Original Research Article

A study of inflammatory biomarkers in the patients of rheumatoid arthritis at tertiary health care centre

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Abstract

Background: Rheumatoid arthritis (RA) is a long-term autoimmune disorder that primarily affects joints. It typically results in warm, swollen, and painful joints. Pain and stiffness often worsen following rest. **Aims and Objectives**: To Study Inflammatory Biomarkers in The patients of Rheumatoid arthritis at tertiary health care centre**. Methodology:** This was a cross-sectional study carried out in the patients of Rheumatoid arthritis at tertiary health care centre during the one year i.e. January 2017 to January 2018 in the one year period there were 15 patients rheumatoid arthritis were confirmed by clinical and RA test were included into the study Group A and those who are not having disease confirmed clinically and RA test were enrolled to Group B . All details of the patients like age, sex, were noted . All the patients assessed by serological investigations for inflammatory biomarkers like hs-CRP (m/L), IL-6 (pg/mL) IL-10 (pg/mL), TNF-α(pg/mL) . The statistical analysis done by Chi-sqaure test, unpaired t-test calculated by SPSS 19 versions. **Result:** In our study we have seen that the average age of the patients in both the groups was 48.23 ± 3.45 and 49.23 ± 4.12 (p p>0.05, df=68, Unpaired - t= 1.74) was comparable to each other. The Female: Male sex ratio was 2:1 and 2.75: 1 was comparable to each other (X2=0.24, df=1, p>0.05) in both the groups. The inflammatory bio-markers like hs-CRP (m/L) were in Group A were significantly higher i.e. 9.23 ±3.45 and in Group B were 1.23 ± 0.92 (p<0.05); IL-6 (pg/mL)-60.12 ± 4.56 and 13.45 ± 5.12 (p<0.01); IL-10 (pg/mL) - 24.45± 5.12 and 14.52 ±6.72 (p<0.001);TNF-α(pg/mL)-48.42 ± 19.23 and 15.23 ± 6.54 (p<0.05) respectively. **Conclusion:** It can be concluded from our study that the majority of the patients in the age group of was 48.23 ± 3.45 Years, majority of the patients were Female. The inflammatory biomarkers like hs-CRP (m/L), IL-6 (pg/mL), TNF-α(pg/mL) were significantly higher in the Rheumatoid arthritis patients .

Key Words: Rheumatoid arthritis, Inflammatory Biomarkers , hs-CRP, IL-6 , TNF-α

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INTRODUCTION

Rheumatoid arthritis (RA) is a long-term autoimmune disorder that primarily affects joints.[1] It typically results in warm, swollen, and painful joints.[1] Pain and stiffness often worsen following rest.[1] Most commonly, the wrist and hands are involved, with the same joints typically involved on both sides of the body.[1] The disease may also affect other parts of the body.[1] This may result in a low red blood cell count, inflammation around the lungs, and inflammation around the heart.[1]Fever and low energy may also be present.[1] Often, symptoms come on gradually over weeks to months.[2]While the cause of rheumatoid arthritis is not clear, it is believed to involve a combination of genetic and environmental factors.[1] The underlying mechanism involves the body's immune system attacking the joints.[1] This results in inflammation and thickening of the joint capsule.[1] It also affects the underlying bone and cartilage.[1] The diagnosis is made mostly on the basis of a person's signs and symptoms.[2] X-rays and laboratory testing may support a diagnosis or

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exclude other diseases with similar symptoms.[1] Other diseases that may present similarly include systemic lupus erythematosus, psoriatic arthritis, and fibromyalgia among others.[2]RA primarily starts as a state of persistent cellular activation leading to autoimmunity and immune complexes in joints and other organs where it manifests The initial site of disease is the synovial membrane, where swelling and congestion lead to infiltration by immune cells. Three phases of progression of RA are an initiation phase (due to non-specific inflammation), an amplification phase (due to T cell activation), and chronic inflammatory phase, with tissue injury resulting from the cytokines, IL–1, TNF-alpha and IL–6.4 Non-specific inflammation Factors allowing an abnormal immune response, once initiated, become permanent and chronic. These factors are genetic disorders which change regulation of the adaptive immune response.[3] Genetic factors interact with environmental risk factors for RA, with cigarette smoking as the most clearly defined risk factor.[5,6,7]Other environmental and hormonal factors may explain higher risks for women, including onset after childbirth and hormonal medications. A possibility for increased susceptibility is that negative feedback mechanisms – which normally maintain tolerance – are overtaken by positive feedback mechanisms for certain antigens, such as IgG Fc bound by rheumatoid factor and citrullinated fibrinogen bound by antibodies to citrullinated peptides (ACPA - Anti–citrullinated protein antibody). A debate on the relative roles of B-cell produced immune complexes and T cell products in inflammation in RA has continued for 30 years, but neither cell is necessary at the site of inflammation, only autoantibodies to IgGFc, known as rheumatoid factors and ACPA, with ACPA having an 80% specificity for diagnosing RA.7 As with other autoimmune diseases, people with RA have abnormally glycosylated antibodies, which are believed to promote joint inflammation.[8]

Amplification in the synovium: Once the generalized abnormal immune response has become established – which may take several years before any symptoms occur – plasma cells derived from B lymphocytes produce rheumatoid factors and ACPA of the IgG and IgM classes in large quantities. These activate macrophages through Fc receptor and complement binding, which is part of the intense inflammation in RA.9 Binding of an autoreactive antibody to the Fc receptors is mediated through the antibody's N-glycans, which are altered to promote inflammation in people with RA.8

So, we have done Study of Inflammatory Biomarkers in The patients of Rheumatoid arthritis at tertiary health care centre

METHODOLOGY

This was a cross-sectional study carried out in the patients of Rheumatoid arthritis at tertiary health care centre during the one year i.e. January 2017 to January 2018 in the one year period there were 15 patients rheumatoid arthritis were confirmed by clinical and RA test were included into the study Group A and those who are not having disease confirmed clinically and RA test were enrolled to Group B . All details of the patients like age, sex, were noted. All the patients assessed by serological investigations for inflammatory biomarkers like hs-CRP (m/L), IL-6 (pg/mL) IL-10 (pg/mL), TNF-α(pg/mL) . The statistical analysis done by Chi-sqaure test, unpaired t-test calculated by SPSS 19 versions.

RESULT

Table 1: Distribution of the patients as per age in two different groups

	Group A(n=15)	Group B(n=15)	p-value
Average age (mean±SD)	48.23 ± 3.45	49.23 ± 4.12	p>0.05,df=68, Unpaired -t= 1.74.

The average age of the patients in both the groups was 48.23 ± 3.45 and 49.23 ± 4.12 (p p>0.05, df=68, Unpaired - t= 1.74) was comparable to each other.

Table 2: Distribution of the patients as per the sex

Sex	Group A(n=15)	Group B(n=15)	
Male	5	4	X^2=0.26, df=1,p>0.05
Female	10	11	

The Female: Male sex ratio was 2:1 and 2.75: 1 was comparable to each other (X^2=0.24, df=1, p>0.05) in both the groups.

Table 3: Distribution of the patients as per the various inflammatory Biomarkers

Biomarker	Group A	Group B	p-value
hs-CRP (m/L)	9.23 ±3.45	1.23 ± 0.92	p<0.05
IL-6 (pg/mL)	60.12 ± 4.56	13.45 ± 5.12	p<0.01
IL-10 (pg/mL)	24.45± 5.12	14.52 ±6.72	p<0.001
TNF-α(pg/mL)	48.42 ± 19.23	15.23 ± 6.54	p<0.05

The inflammatory bio-markers like hs-CRP (m/L) were in Group A were significantly higher i.e. 9.23 ±3.45 and in Group B were 1.23 ± 0.92 (p<0.05); IL-6 (pg/mL)-60.12 ± 4.56 and 13.45 ± 5.12 (p<0.01); IL-10 (pg/mL) - 24.45± 5.12 and 14.52 ±6.72 (p<0.001);TNF-α(pg/mL)-48.42 ± 19.23 and 15.23 ± 6.54 (p<0.05) respectively.

DISCUSSION

Rheumatoid arthritis (RA) is the most common autoimmune inflammatory arthritis, affecting approximately 1% of the population. Its etiology is unknown but it is presumed to be an immunologic disease

with contributing genetic and environmental factors, such as cigarette smoking [8] and reproductive factors in women.[9–12] A growing body of evidence suggests that there are three phases to the development of RA, an asymptomatic period of genetic risk, a preclinical phase in which RA-related autoantibodies can be detected [12, 13], and a clinical phase with acute signs and symptoms of inflammatory arthritis.[15] Similar phases of development have been proposed in other autoimmune diseases such as type 1 diabetes and systemic lupus erythematosus.[15, 16] In acute and chronic inflammation, cytokines are instrumental in regulating the magnitude and duration of the inflammatory response. Tumor necrosis factor α (TNFα), and interleukin-6 (IL-6) are pleiotropic cytokines produced predominantly by macrophages, that initiate the T cell and synovial proliferation, and are responsible for joint destruction in RA[17] ; and levels are elevated in the serum and the joints during active RA.[18–21] Since TNFα degrades rapidly in stored samples, we studied soluble TNF Receptor 2 (sTNFR2) levels. Soluble TNFR2 expression parallels TNFα levels and is a surrogate marker for inflammation[21].In our study we have seen that the average age of the patients in both the groups was 48.23 ± 3.45 and 49.23 ± 4.12 (p p>0.05, df=68, Unpaired - t=1.74) was comparable to each other. The Female: Male sex ratio was 2:1 and 2.75: 1 was comparable to each other (X^2=0.24, df=1, p>0.05) in both the groups. The inflammatory bio-markers like hs-CRP (m/L) were in Group A were significantly higher i.e. 9.23 ±3.45 and in Group B were 1.23 ± 0.92 (p<0.05); IL-6 (pg/mL)-60.12 ± 4.56 and 13.45 ± 5.12 (p<0.01); IL-10 (pg/mL) - 24.45± 5.12 and 14.52 ±6.72 (p<0.001);TNF-α(pg/mL)-48.42 ± 19.23 and 15.23 ± 6.54 (p<0.05) respectively. These findings are similar to Shrivastava AK [22], *et al*, they found significantly higher level of t RA patients had significantly higher levels of serum hs-CRP (p < 0.001), IL-6 (p < 0.001), TNF- (p < 0.001), and IL-10 (p < 0.01) as compared to healthy controls. hs-CRP, IL-6 and TNF- correlated positively (p < 0.001) and IL-10 correlated negatively (p < 0.01)

CONCLUSION

It can be concluded from our study that the majority of the patients in the age group of was 48.23 ± 3.45 Years, majority of the patients were Female The inflammatory biomarkers like hs-CRP (m/L), IL-6 (pg/mL), TNF-α(pg/mL) were significantly higher in the Rheumatoid arthritis patients .

REFERENCES

1. "Handout on Health: Rheumatoid Arthritis" (http://www.niams.nih.gov/health_info/Rheumatic_Disease/default.asp). National Institute of Arthritis and Musculoskeletal and Skin Diseases. August 2014. Archived (https://web.archive.org/web/20150630212818/http://niams.nih.gov/Health_Info/Rheumatic_Disease/default.asp) from the original on June 30, 2015. Retrieved July 2, 2015.
2. Majithia V, Geraci SA (2007). "Rheumatoid arthritis: diagnosis and management". Am. J. Med. 120 (11): 936–9. doi:10.1016/j.amjmed.200
3. Smolen, Josef S.; Aletaha, Daniel; McInnes, Iain B. (2016-10-22). "Rheumatoid arthritis". Lancet. 388 (10055): 2023– 2038
4. Shah, Ankur (2012). Harrison's Principles of Internal Medicine (18th ed.). United States: McGraw Hill. p. 2738.
5. Sugiyama, D.; Nishimura, K.; Tamaki, K.; Tsuji, G.; Nakazawa, T.; Morinobu, A.; Kumagai, S. (2010). "Impact of smoking as a risk factor for developing rheumatoid arthritis: A meta-analysis of observational studies". Annals of the Rheumatic Diseases. 69 (1): 70–81
6. Padyukov L, Silva C, Stolt P, *et al*. (2004). "A gene-environment interaction between smoking and shared epitope genes in HLA-DR provides a high risk of seropositive rheumatoid arthritis". Arthritis Rheum. 50 (10): 3085–92.
7. Hua, C; Daien, C. I; Combe, B; Landewe, R (2017). "Diagnosis, prognosis and classification of early arthritis: Results of a systematic review informing the 2016 update of the EULAR recommendations for the management of early arthritis". RMD Open. 3 (1): e000406.
8. Maverakis E, Kim K, Shimoda M, Gershwin M, *et al*. (2015). "Glycans in the immune system and The Altered Glycan Theory of Autoimmunity". J Autoimmun. 57 (6): 1–1
9. Costenbader KH, Feskanich D, Mandl LA, Karlson EW. Smoking intensity, duration, and cessation, and the risk of rheumatoid arthritis in women. Am J Med. 2006; 119(6):503 e1–503 e9.
10. Brennan P, Bankhead C, Silman A, Symmons D. Oral contraceptives and rheumatoid arthritis: results from a primary care-based incident case-control study. SeminArthritis Rheum. 1997; 26(6): 817–823.
11. Hannaford PC, Kay CR, Hirsch S. Oral contraceptives and rheumatoid arthritis: new data from the Royal College of General Practitioners' oral contraception study. AnnRheumDis. 1990; 49(10): 744–746.
12. Karlson EW, Mandl LA, Hankinson SE, Grodstein F. Do breast-feeding and other reproductive factors influence future risk of rheumatoid arthritis? Results from the Nurses' Health Study. Arthritis Rheum. 2004; 50(11):3458–3467.
13. Rantapaa-Dahlqvist S, de Jong BA, Berglin E, *et al*. Antibodies against cyclic citrullinated peptide and IgA rheumatoid factor predict the development of rheumatoid arthritis. Arthritis Rheum. 2003; 48(10):2741–2749.
14. Nielen MM, van Schaardenburg D, Reesink HW, *et al*. Specific autoantibodies precede the symptoms of rheumatoid arthritis: a study of serial measurements in blood donors. Arthritis Rheum. 2004; 50(2):380–386.
15. Majka DS, Holers VM. Can we accurately predict the development of rheumatoid arthritis in the preclinical phase? Arthritis Rheum. 2003; 48(10):2701–2705.

16. Leslie D, Lipsky P, Notkins AL. Autoantibodies as predictors of disease. J Clin Invest. 2001; 108(10):1417–1422.
17. Arbuckle MR, McClain MT, Rubertone MV, *et al*. Development of autoantibodies before the clinical onset of systemic lupus erythematosus. N Engl J Med. 2003; 349(16):1526–1533.
18. Feldmann M, Brennan FM, Maini RN. Role of cytokines in rheumatoid arthritis. [Review] [226 refs]. Annual Review of Immunology. 1996; 14:397–440.
19. Cope AP, Aderka D, Doherty M, *et al*. Increased levels of soluble tumor necrosis factor receptors in the sera and synovial fluid of patients with rheumatic diseases. Arthritis and Rheumatism. 1992; 35(10):1160–1169.
20. Steiner G, Studnicka-Benke A, Witzmann G, Hofler E, Smolen J. Soluble receptors for tumor necrosis factor and interleukin-2 in serum and synovial fluid of patients with rheumatoid arthritis, reactive arthritis and osteoarthritis. Journal of Rheumatology. 1995; 22(3):406–412.
21. Cutolo M, Montecucco CM, Cavagna L, *et al*. Serum cytokines and steroidal hormones in polymyalgia rheumatica and elderly-onset rheumatoid arthritis. Ann Rheum Dis. 2006; 65(11): 1438–1443.
22. Klimiuk PA, Sierakowski S, Latosiewicz R, *et al*. Interleukin-6, soluble interleukin-2 receptor and soluble interleukin-6 receptor in the sera of patients with different histological patterns of rheumatoid synovitis. Clin Exp Rheumatol. 2003; 21(1):63–69.
23. Dibbs Z, Thornby J, White BG, Mann DL. Natural variability of circulating levels of cytokines and cytokine receptors in patients with heart failure: implications for clinical trials. J Am Coll Cardiol. 1999; 33(7):1935–1942.
24. Shrivastava AK, *et al*. Inflammatory markers in patients with rheumatoid arthritis. Allergol Immunopathol (Madr). 2014.

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