TAJ December 2020; Volume 33 Number-2

ISSN 1019-8555
The Journal of
Teachers Association
RMC, Rajshahi

Original Article

Anemia of Chronic Disease in Rheumatoid Arthritis and its Relationship with Disease Activities

Md. Rofiqul Islam,[1] Md. Shafiqul Islam,[2] Mst. Musarrat Sultana[3]

Abstract

Background: Rheumatoid arthritis is the most common form of inflammatory arthritis. Anemia is a common extra-articular manifestation and anemia of chronic disease (ACD) is the most common form of anemia in rheumatoid arthritis that reduces the quality of life.

Objectives: The purpose of this study was to find out the prevalence of anemia of chronic disease (ACD) in Rheumatoid arthritis and to determine the relationship between ACD and disease activity of rheumatoid arthritis patients and to Identify the relationship between ACD and disease activity of rheumatoid arthritis patients.

Methods: This was an observational cross-sectional study was conducted at the Department of Medicine, Rajshahi Medical College Hospital, Rajshahi. Consecutive 165 patients of rheumatoid arthritis with anemia who fulfilled the inclusion and exclusion criteria were enrolled in this study.

Results: In this study mean age of these patients was 43.2±13.5 years. Male were 27(16.4%) and female 135(83.6%) with male: female ratio was 1:5.1. Most of the patients (29.1%) were illiterate, maximum participants (81.8%) were married and housewife 73.3%. DAS- 28 score (p< 0.001), tender and swollen joint count (p<0.001 for both tender and swollen joint count), ESR (p< 0.001) and HAQ score (p< 0.001) were significantly higher in anemic group of patients as compared to non-anemic. But there was no significant difference in terms of disease duration, morning stiffness and RF positivity between mentioned groups (p> 0.05). Comparing disease activity related characteristics between pure ACD and ACD with co-existent IDA sub group of patients, DAS 28 (p< 0.001), tender joint count (p= 0.03), swollen joint count (p= 0.03) and HAQ score (p= 0.03) were significantly higher in pure ACD patients than ACD and concomitant IDA patients with RA. But no significant difference was observed between two subgroups in terms of disease duration, morning stiffness, ESR and RF positivity (p> 0.05).Comparison of disease activity indices at different cut off levels between two groups and subgroups. Higher DAS- 28 score, tender joint count, swollen joint count and HAQ score was significantly found in anemic group of patients as compared to non-anemic. No significant difference was found between two groups at differing levels of morning stiffness (p= 0.337).

Conclusions: ACD is frequently encountered with high frequency of iron deficiency anemia among rheumatoid arthritis patients and RA patients with anemic tend to have more severe disease than non-anemic RA patients.

Key words: Anemia of chronic disease, rheumatoid arthritis, disease activity

TAJ 2020; 33: No-2: 85-93

[1] Assistant Professor, Department of Hepatology, Rajshahi Medical College, Rajshahi.
[2] Assistant Professor, Department of Gastroenterology, Rajshahi Medical College, Rajshahi.
[3] Resident Physician, Pediatrics, Rajshahi Medical College Hospital.

Introduction

Rheumatoid arthritis (RA) is an autoimmune disorder of unknown etiology characterized by symmetric erosive synovitis and in some cases extra-articular involvement.[1] The prevalence of RA is approximately 0.8% of the population (range 0.3%-2.1%). Women are affected approximately three times more often than men. It is a significant cause of disability and mortality and carries a high socioeconomic cost. Anemia is a common extra-articular manifestation of rheumatoid arthritis that reduces quality of life. The estimated prevalence of anemia in rheumatoid arthritis ranges from 33.3 to 59.1%.[2] In an Indian study, prevalence of anemia in RA is 71% which is higher western countries.[3] Improvement in hemoglobin levels is associated with significant improvement in quality of life of anemic patients with rheumatoid arthritis.[4]

Anemia in rheumatoid arthritis has multi factorial causes such as anemia of chronic disease (ACD) and iron deficiency anemia (IDA), which comprise the majority of forms.[5] ACD is more common than IDA in rheumatoid arthritis, occurring in up to 77% of anemic RA patients (Song et al 2001).[6] The exact mechanisms underlying ACD in rheumatoid arthritis is unknown but is possibly related to inflammatory cytokines, defective production of erythropoietin, reduced bone marrow response to erythropoietin or to defective reticulo-endothelial release of iron causing erythroblast iron deficit.[7]

Identification and differentiation of anemia in rheumatoid arthritis is important in planning diagnostic and therapeutic modalities. The tests most commonly used are serum ferritin, serum iron, Total iron binding capacity (TIBC), Transferrin saturation, Mean corpuscular volume (MCV) and reticulocyte count. In the general population, serum ferritin has been used as the most reliable indicator of iron deficiency.[8] It's value may be falsely high due to recent infections, inflammatory diseases, liver diseases or starvation. A higher cut off level of serum ferritin has been proposed to overcome this problem. Patients with serum ferritin levels > 50 µg/l are likely to have anemia of chronic disease (ACD) while those with a lower value of serum ferritin are likely to be iron deficient.[3] The anemia of chronic disease is primarily an anemia due to underproduction of red cells, with low reticulocyte production, and is most often a normochromic, normocytic anemia. However, in 30% to 50% of patients, the red cells are hypochromic and microcytic and most often, the serum iron, total iron-binding capacity, and transferrin saturation are reduced in the presence of adequate iron stores. Although the differential diagnosis includes other underproduction anemias, such as those caused by vitamin and mineral deficiencies, renal failure, endocrinopathies, and myelodysplasia, ACD is generally easily distinguished from these conditions. Nevertheless, an understanding of the pathogenesis of this condition, as well as a means of alleviating the anemia when the chronic disorder persists, has remained elusive.[10]

Estimates of the prevalence of mild anemia ranged between 33% and 60%; however, the 2 studies that examined demographics in patients with RA did not identify subpopulations at particular risk for anemia. Twelve articles assessed the impact of the resolution of anemia on symptoms and quality of life (QOL) in patients with RA. For many of the parameters assessed-including tender joint count, swollen joint count, DAS-28 score and HAQ score, a positive correlation was observed between improvement of symptoms and the resolution of anemia.[9] Patients with rheumatoid arthritis who have anemia are likely to have more severe joint disease than patients without anemia.[9] There are number of reports from different studies observed that anemia of chronic disease has been found to be associated with greater disease activity than iron deficiency anemia of rheumatoid arthritis patients.[10] In the present study, prevalence of anemia of chronic disease (ACD) among rheumatoid arthritis patients and relationship between ACD with disease activity of rheumatoid arthritis will be addressed.

Materials and Methods

The study was a cross-sectional analytical study which carried out in the Department of Medicine, Rajshahi Medical College Hospital, Rajshahi from September, 2015 to March, 2016. Sample size was 165. All patients fulfilling the inclusion and exclusion criteria were included in this study.

Patients fulfill American College of Rheumatology (ACR) 1987 revised criteria for rheumatoid arthritis and age- 18-70 years were included in this study. Patient age- <18, and >70 years, Known malignancy. renal failure, hemolytic conditions, pregnancy, lactating mother, other causes of chronic blood loss not related to RA (hemorrhoids, anal fissure, menorrhagia etc) were excluded from this study. Sampling technique was purposive sampling.

Results: in this study maximum 95(57.6%) patients were 31-50 years of age with mean age was 43.2±13.5 years. Male were 27(16.4%) and female 135(83.6%) with male: female ratio was 1:5.1. Most of the patients (29.1%) were illiterate, maximum participants (81.8%) were married and 73.3% were housewife. Comparison of disease and disease activity related characteristics between anemic and non-anemic RA patients are illustrated in Table- 3.7. DAS- 28 score ($p< 0.001$), tender and swollen joint count ($p<0.001$ for both tender and swollen joint count), ESR ($p< 0.001$) and HAQ score ($p< 0.001$) were significantly higher in anemic group of patients as compared to non-anemic. But there was no significant difference in terms of disease duration, morning stiffness and RF positivity between mentioned groups ($p> 0.05$). The entire hematological feature i.e. hemoglobin, MCV, MCH, MCHC and platelet count showed statistically significant difference between anemic and non-anemic group.

Table-1: Demographic characteristics of RA (n= 156)

Parameter	Frequency	Percentage (%)
Age in years		
18-20	9	5.5
21-30	25	15.2
31-40	53	32.1
41-50	42	25.5
51-60	29	17.6
61-70	7	4.2
Mean±SD	43.2±13.5 (18-67) years	
Sex		
Male	27	16.4
Female	138	83.6
Education		
Illiterate	48	29.1
Primary	37	22.4
SSC	32	19.4
HSC & above	48	29.1
Marital status		
Married	135	81.8
Unmarried	18	10.9
Others	12	7.3
Occupation		
House wife	121	73.3
Service holder	17	10.3
Student	7	4.2
Businessman	9	5.5
Labourer	6	3.6
Others (Driver, Cultivator, Mechanic etc)	5	3.0

Laboratory and disease activity parameters

Table- 2: Comparison of disease and disease activity related characteristics between ACD and non-anemic RA patients (n=165)

Disease and disease activity parameters	Anemic (n=97) Mean±SD	Non-Anemic (n=68) Mean±SD	*P-Value
Duration of disease (in month)	4.25±1.2	4.12±1.4	0.259
Hematological feature			
Hemoglobin (gm/dl)	9.2±1.2	14.1±1.1	< 0.001*
MCV (fl)	78.2±9.5	88.3±5.6	<0.001*
MCH (pg)	24.3±3.9	28.7±2.2	<0.001*
MCHC (gm/dl)	30.0±5.8	33.5±8.1	0.001*
Platelet count ($\times 10^9$/L)◆	280(190-450)	350(162-610)	< 0.001*
Disease activity parameters			
DAS 28	6.5±1.1	5.6±0.84	< 0.001*
Tender Joint Count	31.6±11.9	21.3±9.0	< 0.001*
Swollen Joint Count	4.4±3.7	1.9±2.4	< 0.001*
Morning Stiffness (in minutes)◆	90(10-300)	60(10-180)	0.100
HAQ	1.3±.83	0.83±0..33	< 0.001*
Erythrocyte Sedimentation Rate◆ (mm in 1st hour)	60(20-140)	40(10-105)	< 0.001*
RF (Positive)#	62 (63.9%)	39(57.4)	0.394
Drug used#			
NSAID	97(100.0%)	63 (92.6%)	0.006*
Steroid	35 (36.1%)	11 (16.2%)	0.005*
DMARD	53 (54.6%)	25 (36.8)	0.023*

p value reached from unpaired student's 't' test/χ^2 test, #No. (%), ◆Median (range), *significant

Table-3: Comparison of disease and disease activity related characteristics between pure ACD and ACD with co-existent IDA patients (n=97).

Disease and disease activity parameters	**Pure ACD (n=16)**	**ACD+IDA (n=81)**	***P-Value**
	Mean±SD	**Mean±SD**	
Duration of disease (in month)◆	30(09-120)	36(04-180)	0.16
Hematological feature			
Hemoglobin (gm/dl)	9.9±0.6	9.1±1.3	0.018*
MCV (fl)	85.6±4.4	76.4±9.6	< 0.001*
MCH (pg)	26.4±1.4	23.8±4.1	0.014*
MCHC (gm/dl)	30.8±6.9	30.8±7.8	0.98
Platelet count ($\times 10^9$/L) ◆	270(240-450)	265(160-610)	0.99
Disease activity parameters			
DAS 28	7.2±0.3	6.5±0.8	< 0.001*
Tender Joint Count	38.3±6.7	30.5±12.1	0.03*
Swollen Joint Count	6.6±2.7	4.0±3.8	0.03*
Morning Stiffness (in minutes) ◆	90(30-240)	90(30-300)	0.65
HAQ	1.6±0.5	1.3±0.5	0.031*
Erythrocyte Sedimentation Rate◆ (mm in1st hour)	60(50-110)	65(20-140)	0.61
RF (Positive)# No (%)	10(62.5%)	55(67.9)	0.674
Drug used# No. (%)			
NSAID	16(100.0)	81(100.0)	-
Steroid	2(12.5)	37(45.7)	0.013*
DMARD	8(50.0)	47(58.0)	0.553

*P values are based on unpaired 't' test /χ^2 test, #No. (%), ◆ Median (range)

Table showed the comparing disease activity related characteristics between pure ACD and ACD with co-existent IDA sub group of patients, DAS 28 (p< 0.001), tender joint count (p= 0.03), swollen joint count (p= 0.03) and HAQ score (p= 0.03) were significantly higher in pure ACD patients than ACD and concomitant IDA patients with RA. But no significant difference was observed between two subgroups in terms of disease duration, morning stiffness, ESR and RF positivity (p> 0.05).

Table-4: Comparison of disease activity indices at different cut-off levels between ACD and non-anemic RA patients.

Disease activity indices	Anemic (n=97)	Non anemic (n=68)	P value*
DAS-28			
3.2 – 5.1	7(7.2)	14(20.6)	0.011*
> 5.1	90(92.8)	54(79.4)	
Morning stiffness (in min)			
< 60	44(45.4)	36(52.9)	0.337
≥ 60	53(54.6)	32(47.1)	
Tender joint count			
0-10	3(3.1)	7(10.3)	
10-20	18(18.6)	29(42.6)	0.001*
20-30	35(36.1)	19(27.9)	
≥ 30	41(42.3)	13(19.1)	
Swollen joint count			
0-10	90(92.8)	68(100.0)	0.023*
10-20	7(7.2)	0(0.0)	
HAQ			
0-1	32(33.0)	60(88.2)	
1-2	57(58.8)	8(11.8)	<0.001*
2-3	8(8.2)	0(0.0)	

Values are No. (%), *p values are based on chi-square (χ^2) test.

Table showed the comparison of disease activity indices at different cut off levels between two groups and subgroups. Higher DAS- 28 score, tender joint count, swollen joint count and HAQ score was significantly found in ACD group of patients as compared to non-anemic. No significant difference was found between two groups at differing levels of morning stiffness (p= 0.337)

Discussion

This cross-sectional hospital based descriptive study was conducted among 165 patients with rheumatoid arthritis who admitted at the Department of Medicine, Rajshahi Medical College Hospital, Rajshahi during the study period. The study was aimed to find out the prevalence of anemia of chronic disease (ACD) in Rheumatoid arthritis and to determine the relationship between ACD and disease activity of rheumatoid arthritis patients.

In present study, the socio-demographic characteristics of RA patients are summarized, maximum 95(57.6%) patients were 31-50 yrs. The mean age was 43.2±13.5 years, male were 27(16.4%) and female 135(83.6%) cases. Female

were predominant in this study, male: female ratio was 1:5.1. A study done by Basak (2013)[13] demonstrate similar findings, mean (±SD) age was 41.2±12.2 years, 110 (84.6%) were female and 20 (15.4%) were male and female to male ratio was about 5.5:1.[13]

In present study the prevalence of anemia in RA is 58.9% which is comparable to the other studies; Basak (2013)[13] revealed 59%, Davis et al. (1997)[21] described 60%. The frequency of ACD and the relative frequency of co-existent IDA in rheumatoid arthritis patients similar to previous studies.[2,3,18] We observed higher prevalence of disease activity indices in ACD patients with RA as compared to non-anemic RA patients. Using cut off levels of different severity indices of RA did not show significant differences in the prevalence of pure ACD and ACD with co-existent IDA.

In our study estimated frequency of ACD was 58.9%. In various cross sectional studies, ACD has been reported to be present in 30% to 70% of patients with RA.[2,5,19,20] The difference in prevalence rate in various studies is related to the difference in the definition of anemia. In India, Borah et al. (2007)[17] showed that anemia (ACD) was present in 64% of patients, which is nearly comparable to present study. If the WHO criterion (men Hb $\leq$ 13gm/dl and women $\leq$ 12g/dl) has been used to define anemia, frequency of ACD in our study would be 86.5% which is much higher than prevalence reported in RA patients from western countries. This may be related to high background prevalence of anemia in our country as well as poor access to medical care leading to poor disease control of RA. We excluded various causes of anemia such as renal failure, hemolysis, pregnant and lactating mother, menorrhagia, hemorrhoids etc. otherwise actual frequency of anemia in RA would be much higher.

Identification and sub-classification of anemia in RA may be important in planning diagnostic and therapeutic modalities. The definitive method to distinguish between IDA and ACD is the assessment of stainable iron in bone marrow which is invasive, expensive and time consuming.[18] We have tried to use soluble transferrin receptor /log ferritin ratio (sTfR-F index) which we have been described as a promising new diagnostic tool to sub-classify pure ACD and IDA in anemic RA patients. Patients with sTfR-F index value < 1 were classified as pure ACD and sTfR-F index value >1 were classified as ACD with co-existent IDA.[22] Using this criteria, 16.5% patients were found to have pure ACD and 83.5% patients had co-existent IDA and ACD. Almost similar results were observed in Barak et al. (2013)[13] who revealed 16.0% patients were pure ACD and 84.0% patients had co-existent IDA and other similar study done Goyal et al. (2008)[18] who using these criteria, 20% patients were found to have pure ACD and 80% patients had coexistent ACD and IDA. Thus sTfR-F index should be utilized regularly to classify ACD when conventional laboratory test such as serum iron, transferrin /total iron binding capacity, transferrin saturation and serum ferritin are influenced by acute phase response.[22]

Ravindron et al. (2007)[23] showed that, among the anemic patients with RA, anemia was significantly worse in IDA group as compared to ACD group which was nearly similar to our study findings. Iron deficiency in RA is mainly related to non-steroidal anti-inflammatory drugs and steroid induced occult gastrointestinal blood loss. High female predominance (84.6%) and poor intake as well as other dietary factors may contribute to iron deficiency in RA patients from our study.

In present study, drug history that included NSAID, steroid and DMARD was also recorded and showed that anemic (ACD) RA patients more often received treatment with NSAID, steroid and DMARD's than non-anemic patients. No significant difference was observed in taking drugs between pure ACD and ACD with co-existent IDA subgroups of patients. Intake of drugs particularly NSAID and steroid may contribute to development of anemia in RA patients. These findings correlate with Basak (2013)[13] who similar results were focused.

We also assessed disease activity in both anemic (ACD) and non-anemic RA patients. A variety of parameters have been used for this purpose,

including DAS-28, tender joint count, swollen joint count, Bengali HAQ, morning stiffness, ESR, RF positivity etc. Agrawal et al. (2006)[3], Barak (2013)[13] and Borah et al. (2007)[17] found that anemic patients with RA had significantly higher mean DAS-28 score, tender joint count, swollen joint count, morning stiffness, mean ESR as compared to non-anemic patients which was nearly comparable to our study. We also found significantly higher mean HAQ score in anemic (ACD) RA patients than non-anemic patients with RA. Borah et al. (2007)[17]and Barak (2013)[13] reported similar study findings. Doube et al.[24] did not find statistically significant difference between mentioned groups in mean HAQ score. Agrawal et al. (2006)[3] also found significantly higher mean morning stiffness in anemic RA patients than non-anemic one which was not correlated with our study findings. Mentioned disease activity indices were compared with different cut-off levels between two groups. Most ACD patients (92%) have higher cut-off levels of DAS-28 (> 5.1) though moderate levels of DAS-28 (3.2-5.1) were significantly higher in non-anemic group. In terms of HAQ score, maximum percentage (67.5%) of patients with ACD have higher HAQ score (>1) which indicate ACD patients with RA are more disabled than non-anemic one. Tender and swollen joint count when compared with different cut-off levels was found to be significantly higher in RA patients with ACD. So it can be said that when disease activity indices were compared with mean values and different cut-off levels, it may reveal RA patients with ACD are more active as compared to non-anemic one.

In present study, the comparing disease activity related characteristics between pure ACD and ACD with co-existent IDA sub group of patients, DAS 28 ($p< 0.001$), tender joint count ($p= 0.03$), swollen joint count ($p= 0.03$) and HAQ score ($p= 0.03$) were significantly higher in pure ACD patients than ACD and concomitant IDA patients with RA. But no significant difference was observed between two subgroups in terms of disease duration, morning stiffness, ESR and RF positivity ($p> 0.05$). Mentioned disease activity parameters were also compared between pure ACD and ACD with co-existent IDA subgroups of patients with RA. We observed that patients with pure ACD had higher DAS-28 score, tender joint count, swollen joint count and HAQ score as compared to ACD with co-existent IDA sub group of patients with RA. The results were similar to that of other study.[3,13] Our study did not find significant difference in morning stiffness between mentioned subgroups which was almost similar to another study conducted by Doubel et al.[24]. But Agrawal et al.[3] found significantly higher morning stiffness in pure ACD group of patients than IDA patients with RA. When mentioned disease activity indices were compared between two subgroups with differing levels of disease activity, we found no significant difference between pure ACD and ACD with co-existent IDA patients with RA. This may be possibly due to smaller scale study in a tertiary hospital which may not represent whole population & interruption of disease activity by irregular intake of multiple drugs.

Conclusion

ACD is frequently encountered along with high frequency of iron deficiency anemia among rheumatoid arthritis patients. RA patients with ACD tend to have more severe disease than non-anemic RA patients. But, disease activity was not different in pure ACD and ACD with co- existent IDA patients with RA. Anemia is a common extra articular manifestation of rheumatoid arthritis and anemia of chronic disease is the commonest type of anemia in rheumatoid arthritis, however there is a high prevalence of iron deficiency anemia in RA in this part of country. Anemic patients tend to have more severe disease as reflected by high disease activity score and HAQ scores and thus there may be justification at early and aggressive treatment in this group of patients.

References

1. Harris ED. Rheumatoid arthritis: pathophysiology and implications for therapy. N Engl J Med. 1990; 322: 1277-89.

2. Remacha, A.F, Rodriguez-de-la Serna, A, Gracia-Die, F, Geli C, Diaz C, Gimferrer E. Erythroid abnormalities in rheumatoid arthritis: the role of erythropoietin. J Rheumatol. 1992; 19: 1687-1691

3. Agrawal S, Misra R, Aggarwal A. Anemia in rheaumatoid arthritis: high prevalence of iron deficiency anemia in Indian patients. Rheumatol Int. 2006; 26: 1091-1095.

4. Kaltwasser JP, Kessler U, Gottschalk R, Stucki G, Moller P. Effect of recombinant human erythropoietin and intravenous iron on anemia and disease activity in rheumatoid arthritis. J Rheumatol. 2001; 28: 2430-2366

5. Vreugdenhil G, Swaak AJ. Anemia in rheumatoid arthritis. Pathogenesis, diagnosis and treatment. Rheumatol Int. 1990; 9: 243-257.

6. Song JS, Park W, Bae SK, Kim SS, Lee YH., Choi JW, Kim SK. The usefulness of serum transferrin receptor and ferritin for assessing anemia in rheumatoid arthritis: Comparison with bone marrow iron study. Rhemotol Int. 2001; 21: 24-29

7. Means RT, Krantz SB. Progress in understanding the pathogenesis of anemia of chronic disease. Blood. 1992; 7: 1639-47.

8. Lipschitz DA, Cook JD, Finch CA. A clinical evaluation of serum ferritin as an index of iron stores. N Engl J Med. 1974; 290: 1213-1216.

9. Wilson A, Ting YH, Goodnoug, LT, Nissenson AR. Prevalence and outcomes of anemia in rheaumatoid arthritis: A systemic review of the literature. Am J Med. 2004; 116 (7A): 50-57.

10. Krantz SB. Pathogenesis and treatment of the anemia of chronic disease [Review]. Am J Med & Sci. 1994; 307: 353-9.

11. Sox HC, Liang MH. The erythrocyte sedimentation rate. Ann Internal Medicine. 1986; 104: 515-523.

12. Robert T, Means JR, Bertil G. Anemia: General considerations. Wintrobes clinical hematology, 12th edition, 2009; 26: 792.

13. Basak TB, Talukder SI. Anemia of Chronic Disease in Rheumatoid Arthritis and its Relationship with Disease Activities. Dinajpur Med Col J. 2013; 6 (2):113-122.

14. Hajar TL, Rostom S, Hari A, Lahlou R, Bahiri R, et al. Prevalence of Anemia and its Association with Parameters of Rheumatoid Arthritis Patients: A Study from the Moroccan Quest - RA Data. J Palliat Care Med. 2015; 5: 221.

15. Furst DE, Chang H, Greenberg JD, Ranganath VK, Reed G et al. Prevalence of low hemoglobin levels and associations with other disease parameters in rheumatoid arthritis patients: Evidence from the CORRONA registry. Clinical and Experimental Rheumatology. 2009; 27: 560-566.

16. Mital P, Goyal LK, Sherawat K, Agarwal A, Renu Saigal. Nutritional Status and its Relation with Disease Activity in Rheumatoid Arthritis: A Study from North India. Sch. Acad. J. Biosci. 2014; 2(11): 788-792.

17. Borah DJ, Iqbal F. Anemia In Recent Onset Rheumatoid Arthritis. J K Science. 2007; 9(3): 120-123.

18. Goyal R, Das R, Bambery P, Garewal G. Serum transferrin receptor- ferritin index shows concomitant iron deficiency anemia and anemia of chronic disease is common in patients with rheumatoid arthritis in North India. Indian J Pathol Microbiol. 2008; 51:102-4.

19. Hansen TM, Hansen NE, Birgens HS. Serum ferritin and the assessment of iron deficiency in rheumatoid arthritis. Scan J Rheumatol. 1983; 12: 353-359.

20. Baer AN, Dessypris EN, Krantz SB. The pathogenesis of anemia in rheumatoid arthritis: a clinical and laboratory analysis. Semin Arthritis Rheum. 1990; 19: 209-23.

21. Davis D, Charles PJ, Potter A, Feldann M, Maini RN, Elliott MJ. Anaemia of chronic disease in rheumatoid arthritis: in vivo effects of tumour necrosis factor Alfa blockade. British Journal of Rheumatology. 1997; 36: 950-956.

22. Punnonen K, Irjala K, Rajamaki A. Serum transferrin receptor and its ratio to serum ferritin in the diagnosis of iron deficiency. Blood. 1997; 89: 1052-9

23. Ravindran V, Jain S, Mathur DS. The differentiation of anaemia in rheumatoid arthritis: parameters of iron-deficiency in an Indian rheumatoid arthritis population. Rheumatol Int. 2007; 28:507-511.

24. Doube A, Davis M, Smith JG, Maddison PJ, Collins AJ. Structured approach to the investigation in patients with rheumatoid arthritis. Ann Rheum Dis. 1992; 51:469472

All correspondence to
Md. Rofiqul Islam
Assistant Professor
Department of Hepatology
Rajshahi Medical College, Rajshahi
Email: smairofiq@gmail.com