies in people with RA and associated diabetes, accounting for diabetes complications, showed that patients with diabetes significantly more often than in the control group had cheiroarthropathy - isolated ($p < 0.001$) or coexisting with involvement of the shoulder ($p < 0.001$) and they occurred in more than half of patients with diabetes. Changes associated with diabetic limited joint mobility syndrome were significantly more often in the elderly, with longer-lasting diabetes and worse metabolic control.

Conclusions: Disorders of glucose metabolism in patients with rheumatoid arthritis are twice more likely than in the general population, and therefore RA patients should be regularly and routinely screened for diabetes. In the population of rheumatoid arthritis patients autoimmune diabetes is much more common than in the general population. The prevalence of autoimmune diabetes LADA with the presence of anti-GAD antibodies in RA-patients presenting with Type 2 diabetes is 13%. Patients with LADA are not phenotypically different from patients with type 2 diabetes, therefore the testing for anti-GAD autoantibodies should be considered as a part of diagnostic process in patients with rheumatoid arthritis and diabetes, especially in case of difficulty in obtaining good metabolic control. Insulin resistance indices determined under basal conditions confirmed that approximately 40% of patients with rheumatoid arthritis are insulin resistant. Patients should be educated in the field of prevention, diet and physical activity. In the vast majority of patients with rheumatoid arthritis vitamin D concentrations did not reach proper levels. All patients should have adequate vitamin D supplementation. Patients with RA and diabetes do not obtain good control of metabolic disorders, therefore treatment of comorbid diseases should be intensified to achieve target values both for glycemic and lipid disorders. The most common form of musculoskeletal changes occurring in patients with rheumatoid arthritis with concomitant diabetes is cheiroarthropathy and shoulder pain syndrome; these changes affect more than half of the patients. The presence of lesions characteristic for diabetic limited joint mobility in a

patient with RA requires a detailed diagnosis of diabetes, because these changes may precede the onset of clinical symptoms of hyperglycemia.

Keywords: rheumatoid arthritis, Type 2 diabetes, LADA, insulin resistance, diabetic cheiroarthropathy