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ORIGINAL RESEARCH

A HOSPITAL-BASED INVESTIGATION OF THE PREVALENCE AND RISKS OF VENTRICULAR DYSFUNCTION IN CONNECTIVE TISSUE DISORDERS

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ABSTRACT

Background: The incidence of cardiac anomalies in patients with connective tissue disorders (CTD) and related risk factors are poorly understood in modern India.

Methods: 35 consecutive CTD patients who presented to our outpatient department and had no substantial cardiovascular risk factors at baseline were prospectively tracked. We also kept track of data from controls who were matched for age and gender. Following normal investigations, echocardiography and a 12-lead electrocardiogram were performed on all patients and controls.

Results: 19 (54.3%) patients with systemic lupus erythematosus, 12 (34.3%) patients with systemic sclerosis, 2 (5.7%) patients with mixed CTD, and one (2.9%) patient with overlap syndrome and dermatomyositis made up the CTD group. 71.4 percent of CTD patients had cardiovascular involvement on echocardiography, despite the fact that the majority of them had no cardiac symptoms. Three (8.6%) CTD patients showed overt left ventricular (LV) systolic dysfunction, whereas 13 (37.1%) showed subclinical LV systolic dysfunction. 11.4 percent (n = 4) of the patients had LV diastolic dysfunction. Rv systolic dysfunction affected 20% of the individuals (n = 7). Forty percent (n = 14) of CTD patients had pulmonary hypertension.

Conclusion: In the current investigation, roughly one-third of CTD patients had subclinical LV systolic dysfunction and pulmonary hypertension. In order to guarantee prompt diagnosis and treatment for CTD, it is essential to test for certain abnormalities.

INTRODUCTION

An antibody or T-cell reaction against a self-antigen causes connective tissue disorders (CTD), a set of autoimmune, multisystem, chronic inflammatory diseases that ultimately cause tissue destruction and organ failure. An overt CTD is the result of the immune system's genetic predisposition and environmental stimuli. The pulmonary, renal, musculoskeletal, gastrointestinal, neurological, and haematological organ systems are among the specific or multiple organ systems that the antibodies target. The involvement of the cardiovascular system is one of the main causes of morbidity and mortality in CTD patients [2]. All of the

heart's structural elements, including the pericardium, conduction system, myocardium, valves, and coronary arteries, may be targeted by cardiac involvement in CTDs [3].The most typical cardiac anomaly in SLE is Libman-Sacks endocarditis, which has been detected in up to 50% of patients at necropsy in the past [4]. Pericarditis is a typical cardiac symptom of CTDs that can occur in up to 39% of patients of SLE5 and up to 43% of cases of MCTD [6]. At the time of diagnosis in the past, cardiac symptoms were severe, frequently fatal, and frequently discovered through postmortem exams [4].However, because to advancements in diagnostic technology, cardiac symptoms are now frequently modest and asymptomatic as they can be detected early by non-invasive procedures like echocardiography during the beginning stages of CTDs [7]. However, there are few recent data from India about the incidence of structural and functional heart abnormalities in CTD patients and associated risk factors.

METHODS

STUDY DESIGN

This study was carried out as a case-control experiment at the dermatology and cardiology departments of our institute, a tertiary care hospital.

PATIENT SELECTION

All patients with CTD who had been diagnosed repeatedly over the course of a year in the dermatology department of our institute using accepted criteria were screened for enrollment, and those who were willing to participate were included. The control population was comprised of the patient's attendants, family members, friends, and patients who visited the dermatology out-patient department for minor skin conditions like fungal infections, common warts, acne patients, etc. They were screened to be enrolled as age- and sex-matched controls. Patients with congenital heart conditions, a history of coronary artery disease, associated malignancies, chronic obstructive pulmonary diseases, pulmonary fibrosis brought on by infections, patients older than 60, patients with poor echo windows, and patients who were unwilling to participate were among the exclusion criteria.Patients with additional complicating conditions were also disqualified, including diabetes, hypertension, and smoking.

DATA COLLECTION

Demographic information and medical history were self-reported, and was captured using a structured data recording format. Anthropometric and blood pressure measurements were then performed using verified instruments and according to accepted protocols. Body mass index (BMI) is determined by dividing a person's weight in kilogrammes by their height in square metres (kg/m^2). According to the defined data format, the mucocutaneous examination was conducted. Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and modified Rodnan skin score were used to measure the severity of the disease in SLE and SSc, respectively. In a fasted state, approximately 10 cc of blood was extracted and collected in separate vials with the proper reagents for biochemistry and hemogram. The creatinine clearance was calculated using the Cockcroft-Gault equation.Pneumopulmonary function tests were also used to assess pulmonary health. To examine the heart rate, rhythm,

characteristics of ventricular hypertrophy, previous myocardial infarction, and conduction anomalies, all participants had 12-lead "electrocardiograms" (ECG). In order to record various parameters, "echocardiography" was performed using an I33 echo machine from Philips medical system equipped with a 2 to 5 broad band phased array probe.

STATISTICAL ANALYSIS

For categorical variables, absolute frequency, relative frequency, mean ±SD (standard deviation), and continuous variables with non-normal distribution, median and interquartile range, respectively, were presented. Using the unpaired t test and the chi-square test, respectively, the difference between case and control groups of continuous variables and categorical variables was examined. To ascertain the independent association of the clinical parameters, multivariable logistic regression was used to model variables that were found to have a significant association with outcomes in univariate analysis. Software called Epi-info, version 3.4.3, was used to examine the data. Statistical significance was defined as a P value of less than 0.05.

RESULTS

DEMOGRAPHICS

The study explored enrolling 46 consecutive CTD patients, of whom 11 satisfied the exclusion criteria, leaving 35 CTD patients for the final analysis. The study also included an equal number (n = 35) of controls who were matched for age and sex. There were 19 (54.3%) patients with SLE, 12 (34.3%) with SSc, 2 (5.7%) with MCTD, and one (2.9%) with overlap syndrome and diabetes mellitus. The average age of CTD patients and the control group was 33.7 ±11.9 years for the former and 36.9 ±12.5 years for the latter. As seen in Table 1, there were 33 (94.3%) more female subjects than male.

Table 1: Characteristics of the Patient and Control Group

Characteristics	CTD Group	Control Group	P value
Age	37.0±12.6	33.6±12.0	.26
Female	32	32	.70
History	10	1	.0001*
BMI	20.0± 3.05	20.6± 2.98	.47
Chestpain	12	1	.0001*
Breathlessness	2	0	.49
Palpitation	3	0	.07
Thrombotic events			
Hemoglobin	11.4±1.6	12.0±1.3	.09
DiastolicBP	72.4±7.5	73.6±6.7	.43
SystolicBP	111.3 ±14.0	112.0±9.8	.77
S. Triglyceride	130.6 ± 49.2	97.7 ± 18.6	.003*
S. Cholesterol	159.6 ± 36.8	158.6 ± 28.7	.79
S.uricacid	4.1±0.7	4.6±0.5	.10
S.LDL	85.5± 22.1	86.0±19.7	.91
S. HDL	42.3 ± 10.3	45.3 ± 9.1	.20

S.creatinine	0.6±0.02	0.6±0.03	.10
S. Albumin	5 ± 0.6	4.0 ± 0.3	.44
Restrictive Lung disease on pulmonary function test	24	1	.0001
ESR	24	6	.001*
RBS	86.0 ± 14.5	83.3 ± 10.3	.40
Deranged LFT	13	2	.0001*
ECG finding			
LVH	2	1	.4
AF	0	0	
HR	84±9.1	83.8±5.0	.46
ECHO findings			
RVSD	6	0	.005
LVSD	15	3	.0001*
LVDD	5	0	.06
Subclinical	12	3	
Overt	4	0	
PAH	15	2	.003

LEFT VENTRICULAR AND RIGHT VENTRICULAR SYSTOLIC DYSFUNCTION

There was no discernible change in the LVEF between the CTD group and the controls when the LV systolic function was evaluated by recording LVEF (64.2 ±6.3 vs. 66.3 ±4.9, P = 0.31). In CTD patients compared to controls, the absolute value of global longitudinal on strain imaging was reduced (-20.1 ±2.5 vs -22.5 ± 1.4, P <0.0001). There was no discernible difference between the two groups' absolute values of global circumferential strain (-21.5 ± 3.9 vs. -22.8 ± 2.4; P =0.1). Three (8.6%) of the patients, who were thought to have overt LV systolic dysfunction, had aberrant LVEF.Additionally, systolic dysfunction was detected by global strain imaging in the longitudinal plane and circumferential plane in 9 (28.1%) and 7 (25.9%) patients, respectively. As a result, the prevalence of LV systolic dysfunction in the current study was 45.7 percent (n = 16). LVSD was observed in 45.7 percent of SLE patients (n = 9) and 33.3 percent of SSc patients (n = 4) among subsets of CTD.

Table 2: Risk determinants of LV and RV systolic dysfunction

	LV systolic dysfunction		**RV systolic dysfunction**	
	CTD without LVSD	**CTD with LVSD**	**CTD with RVSD**	**CTD with RVSD**
Age	38.7±10.1	35.6±14.5	37±13.2	32.7±8.0
History	4	5	5	2
Disease duration	7	4	4.0	4
ESR	26	22.4	14	3
Dyspnea Chest pain	2	1	2	1
ANA	13	3	14	3
Hypertriglyceridemia	6	5	8	3

Hematology abnormalities	5	5	9	1
Deranged PFT	12	10	19	4
Deranged LFT	7	7	11	1
Type of CFT-SSc/SLE	13	5	15	4
GFR	84.3±28.7	90.4±26.8	86.1±29.6	90.6±17
Photosensitivity	10	14	3	4
GIT involvement	5	3	4	3
Discoid rash	4	8	9	1
Arthritis	3	6	5	2
Parenchymal lung changes on CXR	2	5	-	-
ILD on HRCT	4	7	9	2
Sclerodactyly	7	7	-	-
Oral mucosal ulcers	2	2	-	-
On treatment at enrolment	9	14	-	-
Urine proteins	-	-	7	2

DISCUSSION

The structural harm to the myocardium, pericardium, and valves may be caused by autoimmune immunoinflammatory injury. As a result, patients with CTD who exhibit signs of a systemic inflammatory state are prone to experience cardiovascular system involvement. [8,9] There aren't any case-control prospective studies from an Indian population that show the same thing, though.

In the current investigation, which included 35 CTD patients and 35 age- and sex-matched controls, we looked into the cardiac involvement in CTD patients who were mostly SLE and SSc patients who mainly displayed cutaneous symptoms. There were no RhA, Sjögren's syndrome, or PM patients in the current study population of CTD. Overall, 25 individuals (71.4 percent) had structural and functional abnormalities in their hearts, which is a result of cardiac involvement. 16 (45.7%) and 7 (20%) patients, respectively, had systolic dysfunction (overt and/or subclinical) of the LV and RV, and 4 (11.4%) patients had diastolic dysfunction of the left ventricle. There were 9 (25.7%) and 2 (5.7%) individuals with tricuspid and mitral valve valvular incompetence, respectively.

Overall, CTD has been linked to both conventional and unconventional cardiovascular involvement risk factors. Traditional risk factors for cardiovascular disease include high blood pressure, diabetes mellitus, dyslipidemia, male gender, metabolic syndrome, obesity, smoking, advanced age, menopause status, family history of the disease, HRT, and hyperhomocysteinemia. [10] Polyautoimmunity, elevated ESR and C-reactive protein, higher disease activity, organ damage, longer disease duration, medication, long-term steroid therapy, and renal involvement are non-traditional variables. [10]To assess the consistent prevalence of cardiac involvement among CTD patients, we had all smokers, people with

hypertension and diabetes, and people over 60 years old eliminated from the study. Additionally, 94.6 percent of the participants were female. We found that patients with SLE had a greater prevalence of ventricular dysfunction among various subsets of the CTD population, but no statistical evidence could be found to support this link.

In a retrospective case-control research involving 436 patients with CTD and 436 controls, Wang et al. [2] found that 42.4% of patients had LV systolic dysfunction. The presence of ventricular dilatation, regional wall motion abnormalities, and a decreased LVEF, however, were the criteria employed to define myocardial function restriction. Imaging of strain was not used. Similar to these researchers, numerous additional researchers [11-13] studied LVSD in a diverse population of CTD and found worse systolic function as compared to healthy controls. They did not, however, mention the common clinical and subclinical systolic dysfunctions.Only 3 (8.6%) of the CTD patients in the current investigation had overt LV systolic dysfunction, although strain imaging revealed subclinical LV systolic dysfunction in 13 (37.1%) of the patients. In a case-control study including 22 patients with SSc, Spethmann et al.18 found subclinical LV systolic dysfunction using strain imaging and reported a prevalence of 40.9 percent. Our findings show how strain imaging can help patients with CTD discover LV dysfunction early on, before it becomes clinically obvious [15-18, 20].

In this study, we discovered a statistically significant relationship between photosensitivity and the kind of treatment, i.e., high dose, long-term steroid therapy at the time of enrolment with LVSD. On univariate analysis, discoid rash also had significant results. However, none of the prior research have identified photosensitivity and discoid rash as significant predictors of cardiac involvement in CTD. Previous studies have detected disease duration as a factor for LVSD. Curiosity is sparked by this, but larger research are required to confirm and uncover the potential cause of this correlation.

Patients with CTD also experience problems with the right ventricle's systolic functions. According to Karna et al. [19], the patient group's MPI values were substantially higher than those of the controls (0.54 + 0.26 vs. 0.35 + 0.07, P <.001), indicating overall worsened right ventricular performance.In the current study, patients with CTD also had higher MPI values. Similar to our investigation, Buss et al. [14] showed significantly lower TAPSE levels among the CTD group. Due to the small sample size of CTD patients with RV dysfunction, it is possible that no statistically significant RVSD determinants were found, despite RVSD being present in 20% (n = 7) of the study's CTD patients. Therefore, to assess the risk drivers, larger sample size research in the future are needed [21-23].

CONCLUSION

71.4 percent of CTD patients have cardiovascular problems, the majority of whom are asymptomatic. Utilizing strain imaging, the most prevalent sign was subclinical LV systolic failure. Patients who received long-term steroid therapy and photosensitivity were more likely to have LV systolic dysfunction. In almost one-third of CTD patients, pulmonary hypertension was discovered. Only a small number of CTD patients had significant cardiac involvement, as evidenced by overt LV systolic failure and mild valvular incompetence. Furthermore, to verify these results, long-term studies with a larger population of CTD patients are required. Such information is required to develop cardiovascular problems screening techniques for CTD patients.

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