Original Article

Anemia in Rheumatoid Arthritis Patients

Frequency of Anemia in Rheumatoid Arthritis Patients Presenting in Various Hospitals of Peshawar, Khyber Pakhtunkhwa

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ABSTRACT

Objective: Anemia is a chronic complication of rheumatoid arthritis that is produced by a number of causes.Very little interest in research is shown in this field by researchers both nationally and internationally. The main objective of the study was to determine the frequency of anemia in rheumatoid arthritis patients.

Study Design: Descriptive, cross sectional study.

Place and Duration of study: This study was conducted at the Hayatabad Medical Complex (HMC), Rehman Medical Institute (RMI) and Khushal Medical Center, Peshawar, from April 2015 to March 2016.

Materials and Methods: Two hundred and thirty patients with rheumatoid arthritis visiting medical outdoor clinics in different hospitals of Peshawar were enrolled from April 2015 to March 2016. Detailed history was taken and clinical examination was performed. After taking consent, diagnosis of anemia was madeby performing peripheral smear tests using digital sysmex XT-4000i hematology analyzer. The identity of patients was kept confidential. The demographic informations such as name, age and gender were recorded.

Results: Among 230 patients, with mean age of 50 years, male-female ratio was 30%(n=70) and70%(n=160) respectively. Anemia was diagnosed in 26%(n=60) patients, while 74%(n=170) patients had no anemia among the study group. Out of 60 patients with anemia, 30%(n=18) patients were male and 70%(n=42) patients were female. Anemia association with the duration of rheumatoid arthritis was analyzed, which shows that anemia increases as duration of rheumatoid arthritis increases

Conclusion: It is concluded from the study that rheumatoid arthritis is a chronic disorder affecting multiple organs of the body and anemia is a well-known significant complication of rheumatoid arthritis as shown by the results of this study.

Key Words: Rheumatoid arthritis, anemia, hematology analyzer

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INTRODUCTION

Rheumatoid arthritis is a chronic autoimmune disorder, affecting almost every organ system of the body and need lifelong treatment. Both the disease and its treatment have got significant hematological complications, "including anemia, leukopenia and thrombocytopenia". There are multiple causes of anemia in patients with rheumatoid arthritis including "anemia due to inflammatory mediators, anemia of chronic disorder, macrocytic anemia due to methotrexate and other anti-rheumatic drugs, anemia due to gastro-intestinal bleeding as adverse effect of painkiller and steroids, anemia due to renal involvement and anemia due to poor appetite"[1,2]. There are a number of inflammatory cytokines including interleukin-10, ilterleukin-1B and interleukin-6 (IL-6), which have profound effect on iron metabolism and development of anemia in rheumatoid arthritis"[3,4,5].They facilitate "production of hepcidine, which is a peptide produced by liver leading to disturbed metabolism of iron via ferroportin and anemia of chronic inflammatory disease". That is why "treatment of rheumatoid arthritis by targeting cytokines improves hematological picture of the patients"[3,4].It has been observed that anemia is a significant hematological complication of rheumatoid arthritis. However, no research data are available in Pakistan regarding this association. Keeping in mind this important association, this study was conducted to determine the association of anemia with rheumatoid arthritis, so that physicians can anticipate anemia earlyand enhance patient care by supplementing iron

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and targeting the possible cause. Considering "anemia as important complication of rheumatoid arthritis can reduce morbidity, functional disability and disease related other complications"[6].

MATERIALS AND METHODS

This study was conducted in Hayatabad Medical Complex (HMC), Rehman Medical Institute (RMI) and Khushal Medical Center, Peshawar, from April 2015 to March 2016. Two hundred and thirty patients were selected by non-probability consecutive sampling, having rheumatoid arthritis for a minimum of 5 years with age of ≥20 years, comprising 30% male and 70% female patients. All those patients who had bleeding disorder, history of major gut and stomach surgery, concomitant other major chronic disease like diabetes mellitus and chronic renal failure were excluded from the study. The patients with hematological and solid organ malignancy were excluded from the study. The descriptive- cross sectional design was used in the study.

Data Collection: The patients with rheumatoid arthritis, visiting outdoor clinics of different public and private hospitals of Peshawar fulfilling the inclusion criteria were enrolled in the study in a consecutive manner. Ethical committee approval was obtained. Informed consent was taken from the subjects for undergoing peripheral smear test. Patient's identity was kept confidential and risk and benefits of the study were explained to the subjects. The demographic information of the subjects such as name, age and gender were recorded. Peripheral smear tests were performed using digital sysmex XT-4000i hematology analyzer. All patients with hemoglobin (Hb) recorded as<12gm/dL in case of males and< 11gm/dL in case of females were labeled as having anemia. All collected information was recorded on pre-designed performa.

Data Analysis: Data were entered and analyzed by using SPSS version 17.0 statistical program. The data were expressed as mean and presented in a tabulated form.

RESULTS

Out of 230 studied patients, 30 %(n=70) were males and 70 %(n=160) were females, with mean age of 50±1.26 years. Age distribution among 230 patients was analyzed as n=18(8%) patients were in age group of20-30 years, n=35(15%) patients were in age group of 31-40 years, n=92(40%) patients were in age group of 41-50 years, n=69(30%) patients were in age group of 51-60 years and n=16(7%) patients were above 61 years of age as shown in Table No. 1.

Status of anemia among 230 patients was analyzed as n=170(74%) patients with normal Hb, while in n=60 (26%) patients, Hb was below normal level, as<12gm/dL(in case of males) and <11gm/dL(in case of females) as shown in Table No. 2.

Mean duration of rheumatoid arthritis among the study populationwas 11 years with standard deviation of ± 2.14.

Age groups of rheumatoid arthritis patient having confirmed anemia were further analyzed as shown in Table No. 3. Among 60 patients with anemia, n=01 patient was in age range of 20-30 years, n=03 patients were in age range of 31-40 years, n=28 patients were in age range of 41-50 years, n=20 patients were in age range of 51-60 years, and n= 08 patients were in age range of >61 years.

Table No.1: Age distribution of study population

Age	Frequency	Percentage
20-30 Years	18	8%
31-40 Years	35	15%
41-50 Years	92	40%
51-60 Years	69	30%
> 61 Years	16	7%
Total	**230**	**100%**

Table No.2: Anemia distribution in study population

Hemoglobin ratio	Frequency	Percentage
Normal range	170	74%
Anemia range	60	26%
Total	**230**	**100%**

Table No.3: Association of anemia with different age groups

Anemia presence	20-30 Years	31-40 Years	41-50 Years	51-60 Years	>61 years	Total
Yes	01	03	28	20	08	60
No	17	32	64	49	08	170
Total	18	35	92	69	16	230
p-value						**0.002**

Table No.4: Association of anemia with duration of rheumatoid arthritis

Presence of Anemia	Duration of rheumatoid arthritis			Total
	5-15 Years	16-25 Years	>25 Years	
Yes	25	23	12	60
No	115	53	02	170
Total	**140**	**76**	**14**	230
p-value				**0.003**

Table No.5: Anemia Distribution in different sex groups

Sex groups	Frequency	Percentage
Male (i.e. Hb<12 mg/dL)	18	30%
Female (i.e. Hb<11 mg/dL)	42	70%
Total	**60**	**100%**

Anemia association with the duration of rheumatoid arthritis was analyzed, which shows that anemia

increases as duration of rheumatoid arthritis increases (Table No. 4).

Among 60 patients with anemia and rheumatoid arthritis, n=18(30%) patients observed were males and n= 42(70%) were females (Table No. 5).

DISCUSSION

Anemia in rheumatoid arthritis has attracted growing interest as a potential complication of this chronic inflammatory disease. Many cross sectional studies, conducted on this topic have consistently shown that "all adults especially female with rheumatoid arthritis have some level of iron deficiency than their normal counterparts and significant number of these patients develop frank anemia of sometype"[7].

In our present study, 26% patients had frank anemia, while the rest 74% had Hb levels less than normal individuals, but was not falling in the defined range for anemiawhichwasclose to the study results of Wolfe and Santen, who found that anemia was present in31.5% and 37.7% patients respectively[8,9]. There is another community- based study conducted on adultpatients with rheumatoid arthritis by Agrawal S. et al,2006, and it was found that rheumatoid arthritis caused anemia up to some level in more than 70% of patients. Iron replacement and treatment of the underlying disease can prevent this complication of rheumatoid arthritis[10].In another study conducted by Yildirim K et al.2004, showing that "severity of anemia is also related with the disease activity which can be measured by Disease Activity Score 28 (DAS 28). The more is the DAS 28score and raised level of ESR and CRP, the more severe is the anemia and thus showing very good response to the treatment of underlying disease"[11].There is another study conducted by Han et al., which shows "that more severe anemia at baseline was associated with more severe physical disability and thus increase of Hb with treatment was an independent predictor of improvement in physical function of the patient" [12]. Going into detailed research revive and advanced study, it was found that although the underlying mechanism relatedto pathogenesis of anemia in rheumatoid arthritis is multi factorial and still needs confirmation, but it also became clear"that each patient with rheumatoid arthritis has different single or multiple mechanisms for the development of anemia"[13].Various studies suggest several possible mechanisms for the development of anemia in rheumatoid arthritis. The causative mechanism include;

1. Disturbed iron metabolism due to IL-6, IL10 and other cytokines.
2. Anemia of chronic disease.
3. Poor intake of iron and diet due to loss of appetite, chronic disease and depressed mood in these patients.
4. Loss of iron due to bleeding peptic ulcer as a complication of steroids, NSAIDs and anti-rheumatic drugs[14].
5. Anemia due to renal involvement in rheumatoid arthritis and deficiency of erythropoietin.
6. Megaloblastic anemia as a complication of direct anti-rheumatic drugs like methotrexate.

There are some limitations of present study including, hospital-based population, cross-sectional study design, lack of data on potential confounders and poor addressing of different inflammatory markers that can potentially decrease precision of our estimates. Finally, the prevalence of anemia in rheumatoid arthritis especially in female patients leaves concern about the possibility of confounding, as number of parity and socioeconomic background may have impact on the development of iron deficiency in these patients. The strength of our study can be improved by using "multivariate study analysis, taking into account the potential confounders by using logistic regression and using a case control study design for comparing type of anemia nature in rheumatoid patientswith anemia in normal population". All these findings make it clear that "anemia should be considered as a potential complication of rheumatoid arthritis and every patient with rheumatoid arthritis must be treated for anemia to improve this/her physical functionality". However, the clinical relevance of these findings, in terms of the development of anemia has yet to be precisely ascertained.

CONCLUSION

Rheumatoid arthritis is a chronic inflammatory disorder affecting almost every organ of the body and anemia is a known significant complication of this disease. Further study is suggested, both at national and international levels to explore this problem, designtools for early diagnosis and proper treatment to decrease the suffering of the patients.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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