



SYSTEMIC HYPERTENSION IN RHEUMATOID ARTHRITIS

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ABSTRACT There is a significantly higher cardiovascular mortality in Rheumatoid arthritis (RA) patients compared to general population. High prevalence of traditional cardiovascular risk factors like hypertension along with persistent chronic inflammation of vascular endothelium due to high disease activity is thought to be responsible for higher CVD-related morbidity in RA. Another contributing factor could be the widespread use of glucocorticoids, which increase carotid intimal thickening. There are only few studies among Asians on the prevalence of hypertension in RA. Here we describe the prevalence of hypertension in RA patients compared to general population and the effect of corticosteroids on their blood pressure.

Methods: The study was conducted at a Government Medical College in North Kerala, India. RA Patients aged between 16 and 80 years who satisfied the ACR-EULAR 2010 criteria attending the Rheumatology clinic during a period of 1 year were studied in comparison with age and sex matched controls.

Results: There is statistically significant difference (p value 0.003) in the prevalence of hypertension in the RA group (36%) and controls (14.7%). Corticosteroids did not contribute to the development of hypertension in RA patients in our study.

Conclusions: This study highlights the need for control of hypertension in RA patients to improve CVD outcome.

KEYWORDS : Hypertension, Rheumatoid Arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease with both articular and systemic manifestations. Mortality rates in RA is around twice that of general population and is mostly due to premature atherosclerosis-related cardiovascular disease (CVD). Traditional CVD risk factors (hypertension, smoking and dyslipidemia) are responsible for around half of all coronary heart disease (CHD) events in general population. Higher CVD related mortality in RA is due to the combined effect of persistent chronic active inflammation on vascular endothelium secondary to poor disease control along with the increased burden of traditional CVD risk factors. Patients with RA are more prone to recurrent cardiac events and have higher mortality after acute cardiovascular events.¹

Hypertension is one of the most important modifiable risk factors for the development of CVD in the general population.² It affects around 1 billion population worldwide and around 30% of the adult population. Though the reported prevalence of hypertension among RA patients varies widely from 34% to 73%, it is largely under-diagnosed and under-treated.³ The most convincing evidence comes from a large study by Han *et al* involving 28,000 RA patients and almost 113,000 age matched controls in which prevalence of hypertension was significantly higher in RA (34% vs 23.4%).⁴ Several studies in RA patients have demonstrated that hypertension is associated with subclinical atherosclerosis and is one of the most significant independent predictors of CVD. Using data from the Framingham Heart Study in the United States and the Third National Health and Nutrition Examination Survey (NHANESIII), Singh *et al.* projected that a 20mmHg increase in systolic blood pressure (SBP) in RA patients would result in 1572 additional CVD events.⁵ Since RA patients have higher CV mortality compared to matched non-RA controls, the number of deaths that can be attributed to hypertension may be higher amongst RA patients.

Despite the high prevalence of hypertension and the impact of its complications, control of hypertension is far from adequate both in the general population and RA.⁵ In a recent study, the rate of controlled hypertension in RA was significantly lower at 13.2% than the 21–23% observed in the general population.⁶ This is in line with several studies on RA patients, which report prevalence of treated hypertension between 22–34%, a figure much lower than the aforementioned prevalence of hypertension in RA.

In the general population, optimal anti-hypertensive therapy reduces the mortality by 40% in stroke, 20% in MI and >50% in heart failure, emphasizing the importance of optimal BP control in any population,

including RA. NSAIDs used in the management of RA may have deleterious effects on BP control and renal function, and should be avoided as far as possible especially in patients with serum creatinine levels above 2.5 mg/dl or those with known CVD or at risk for CVD.⁷

Some DMARDs like Leflunomide (LEF) can induce hypertension. LEF related hypertension is found in 2–4.7% of prescribed patients even in the absence of renal function abnormalities. A small longitudinal study of consecutive patients on stable doses of NSAIDs and corticosteroids revealed significant increases in SBP and DBP occurring within first 2–4 weeks of LEF therapy.⁸ The mechanisms by which LEF induces hypertension include an increase in sympathetic drive and displacement of free fraction of concomitant NSAIDs from protein binding, increasing NSAID's effect on renal blood flow and retention of salt and water.⁹ So if RA is diagnosed in a person with hypertension (or conversely, when a person with established RA develops hypertension), the choice of DMARD must be carefully considered. The concurrent use of NSAIDs/coxibs and/ or steroids may further exacerbate these side-effects.

Effective management of one of the most important CVD risk factor like hypertension will go a long way in drastically reducing mortality in RA.

The impact of conventional risk factors like hypertension on the development of CVD in RA patients is an area of active interest to the researchers. Very few data is available from India about the prevalence of conventional cardiovascular risk factors like hypertension in RA. Hence we have taken up the study of role of HT as an added cause for CVD in RA patients by comparing with age and sex matched controls.

Materials and methods

The study was conducted at Government Medical College, Calicut which is the largest tertiary referral hospital in North Kerala, India. RA patients (16 to 80 years) who satisfied the ACR-EULAR 2010 criteria¹ attending the Rheumatology clinic during one year period were studied. Patients with pre-existing CHD or hypertension prior to the onset of RA were excluded. The study was approved by the Institutional Ethics Committee, and signed informed consent was taken from all patients. There were 75 patients in the study group and 75 age and sex matched controls. The study measured blood pressure of both RA patients and controls.

Hypertension is defined according to the Joint National Committee on Prevention, Detection, Evaluation and Treatment of Hypertension Guidelines as blood pressure >140/90 mm Hg.

Results

80% of the 75 patients in the study group and 77% of age and sex matched controls were females. This reflects the female preponderance of the disease in our population.

Table 1 Age distribution of RA patients and controls

Age group (Years)	Controlsn (%)	Cases n(%)
<40 years	13 (17.3)	13 (17.3)
40 to 49	25 (33.3)	24 (32.0)
50 to 59	26 (34.7)	25 (33.3)
60 and above	11 (14.7)	13 (17.3)

17.3% patients were below 40 years, 32% were between 40-50 years, 33.3% were 50-60 years and rest were above 60 years. Majority of patients were in the middle age groups.

35% of the RA patients had a disease duration of less than 2 years, while in 33% patients, the duration was between 2-4 years, and in 25% 5-9 years. Only 7% had more than 10 year disease duration.

RA disease activity was assessed using a composite DAS28 score (Disease Activity Score), which included tender joint count, swollen joint count, ESR and patient global assessment of pain.² DAS 28 score less than 2.4 indicates clinical remission, 2.4-3.2 indicate mild disease activity, 3.3-5.1 moderate disease activity and more than 5.1 severe disease activity.

56% of RA patients had mild disease activity while 16% had moderate and 9.3% had severe disease activity. 18.6% patients were in clinical remission.

Prevalence of hypertension

27 RA patients (36%) were hypertensive whereas only 11(14.7%) in the control group had hypertension (Fig 1), the difference being statistically significant (p=0.003). Mean systolic and diastolic blood pressures were also higher in the RA group compared to controls (p=0.001)(Table 2).

The possible role of corticosteroids in development of hypertension was analysed. There was no statistically significant difference in the development of hypertension among steroid users and non-users (p=0.182)(Table 3).

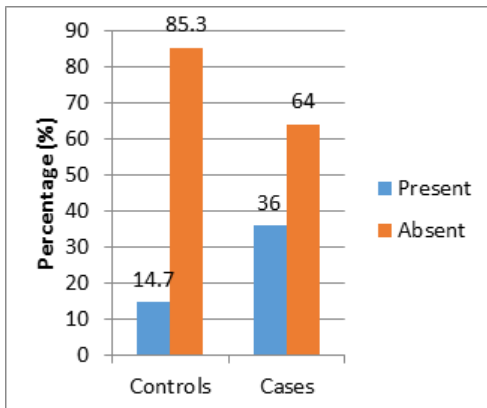


Fig 1 Prevalence of hypertension

Table 2 Mean blood pressure in study and control population

Blood pressure	Control		Cases		p value
	Mean	SD	Mean	SD	
Systolic BP	135.1	14.5	148.6	22.0	0.001
Diastolic BP	80.4	9.6	86.9	13.6	0.001

Table 3: Effect of steroids use on hypertension

Steroid	Hypertension		p value
	Present n (%)	Absent n (%)	
Present	15 (30.6)	34 (69.4)	0.182
Absent	12 (46.2)	14 (53.8)	

Discussion

In our observational case control study to assess prevalence of hypertension in RA, 75 RA patients were compared with age and sex

matched controls. 80% of our patients were female which is consistent with the results of several studies on RA.²

Majority of RA patients (65.3%) were between 40-60 years. The duration of the disease was less than 2 years in 35% and between 2-5 years in 33%. Majority patients (56%) had low disease activity as evidenced by DAAS28 score of 2.4-3.2 and 18.6% were in clinical remission while 9.3% had severe disease.

Hypertension was found in 27 patients (36%) with RA compared to 11(14.7%) in the normal controls. The difference is statistically significant (p 0.003). In various previous studies, the reported prevalence ranged from 29-70%.^{4,10} Mean systolic and diastolic BP also were significantly higher in RA patients compared to controls. Since many RA patients were on steroids, we analyzed the effect of steroid on prevalence of hypertension. The prevalence of hypertension in steroid users and non-users were comparable and there was no statistically significant difference in the groups studied. Majority of the steroid users (71.9%) were taking low dose steroids<10 mg/day. This could be the reason for the lack of difference in the two groups.

Conclusion

1. There is a higher prevalence of hypertension in RA patients compared to normal population which could be contributing to their higher CVD mortality.
2. Medications for RA like corticosteroids did not influence the prevalence of CV risk factors such as hypertension.

Management of traditional CVD risk factors like hypertension in RA patients would significantly reduce the excess cardiovascular mortality in RA contributed by accelerated atherosclerosis due to chronic inflammation.

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