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Original Article

MALONDIALDEHYDE, CALCIUM, PHOSPHORUS LEVELSIN RHEUMATOID ARTHRITIS PATIENTS

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Abstract:

Rheumatoid arthritis (RA) is an inflammatory polyarthritis, leading to joint destruction, deformity and loss of function. Rheumatoid arthritis (RA) is an autoimmune disorder, occurs when there are attacks of the immune system on body's tissues especially the joint, causing a painful, swelling, that finally results in bone deformity, increased free radical level in defect joint and reduce the level of the antioxidant system can cause tissue damage. Serum levels of lipid peroxides, calcium, and phosphorus in RA patients were determined and compared with normal healthy controls. Significant increases in lipid peroxides ($p<0.001$) phosphorus ($p<0.001$) levels were found in patients presenting with RA as compared to controls. Whereas significant decrease in calcium ($P<0.001$) were found in Rheumatoid arthritis patients as compared to controls.

Key words: Rheumatoid Arthritis (RA), Malondialdehyde, Calcium, Phosphorus-Reactive protein, Inflammation,

1. Introduction:

Rheumatoid arthritis (RA) is a chronic progressive autoimmune disorder characterized by symmetric erosive synovitis and sometimes shows multisystem involvement (1). Exact reason behind bone erosion and joint deformities is not fully understood. RA is associated with collection of chronic inflammatory cells occurring adjacent to bone with subsequent bone destruction. It is possible that generated oxygen derived free radicals may be important in bone resorption. (11) There may reduce calcium absorption in RA due to primary malabsorption process (12) prolonged inadequate intake, (10) effects of drugs on calcium metabolism, (8) decreases mean total body calcium levels in RA patients who did not receive corticosteroid drug strongly suggests that this is an integral feature of RA. (5,13)

Rheumatoid arthritis (RA) is a chronic progressive autoimmune disorder characterized by symmetric erosive synovitis and sometimes shows multisystem involvement (1).While lowered concentrations of antioxidants in the blood considerably increase the probability of the occurrence of RA (2). Many investigators have focused on oxidative stress since last few years and suggest that RA patients are more prone to lipid peroxidation (3).The calcium role is not clear in RA, however, the relationship between calcium, vitamin D, and parathyroid hormone suggests the possible role of calcium in RA and there is a change in mineral within bone which are calcium, and phosphorus (3). Changes in lipid profile have been observed in different inflammatory disease such as RA (4). RA patients are in increased risks of atherosclerosis and cardiovascular diseases (CVD) than the overall population (5).

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Bone contains both organic and inorganic material. The organic matter is mainly protein; the inorganic or mineral component is mainly crystalline hydroxyapatite {Ca10 (PO4)6(OH) 2}. Approximately of body's 99% Calcium and 85% Phosphorus are present in bone. The exact reason behind bone erosion and joint deformities is not fully understood.

This study was aimed to study MDA level as a marker of oxidative stress in patients with RA as well as the changes in Ca, and P level in recently diagnosed RA patients compared to healthy subjects and there is continuing interest in the metabolism.

2. Material and Methods:

The sample was collected at Sri Lakshmi Narayana Institute of Medical Sciences from a group of 50 patients with RA (25 male and 25 female), age (45-70 years). The control was diagnosed if they having any diseases such as diabetes, infectious diseases. RA was diagnosis based on clinical histories such as ESR and rheumatoid factor.

Statistical analysis:

Statistical analysis was done by using student t-test to compare between the two groups and statistically significance set at $p<0.05$. The data of this study were given as mean ± standard deviation. Results were diagnosed with rheumatoid arthritis at SLIMS hospital with 50 healthy people who represent controls. In this study patient with RA belonged to the age group of 45-70 years. Among patients of RA 25 patients were males and 25 were females as shown in table 1. The Mean±SD of age in males was 53.20±8.11 and the Mean±SD of the female was 55±11.2.

3. Results:

Table. 1: Serum levels of Malomdialdehyde (MDA), calcium, phosphorus and calcium/phosphorus in control subjects and rheumatoid arthritis patients.**(Mean ± SD).**

S.No	Parameters	No. of Subjects	Control Subjects	Rheumatoid Arthritis patients
1	Serum Malon di aldehyde (MDA) µmol/L	50	1.97 ± 0.66	4.86 ± 1.51*
2	Serum Calcium (mg/dl)	50	10.63 ± 1.84	7.95 ± 1.42*
3	Serum inorganic phosphorus (mg/dl)	50	2.91± 0.40	4.92 ± 0.90*

***P < 0.001**

Our resultsshow comparison of MDA, Calcium and Phosphorus levels in RA with control subjects. Statistically significant increase in levels of lipid peroxide ($P<0.001$) and phosphorus ($P<0.001$) whereas statistically significant decrease in Calcium ($P<0.001$) was found in patients of RA as compared to control subjects. whereas phosphorus level was increased significantly ($P<0.001$) in RA patients as compared to control subjects.

Discussion :

The diseases of the Musculo-skeletal system are common, disabling and costly to economy. Rheumatoid arthritis is a chronic systemic inflammatory disease affecting diarthrodial joints and frequently a variety of other organs. Formation of reactive oxygen species and lipid peroxides because of disease activity may play an important role in rheumatoid arthritis.

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Rheumatoid arthritis (RA) is an inflammatory polyarthritis, leading to joint destruction, deformity and loss of function. Extra-articular features and systemic symptoms usually occur and may accompany the onset of joint symptoms. Lower calcium level may be due to insufficient calcium intake and quicken osteoporosis, more sodium intake in our food may cause calcium depletion (6). Free radical that produced by ROS that case chronic inflammatory cells nearby bone with subsequent bone destruction (7). RA is usually associated with localized or generalized osteoporosis, erosions and hand and generalized bone mineral density (BMD) loss resulting in functional disability and increased risk of clinical fractures. Many drugs shave an affected-on calcium metabolism and cause a low level of calcium in RA. It was assuming that high level of phosphorous was related to tissue hypoxia with an elevated in ATP breakdown resulting in the release of inorganic phosphorous from cells. However, hypoxia create by hypertrophy and hyperplasia within synovial joints (8). It was observed that Calcium in RA a low level in serum whereas Phosphorous has shown a high level in contrast to control, that can be concluded to be a danger factor for RA cases. These results recommend to increase Mg, Ca, P in the dies with a supplement that might be helpful for a patient with RA. Further studying is necessary to estimate various biochemical markers that influences patient with RA. Statistical analysis by unpaired t test shows that the levels of serum calcium were decreased and phosphorus levels were increased statistically, which were highly significant ($p<0.0001$).Low calcium may be due to prolonged inadequate calcium intake and accelerated osteoporosis.In RA patients as compared to healthy controls. These results are in accordance with several other studies (9-13).

As calcium and phosphorous are important constituent of bone, ultimately bone metabolism is altered in RA, the event observed by many workers . Other studies shown Negative correlation between calcium/phosphorus ratio and lipid peroxide ($r = -0.76$) suggests that the generation of reactive oxygen species in excess may be particularly important in the bone resorption that occurs in association with inflammatory diseases (13).RA patients are vulnerable to steroid induced and disease associated osteoporosis. The high salt intake in our population may exacerbate calcium deficiency. At the proximal tubule, were sodium and calcium absorbs option are linked. Although not specifically studied, many disabled people rely heavily on pre-packed food and meals, much of which is high in sodium (14). RA is associated with collection of chronic inflammatory cells occurring adjacent to bone with subsequent bone destruction. It is possible that generated oxygen derived free radicals may be important in bone resorption (15). It is possible that, generation of reactive oxygen species may be particularly important factor for bone resumption in inflammatory process (16). Hypoxic conditions also disrupt an intracellular ionic environment and alter calcium and phosphorus level (17).There is an altered calcium and phosphorous metabolism in RA. As calcium and phosphorous are important constituent of bone, ultimately bone metabolism is altered in RA, the event observed by many workers (18-19).

Generation of reactive oxygen species is an important factor in the development and maintenance of rheumatoid arthritis (RA) in humans. MDA, the product of lipid peroxidation reacts with lysine residues in protein to produce immunogenic molecules, which can exacerbate inflammation (20-21). The longer chain polyunsaturated fatty acids are especially potent at increasing lipid peroxidation and causing cell damage by oxidative stress (22).RA is associated with collection of chronic inflammatory cells occurring adjacent to bone with subsequent bone destruction. It is possible that generated oxygen derived free radicals may be important in bone resorption.

It is postulated that the elevation of phosphorous was related to tissue hypoxia with an increase in ATP degradation resulting in the release of inorganic phosphorous from cells. In RA, hypoxic environment triggers oxygen free radicals generation and alters oxidative metabolism within the cell. It leads to disruption in intracellular ionic environment and altered calcium and phosphorus levels. Some authors suggest that hypocalcemia results due to drugs used in RA, but decreased mean total body calcium levels in RA patients who did not received that corticosteroid drugs strongly suggest that, this is an integral feature of RA (23-25).

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Conclusion:

Biochemical alterations in our study reflect the pathogenesis of RA and support the concept of oxidative stress leading to tissue damage and inflammation, which is evidenced by increased MDA levels. Calcium and Phosphorus level can be studied for the preferable therapeutic management of RA. In patients serum levels of calcium and calcium/phosphorus decreased and further studies on dietary management of calcium and phosphorus are needed. Increased oxidative threat in rheumatoid arthritis is evidenced by raised lipid peroxides. With a better understanding of the pathophysiology of RA, new therapeutic approaches are emerging to provide precision medicine for individuals. We conclude that in patient's serum levels of calcium and calcium/phosphorus decreased and further studies on dietary management of calcium and phosphorus are needed. This study also indicates a strong relationship between oxidative stress and inflammatory markers in RA. Further long-term, in-depth studies about this aspect may help in therapeutic management of RA patients, which may involve correction of inflammation along with correction of oxidative stress with exogenous antioxidants supplementation and dietary modifications.

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Conflicts Of Interest
The authors declare no conflict of interest.
References:

[1]. Taysi, S., Polat, F., Gul, M., Sari, R. A. and Bakan, V. (2002) Lipid peroxidation, some extracellular antioxidants and antioxidant enzymes in serum of patients with rheumatoid arthritis. Rheumatol. Int. 21, 200-204.

[2]. Sklodowska, M., Gromadzinska, J., Biernacka, M., Wasowicz, W., Wolkanin, P., Marszalek, A., Brozik, H. and Pokuszynska, K. (1996) Vitamin E, thiaobarbituric acid reactive substance concentrations and Superoxide Dismutase activity in the blood of children with juvenile rheumatoid arthritis. Clinical and experimental Rheumatology 14, 433-439.

[3]. SerdarOzturk, H., BurakCimen, M.Y., Bolgen Limen, O., Kacmaz, M. and Durak, I. (1999) Oxidant/antioxidant status of plasma samples from patients with rheumatoid arthritis. Rheumatol. Int. 19, 25-37.

[4] Steiner G, Urowitz MB, editors. Lipid profiles in patients with rheumatoid arthritis: mechanisms and the impact of treatment. Seminars in arthritis and rheumatism; 2009: Elsevier.

[5Kaplan MJ. Cardiovascular complications of rheumatoid arthritis: assessment, prevention, and treatment. Rheumatic Disease Clinics. 2010;36(2):40526.

[6] Stone J, Doube A, Dudson D, Wallace J, editors. Inadequate calcium, folic acid, vitamin E, zinc, and selenium intake in rheumatoid arthritis patients: results of a dietary survey. Seminars in arthritis and rheumatism; 1997: Elsevier.

[7] Garrett IR, Boyce BF, Oreffo R, Bonewald L, Poser J, Mundy GR. Oxygenderived free radicals stimulate osteoclastic bone resorption in rodent bone in vitro and in vivo. The Journal of clinical investigation. 1990;85(3):632-9.

ISSN:0975-3583,0976-2833 VOL 11, ISSUE 04,2020

[8] Walwadkar S, Suryakar A, Katkam R, Kumbar K, Ankush R. Oxidative stress and calcium-phosphorus levels in rheumatoid arthritis. Indian Journal of Clinical Biochemistry. 2006;21(2):134.

[9]. Walwadkar SD, Suryakar AN, Katkam RV, Kumbar KM, Ankush RD. Oxidative stress and calcium-phosphorus levels in rheumatoid arthritis. Indian J ClinBiochem 2006;21(2):134-137.

[10]6. Scott DL, Farr M, Howkins CF, Wilkinson R, Bold AM. Serum calcium levels in rheumatoid arthritis. Ann Rheum Dis 1981;40:580-583.

[11]. Ropes MW, Rossmeisl EC, Bauer W. Calcium and phosphorus metabolism in rheumatoid arthritis and degenerative joint disease. Research Paper from Harvard Medical School, Boston P.785-789.

[12]. Bramble MG, Blake DR, White T, Sly J, Kerr DN. Ionised calcium in rheumatoid arthritis: effect of nonsteroidal anti-inflammatory drugs. Br Med J 1980;281:840-841.

[13]. Verstraeten A, Dequeker J. Mineral metabolism in postmenopausal women with active rheumatoid arthritis. J Rheumatol 1986;13(1):43-46.

[14]. Stone J, Doube A, Dudson D, Wtallace J. Inadequate calcium, folic acid, Vitamin E, Zinc and selenium intake in rheumatoid arthritis patients: Results of a dietary survey. Semin Arthritis Rheum 1997;27(3):180-185.

[15]. Garrett IR, Boyce BF, Oreffo ROC, Bonewald L, Poser J, Mundy GR. Oxygen-derived free radicals stimulate osteoclastic bone resorption in rodent bone in vitro and invivo. J Clin Invest 1990;85:632-639.

[16]. Johannes, W. H., Bijlsma, M.D., Johannes, W.G. and Jacobs, M.D. (2000) Hormonal preservation of bone in rheumatoid arthritis. Neuroendocrine mechanisms in Rheumatic disease 26, 897-910.

[17]. Cheesman, K.H. and Slater, T.F. (1993) An introduction to free radical Biochemistry. Br. Med. Bull. 49(3), 481-93.

[18]. Verstraeten, A. and Dequekar, J. (1986) Mineral metabolism in postmenopausal women with active Rheumatoid arthritis. The Journal of Rheumatology 13 (1), 43-46.

[19]. Oelzner, P., Muller, A., Deschner, F., Huller, M., Ahendroth, K., Hein, G. and Stein, G. (1998) Relationship between disease activity of serum levels of vitamin D metabolites and PTH in Rheumatoid arthritis. Calcif. Tissue int. 62(3), 193-198.

[20]. Garrett, R., Boyce, B.F., Oretto, R.O.C., Bonewald, L., Poser, J. and Mundy, G.R. (1990) Oxygen derived free radicals stimulate ostoclastic bone resorption in Rodent Bone in Vitro and in vivo. J. Clin. Invest. 85, 632 - 639.

[21]. Bhogade, R.B., Suryakar, A.N., Katkam, R.V., Sardeshmukh, A.S., Rathi, D.B. (2002) Oxidative stress in Rheumatoid arthritis. Indian medical Gazatte 38-42.

[22]. Darlington, L.G. and Stone, T.W. (2001) Antioxidants and fatty acids in the amelioration of Rheumatoid arthritis and related disorders. Bri.Journal of Nutr. 85, 251-269.

[23].S.D. Walwadkar, A.N. Suryakar, R.V. Katkam, K.M. Kumbar and R.D. Ankush, Oxidative stress and calcium-phosphorus levels in rheumatoid arthritis, Indian J. Clin. Biochem., 21(2), 2006, 134-137.

[24].D. de Carvalho Pereira, R.P.A. Lima, R.T. de Lima, M. da Conceição Rodrigues Gonçalves, L.C.S.L. de Morais, S. do Carmo Castro Franceschini, R.G. Filizola, R.M. de Moraes, L.S.R. Asciutti and M.J. de Carvalho

ISSN:0975-3583,0976-2833 VOL 11, ISSUE 04,2020

Costa, Association between obesity and calcium: phosphorus ratio in the habitual diets of adults in a city of Northeastern Brazil: an epidemiological study, Nutrition J., 12, 2013, 90 (DOI: 10.1186/1475-2891-12-90).

[25]. Arieff, A.I. and Defronzo, R.A. (1985) Fluid electrolyte and Acid base disorders (1); Edited by Allen I. Arieff, Ralph and A. Defronzo. Section 1, Chapter 12, 625-659, published by Churchill Livingstone. 27. Reid, D.M., Kennedy, N.S.J., Smith, M.A., Tothill, P. and Nuki, G. (1982) Total body calcium in Rheumatoid arthritis effects of disease activity and corticosteroid treatment. BMJ. 285, 330-332.