

The Correlation among Osteoporosis, Calcium-Phosphore Metabolism and Clinical Symptoms of Main Disease in Patients with Rheumatoid Arthritis

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Abstract: 110 patients (25 women, 55.5%, 20 men, 44.4%) underwent clinical, laboratory and instrumental examinations to determine parameters of acute phase proteins, iron metabolism blood and bone tissue density in patients with rheumatoid arthritis. So, Physical examinations allowed to detect the specific clinical signs for OP in 17.2–48.0% of patients. Computed tomography with X-ray densitometry showed that 40% of patients had grade I of osteoporosis, 26.7% - grade II of osteoporosis, and 33.3% - grade III of osteoporosis. Hypocalcemia was characteristic of patients with OP. Chronic anemia (CA) was found in 53.7% of RA patients, iron deficiency anemia (IRA) in 39.6%, and both of them in 3.1%. CA leads to aggravation of the main disease, severity of anemia, and it is characterized by profound changes of hematological parameters.

Keywords: rheumatoid arthritis, osteoporosis, computed tomography with X-ray densitometry, hypocalcemia.

RELEVANCE OF THE TOPIC

Rheumatoid arthritis (RA) is a chronic autoimmune disease of the joints characterized by its erosive destruction. RA affects approximately 1% of the population of world [1,5]. In the first 5 years of the disease, more than 40% of patients with RA become disabled due to severe joint damage [2,6].

Osteoporosis (“hollow bone”) is a systemic skeletal process characterized by a decrease of bone mass, disruption of microarchitectonics of bone tissue, increased bone fragility, and growth of risk of bone fractures. Osteoporosis often results in fractures of the humerus, femor (neck), and spine (vertebral bodies) [3,11]. Osteoporosis develops in one out of two women and one out of three men over the age of 50, and socially concedes only to cardiovascular disease, cancer, and diabetes. The disease is more common in women than in men. The prevalence of the disease among women aged 61-70 years is 40-66%, and at the age of 71-89 years - 70-90% [7,9]. Osteoporosis is a background disease for the development of RA . Osteoporosis is the most severe and ubiquitous complication observed in antirheumatic therapy, including treatment with glucocorticoids (GC), methotrexate, sulfasalazine, and delagil [8]. Female gender, age of patients, low body mass index, low density of bone mineral (LDBM), family history, low physical activity, alcohol consumption, smoking, vitamin D and calcium deficiency, hypogonadism, early menopause, risk of long-term immobilization are main factors in the development of OP. Specific factors of RA in the development of OP are

the pathogenesis and course of RA, the systemic course of the disease, the involvement of internal organs in the pathological process. OP and osteoporotic fractures are ones of the most significant complications among other in rheumatoid arthritis [4,10].

Purpose of research is to study the correlation of osteoporosis in rheumatoid arthritis with the results of clinical-laboratory, calcium-phosphorus metabolism and instrumental examination.

MATERIALS AND METHODS OF EXAMINATION

The basis of our work was the materials of clinical, laboratory and instrumental examination of 110 patients aged 40 to 67 years treated with RA in the IIIrd therapy department of MASC (Medical Association of Samarkand city). The examinations included the complaints, anamnesis, general condition of all patients, as well as laboratory and instrumental methods in accordance with the standards. Additionally, the amount of calcium, phosphorus, alkaline phosphatase in the serum of all patients was checked in order to assess the development of osteoporosis in rheumatoid arthritis and to study the statement of metabolism of bone tissue in RA patients. The DAS28 index method was used to determine the RA activity criterion in all patients.

X-rays of the ankle joints and toes in direct projection and Bright Speed 16 MDCT CT densitometry of the lumbar region for diagnosis of secondary OP were used to determine the extent of damage of joint in RA. This test was developed by "General Electric" of the USA. The degree of osteoporosis and density of the lumbar spine as a function of age were determined based on a study conducted by O.R. Baratov (2013) in Samarkand region and in accordance with WHO recommendations. Densitometry of the lumbar spine was performed from the first to the fifth vertebrae (L1-L5). All metal objects were removed from the scanning area prior to examination. It was also noted that the presence of radiographic contrast agents (iodine, barium, thorium, X-ray notine catheters and tubes) had a negative impact on the quality of the imaging, so great care was taken to remove these artefacts in the scanning area initially.

RESULTS ANALYSIS

76 (69,1%) women and 34 (30,9%) men participated in our research, which showed that women suffered from this pathology twice as often. When we analyzed the clinical characteristics of patients with RA, the degree of disease activity was low in 12.7%, moderate in 45.4% and high in 41.9% of patients. Depending on the course of the disease the patients were divided into 2 groups: slow progression of the disease was seen in 67.3% of patients, rapid progression was seen in 32.5% of patients. Radiological studies revealed stage I-II in 65.5% and stage III-IV in 34.5% of patients. Serological examination revealed seropositive RF (+) in 77.2% and seronegative RF (-) in 22.8% of patients. Depending on the degree of joint dysfunction, the number of patients with grade I was 22.7%, grade II in 57.2% and grade III in 20% of patients. When analysing the indicators of acute phase proteins in serum, we observed their significant increase (Table 1). In particular the laboratory values of haptoglobin, ADCP and CRP were statistically significant, exceeding those of the healthy group by 2.75 ($p < 0.001$); 9.35 ($P < 0.001$) and 6.51 ($p < 0.001$) times, respectively. In the

comparison group, there was an increase of 2.74 ($p < 0.001$), 7.83 ($p < 0.001$) and 6.23 ($p < 0.001$) times, respectively, in the same parameters. Serum haptoglobin, ADCP and CRP concentrations increased 2.75 ($p < 0.001$), 9.83 ($p < 0.001$) and 6.54 ($p < 0.001$) in patients with RA and concomitant anaemia, respectively, relative to normal. It should be noted that serum haptoglobin and CRP levels did not differ in all groups, except for ADCP, whose concentration was 1.23 times ($p < 0.05$) higher than in the group without anaemia.

Table 1
Acute phase protein values in patients with RA in different groups, M \pm m

Groups	The amount of haptoglobin, gr/l	ACCP, U/ml	CRP, ng/l
Healthy group, n=20	1.21 \pm 0.11	4.32 \pm 0.28	2.71 \pm 0.18
Patients with RA, n=110	3.33 \pm 0.09 ^a	40.38 \pm 2.29 ^a	17.64 \pm 0.26 ^a
Comparison group, n=20	3.32 \pm 0.30 ^a	33.84 \pm 4.13 ^{a,b}	16.88 \pm 0.54 ^a
Main group, n=90	3.33 \pm 0.09	41.60 \pm 2.56	17.72 \pm 0.29

Note: a - significant relative to the healthy group, b - significant relative to the comparison group.

We also performed a comparative analysis of iron metabolism indicators (Table 2). Thus, the amount of free iron in the serum increased statistically by 2.58 ($p < 0.001$) times, the amount of ferritin increased by 1.53 ($p < 0.01$), and the amount of transferrin increased by 1.19 ($p < 0.05$) times in patients with RA. In the comparison group, the concentration of serum iron decreased by 2.16 ($p < 0.001$) and ferritin increased by 1.52 ($p < 0.001$), although transferrin did not differ from the norm. in the main group of patients, the amount of free iron in the blood serum decreased and was 2.65 times ($p < 0.001$) lower than the norm. The amount of ferritin increased by 1.58 times ($p < 0.001$). Serum transferrin levels remained statistically significant 1.22 ($p < 0.05$). The amount of free iron decreased by 1.23 ($p < 0.05$) times than in the comparative group, as well as the amount of transferrin - by 1.22 ($p < 0.05$) times, the amount of ferritin remained the same. Thus, changes in iron metabolism are observed in patients with RA, but it should be noted that it is more pronounced in patients with anemia.

Table 2
Values of iron metabolism in the blood of patients with RA, M \pm m

Groups	Values of iron metabolism in the serum relative to the group		
	Free iron, mmol/l	Ferritin, ng/ml	Transferrin, mg/dL
Healthy group, n=20	11.44 \pm 0.87	91.14 \pm 7.28	280.71 \pm 20.18
Patients with RA, n=110	4.43 \pm 0.04	139.02 \pm 1.85	234.92 \pm 2.87
Comparison group, n=20	5.30 \pm 0.10	138.39 \pm 5.48	280.50 \pm 6.09
Main group, n=90	4.32 \pm 0.04	144.16 \pm 1.97	229.37 \pm 2.85

Note: a - significant relative to the healthy group, b - significant relative to the comparison group.

When plasma calcium concentration were examined in patients with RA, 11.8% (13 people) of patients had its normal parameter (2.15-2.9 mmol/l), and calcium level of the remaining 88.2% of them were 1.6-1.9 mmol/l. The average calcium concentration was 1.8 ± 0.02 mmol/l. Consequently, it means that patients with RA had lower amount of calcium in the serum (Figure 1).

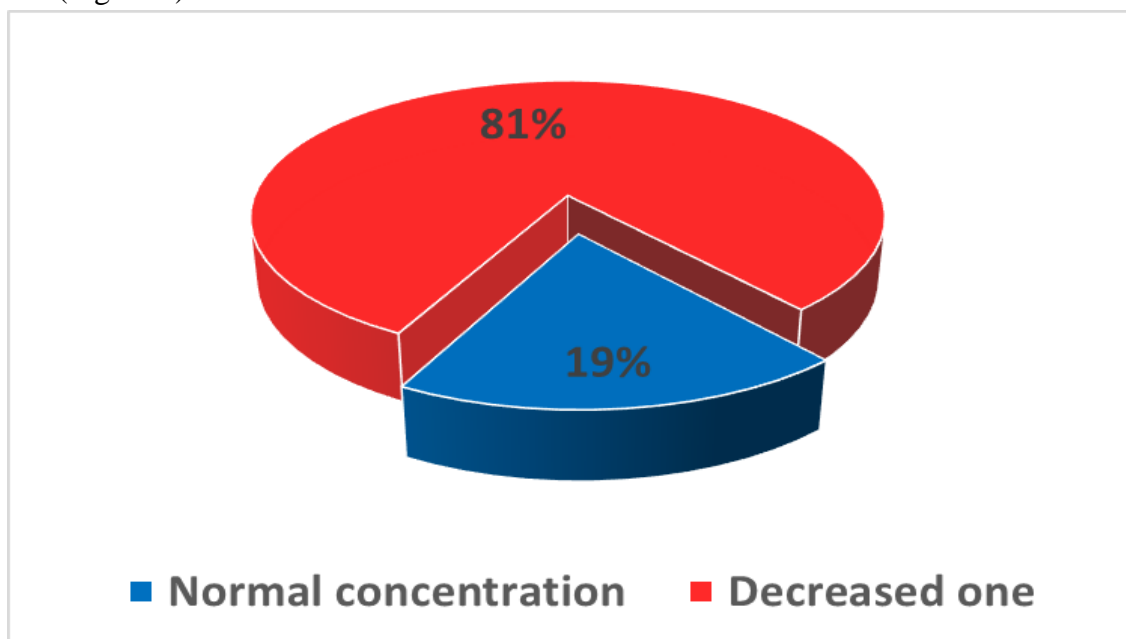


Figure 1. Calcium concentration in blood in patients with RA

Ist group patients with RA had the next amounts of substances in blood plasm: calcium - 1.9 ± 0.02 *, phosphorus - 1.19 ± 0.01 * and alkaline phosphatase - 190.5 ± 10.2 *, group II of them: calcium (mmol / l) 1.7 ± 0.02 *, phosphorus - 1.21 ± 0.02 *(mmol / l), alkaline phosphatase (iu/l) 191.4 ± 13.2 *.

The results of the analysis show that the average values of calcium, phosphorus and alkaline phosphatase had the same value in patients of Ist and IInd groups and was lower than normal.

Calcium level majorly confirmed the presence of OP in both groups of patients (bone density was lower than normal with age). The following levels of OP were detected in patients with HU coefficient of bone density:

I degree: bone tissue density according to HU: 41-50 years - 180-200; 51-60 years - 130-150; 61-70 years - 105-110 HU / cm²

II degree: bone tissue density according to HU: 41-50 years - 160-179; 51-60 years - 110-129; 61-70 years - 100-104 HU / cm²

III degree: bone tissue density according to HU: 41-50 years - 140-159; 51-60 years - 100-109; 61-70 years - 95-99 HU / cm²

The almost identical clinical signs in rheumatoid arthritis and osteoporosis suggest that the diagnosis of osteoporosis cannot be based solely on them. Also, the process of osteoprosis is usually latent for a long time, so the symptoms of the disease are not expressed. However, based on the results of our observations, we can suppose that that back pain during standing or moving is the main symptom of the disease. Later, back pain intensifies and bothers the patient even during lying down. Back pain is accompanied by pain in the ankles and legs,

which are non-permanent, volatile, had varying intensity, could be exacerbated by physical exertion and cold air. As the disease progresses, back pain becomes constant, makes walking difficult, leads to lameness, patients experience "duck walking" and decreased physical activity. Patients are bedridden and constantly in need of help from others.

Treatment and prevention of osteoporosis as a complication of RA is a serious problem. Thus, low physical activity, joint swelling and deformity, low intestinal calcium excretion, muscle atrophy and low body weight, and in most cases the use of glucocorticosteroids (prednisolone, etc.) in the treatment of RA lead to the development and intensification of osteoporosis. Therefore, a number of tasks are crucial for rheumatologists, such as early detection of the disease and initiation of treatment with basic and concentrated calcium drugs, modification of occupational activity, long-term standing, prevention of joint stress, maintaining body mass. In order to prevent the development of osteoporosis in RA, a number of measures should be taken to reduce mechanical stress on the joints, to ensure the safety of patients, to prevent injuries to patients, to protect organism from side effects of drugs.

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