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MORTALITY IN SLE – A RETROSPECTIVE STUDY.

Rheumatology

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ABSTRACT

Aims And Objectives: This retrospective study was conducted in SKIMS Soura Srinagar to study co morbidities associated with SLE as well as to analyse pattern of mortality of SLE patients.

Methods: We analyzed the data of one decade from Jan 2004 to Dec 2014 for total deaths which occurred in SKIMS soura Srinagar during this period. Files of 133 patients on whom Rheumatic disease was mentioned were separately fully analyzed for patient's age, sex, type of rheumatic disease, any other underlying disease and terminal events which lead to death of patient. Particular attention was paid to data of SLE patients.

Observations: There were 41 SLE patients with a male female ratio of 1: 12.6. Mean age at death was 32.46±13.739 years (range 15 – 68). Most of the patients 34 (82.9%) were in the age group of 20-59 years. The main associated co morbidities were HTN in 23 (56.1%), CRF in 20 (48.8%) patients. The common causes of death were sepsis in 12 (29.3%), ARF in 11 (26.8%) , heart failure in 9 (22.0%).

Conclusion: We found that Rheumatic disease patients particularly SLE have premature mortality compared to the non Rheumatic patients and sepsis being the leading cause of death in SLE patients. Mortally of SLE is bimodal with an early mortality due to disease flares and a late mortality due to disease plus other associated co-morbidities like DM, HTN, Malignancy and cardiovascular conditions.

KEYWORDS

SLE: Systemic lupus Erythematosus, Mortality, MCTD: Mixed connective tissue disease, Rheumatic Diseases.

INTRODUCTION:

Systemic Lupus Erythematosus is an autoimmune disease in which organ and cells undergo damage initially mediated by tissue binding autoimmune antibodies and immune complexes. About 90 % of patients at diagnosis are women of child bearing age.[1]

Lupus has long been associated with a bimodal pattern of mortality.[2] Early mortality, less than one year since diagnosis is thought to be more likely related to severe disease activity, and later mortality is more likely associated with complications of long standing disease and treatment with immunosuppressive agents. Infections and accelerated atherosclerosis are causes of later mortality. SLE is associated with an approximate of two to five fold risk of death compared to general population.[3,4]

Premature mortality is the most severe medical outcome of any disease.[5] There is a general belief that cardiovascular and neoplastic diseases are most prominent fatal diseases, while rheumatic diseases generally have been regarded by medical community and general public as non-fatal diseases. Nonetheless most rheumatic diseases have a natural history that includes premature mortality.

AIMS AND OBJECTIVES:

1. To study the pattern of mortality due to Systemic Lupus Erythematosus (SLE).

2. To study the factors affecting mortality due to SLE.

MATERIALS AND METHODS:

The study Mortality in SLE was conducted in the Department of internal medicine division Rheumatology at Sher-I-Kashmir Institute of Medical Sciences Soura (SKIMS) Srinagar J&K India. We analyzed the data of one decade from Jan 2004 to Dec 2014 for total deaths which occurred in SKIMS soura Srinagar during this period. In our study we at first analyzed death register from Jan 2004 to Dec 2014 for the data. We found that in 133 patients rheumatic disease was mentioned as the part of diagnosis at the time of death of patient.

Files of these 133 patients were separately fully analyzed for patient's age, sex, type of rheumatic disease, duration of hospital stay prior to death, any other underlying disease and terminal events which lead to death of patient. Particular attention was paid to mention of pulmonary diseases, cardiovascular diseases, infections, liver diseases and renal diseases. Pattern of mortality of SLE was seen in terms of age at death, any sex predominance, associated co morbidities, terminal events leading to death.

OBSERVATIONS AND RESULTS:

In 10 years from Jan 2004 to Dec 2014 , a total of 4,30,343 admissions to SKIMS were recorded, during which 19,391 (4.51%) patients died, with 133 subjects having recorded a rheumatic cause on the death certificate. Out of total deaths 99.3% had died of non rheumatic diseases while only 0.7% (133) had rheumatic disease mentioned as cause of death on their death certificate (table 1) . There were 41 SLE patients with a male female ratio of 1: 12.6. Mean age at death was 32.46±13.739 years (range 15 – 68). Most of the patients 34 (82.9%) were in the age group of 20-59 years(table2). The main associated co morbidities were HTN in 23 (56.1%), CRF in 20 (48.8%) patients. The common causes of death were sepsis in 12 (29.3%) , ARF in 11 (26.8%) , heart failure in 9 (22.0%)(table3). In 41 SLE patients sepsis was mentioned as immediate cause of death in 12 (29.2%) patients, respiratory failure in 6 (14.6%), encephalopathy in 8 (19.5%), heart failure in 9 (21.9%), ARF in 11 (26.8%), stroke in 3 (7.3%) coagulopathy in 1(2.4%) patient(table4).

DISCUSSION:

The most severe medical outcome of any disease is the premature mortality resulting due to it. Rheumatic diseases have been regarded as non-fatal by the medical community and general public compared to traditional strong belief about cardiovascular and neoplastic diseases as fatal diseases. Nonetheless, majority of Rheumatic diseases run a natural history that reveals their premature mortality. Some inflammatory rheumatic diseases such as systemic lupus Erythematosus (SLE), systemic sclerosis, Polymyositis, and Vasculitis are associated with premature mortality rates comparable to or greater than most cardiovascular and neoplastic diseases. This premature mortality is the outcome of chronic inflammatory burden, infections, organ dysfunction and premature atherosclerosis.

We tried to look into the mortality pattern of SLE in the Indian subcontinent where little is known about mortality of various Rheumatic diseases due to poor medical facility for management of these diseases. The study was carried out in a tertiary care hospital of north India where we analyzed mortality data of one decade from Jan 2005 to Dec 2014. During this decade 19,391 patients died in this institute, out of which 133 had rheumatic disease mentioned as cause of death in the death certificates which constituted 0.7% of total deaths .This lower percentage is understandably due to rareness of Rheumatic diseases especially the inflammatory ones.

The age of rheumatic disease patients ranged from 11 years to 85 years, with majority of patients (83.3%) in the age group of 20-70 years.

Since mortally of certain inflammatory Rheumatic diseases is bimodal with an early mortality due to disease flares and a late mortality due to disease plus other associated co-morbidities like DM , HTN , Malignancy and cardiovascular conditions which may occur earlier than general population in these disorders, the occurrence of most of deaths in the age group of 20-70 years is expected. Jaffrey J Sack and colleagues[6] analyzed death records of rheumatic disease patients who died between 1979-1998 in USA, they found 35.4% patients in the age group of 15-64 years and 63.9% were above 65 years.

In our study the mean age at death of rheumatic disease patients was 43.94 ± 17.79 years against mean age of patients who died of non rheumatic diseases 48.03 ± 23.38. Vanessa E, Rodrignez MD, Esther N et al[7] in their study found the mean age of death of patients who died of SLE was 37 years. In our study SLE constituted 41% of rheumatic disease patients, thus influencing the lower age at mortality.

In our study with a total of 133 rheumatic disease patients 100 (75.2%) were females and 33 (24.81) were males –a finding that is expected as most of the Rheumatic diseases affect the females predominantlty.[8]

Jaffrey J Sack and colleagues[6] also found that women accounted for 68.9% of disease patients between 1979 to 1998 in USA.

The severe inflammatory rheumatic diseases with the highest mortality rates, including Systemic lupus Erythematosus (SLE), systemic sclerosis, Vasculitis, and Polymyositis, are rare diseases, *i.e*., seen in fewer than 1 in 2,000 individuals. Therefore, mortality associated with these conditions has little impact on overall mortality statistics in the general population, compared to mortality in more prevalent chronic diseases such as hypertension or diabetes. Again, due to low prevalence, most settings have too few patients to analyze long-term mortality rates in patients with most rheumatic diseases. Only specialized centers accumulate sufficient patients for analysis of mortality in diseases such as systemic sclerosis or polymyositis.[5] In our study, out of total 133 rheumatic disease patients who died over last decade, 41 (30.8%) had SLE, while 2 (1.5%) had combination of SLE and Rheumatoid arthritis. Rath PD et al[9] in their case review of 20 patients in rheumatology department found out of 20 patients, 12 (60%) had SLE, 5 (25%) had RA, 2 (10%) had Vasculitis and 1 had gout. However, their sample size is far less than that of ours; hence other rare Rheumatic disorders did not figure in their study.

Jaffrey J Sack and colleagues[6] in their study found that out of the 10 categories of AORC 3 accounted for almost 80% of deaths; diffuse connective tissue disease (34% in 1997), other specified rheumatic conditions (23% in 1997) and rheumatoid arthritis (22%in 1997). Most deaths in diffuse connective tissue disease category were from SLE, and systemic sclerosis. Our observations are in agreement with these observations as we too found majority of patients belonged the category of severe inflammatory rheumatic disorders like SLE, Rheumatoid arthritis, Vasculitis, MCTD, and systemic sclerosis.

We found of all 133 Rheumatic disease patients 41 (30.8%) had SLE, out of them 38 (92.6%) were females, only 3 (7.3%) were males with a male female ratio of 1: 12.6. Mean age at death was 32.46±13.739 years (range 15 – 68). Most of the patients 34 (82.9%) were in the age group of 20-59 years. Among 41 SLE patients HTN was present in 23 (46.93%), 20 (48.7%) had CKD. However, Heller T et al[10] found renal failure in only 13% of SLE patients which is lesser that of ours likely due to ethnic difference in study population. Vanessa E, Rodrignez MD et al[11] in their study also found that more females 151 (94%) died of SLE with a male female ratio of 1:15.1. The primary cause of death in SLE patients was infection (27%), uremia (26%) and cardiovascular complications (33%). The mean age at death in their study group was 37 years.

Sepsis was mentioned as immediate cause of death in 12 (29.2%) patients, ARF in 11 (26.8%), respiratory failure in 6 (14.6%), encephalopathy in 8 (19.5%), heart failure in 9 (21.9%). Sepsis, acute renal failure and cardiovascular complications were the main causes of death in these patients. Sepsis as leading cause of death in SLE patients is well-known as these patients are on glucocorticoids and other immune-suppression agents. T. Heller M. Ahmad et al[10] at King Abdul Aziz university hospital Jeddah reviewed 93 patients treated for SLE, 84 females and 9 males. During follow up 8 patients died. They found early deaths (within 2 years) were mainly due to sepsis and PTE; late deaths (after 2 years) were mainly due to sepsis, renal failure and myocardial infarction. Strong association with early mortality was male sex, skin involvement and age < 16 years at diagnosis.

We looked at the year-wise mortality of Rheumatic disorder patients and found that the mortality shows a decreasing trend. This decreasing trend is most likely due to early diagnosis and targeted therapy as a result of improving health care system and awareness about Rheumatic disorders in this part of world.

CONCLUSION

In conclusion we have found that Rheumatic disorder particularly SLE patients have premature mortality compared to the non Rheumatic disease patients. Although rheumatic diseases constitute relatively less proportion of deaths, but the majority of deaths in rheumatic disease patients occur in economically productive age group. Sepses, cardiovascular diseases, organ failure (respiratory failure and acute renal failure) are the main causes of death in SLE patients.

Table1. Number Of Total Admissions, Total Deaths And Deaths Due To Rheumatic Causes.

· Number of total admissions (2005 – 2014)	4,30,343
· Number of total deaths (2005 – 2014)	19,391
· Percent of deaths out of total admissions	4.51%
· Number of deaths with non-rheumatic cause	19,258
· Percent of deaths with non-rheumatic cause	99.3%
· Number of deaths with rheumatic cause	133
· Percent of deaths with rheumatic cause	0.7%

Table 2. Characteristics Of Patients With SLE

Characteristic		
N	41	
Male: Female ratio	1:12.6	
Age of death (years)		
Mean	32.46±13.739	
Median	28.00	
Range	15 – 68	
< 20y	4	9.8%
20 - 39y	28	68.3%
40 - 59y	6	14.6%
60 - 79y	3	7.3%

Table 3: Co Morbidities With SLE Patients: N =41

Co morbidity	HTN	DM	CRF	CLD	Seizure
	23	3	20	1	3

Table 4: Immedate Cause Of Death In SLE Patients: N= 41

Rheumatic disease	Sepsis	Resp. Failure	Encephalopathy	Heart failure	ARF	Stroke	Coagulopathy
SLE(n=41)	12	6	8	9	11	3	1
SLE + RA (n=2)	1	1	0	1	0	0	1

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