

Original Research Article

Clinical profile of patients with cardiac syndrome X in a tertiary care hospital

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Received: 15 May 2017

Accepted: 08 June 2017

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ABSTRACT

Background: Abnormalities in coronary microcirculation may lead to symptoms of chest pain which mimics angina. Symptoms of chest pain along with evidence of ischemia on non-invasive tests like electrocardiography (ECG), echocardiography or treadmill test (TMT) but with normal coronary angiogram (CAG) is referred to as cardiac syndrome X (CSX). Previous studies have shown favourable prognosis in such patients. However recent studies have not shown good prognosis. We intend to understand whether such adverse cardiovascular outcomes could be secondary to any change in the clinical characteristics of patients with CSX in the current era.

Methods: This is a retrospective study which was conducted at a tertiary care hospital. CAG of patients who underwent coronary angiography between November 2013 and October 2016, for suspected ischemic heart disease was reviewed. Clinical characteristics of patients with normal or non-obstructive coronaries (less than 50% stenosis) in angiography with chest pain were analyzed. Further clinical characteristics, ECG, echocardiography, treadmill test and CAG findings were compared among males and females.

Results: 410 patients were included in the study. 212 were females and 198 were males. Mean age of presentation was 53.46±10.5 years for males and 55.04±9.3 years for females. Patients presenting with atypical chest pain were higher (70.7%). There were 195 subjects with systemic hypertension, 103 with diabetes mellitus and 57 had dyslipidemia. In the study, most 260 subjects had ST-T changes on ECG. Abnormal echocardiography was seen in only 35 patients. 30.5% patients showed positive stress test for inducible ischemia.

Conclusions: CSX is prevalent in significant number of patients who present with symptoms of chest pain. Unlike previous studies, there is no significant difference among males and females, in prevalence and risk factors for this syndrome. Further non-obstructive lesions were found to be higher in females.

Keywords: Cardiac syndrome X, Microvascular angina, TMT positive with normal coronary angiogram

INTRODUCTION

Abnormalities of epicardial coronary arteries are known to cause myocardial ischemia. However, it is having been shown that abnormalities in coronary microcirculation may also cause or contribute to myocardial ischemia. Harvey Kemp in 1973 described the term "cardiac syndrome X". The occurrence of typical chest pain and ST-segment changes suggestive of myocardial ischemia

in patients who otherwise have completely normal coronary arteriograms is known as "syndrome X" or "cardiac syndrome X" (CSX).^{1,2} Pathogenic mechanism involved in patients with CSX has not been well understood. Some of the proposed mechanisms include abnormal coronary flow reserve, insulin resistance, abnormal autonomic control, enhanced sodium hydrogen exchange activity, abnormal cardiac sensitivity and microvascular spasm. Myocardial ischaemia because of

coronary microvascular dysfunction is the most accepted. It is possible that the syndrome may result from a combination of coronary microvascular dysfunction and increased sensitivity to painful stimuli.³ There is no uniform definition for diagnosing CSX in the literature.⁴ Diagnosis of CSX requires the exclusion of epicardial abnormalities by coronary angiography (CAG). Though many studies included absolutely normal coronaries, some studies included non-obstructive lesions up to 50% stenosis.⁴⁻⁶ In angina patients suspected to have CSX, attempts should be made not only to rely on this exclusion criterion for the diagnosis but to obtain objective evidence of coronary microvascular disease and possibly, of myocardial ischemia. Some clues in regard to the microvascular origin of symptoms can be derived from clinical findings and non-invasive tests such as ECG, echocardiography and treadmill test (TMT).⁷ It is important to differentiate this condition from metabolic syndrome X which is characterised by hypertension, central obesity, insulin resistance, low HDL and high triglyceride levels. According to prior studies, the prognosis of patients with CSX is generally more favorable than those with obstructive CAD. On the contrary, recent studies have reported adverse cardiovascular outcomes in patients with non-obstructive coronaries. The prognosis of “normal” coronary arteries in the setting of signs and symptoms of myocardial ischemia is not as benign as reported by preliminary cohort studies.⁴ More than 40% of these patients are re-hospitalized for chest pain more than once, and 30% undergo repeat coronary angiography over 1- to 5-year follow-up periods despite demonstration of “normal” coronary arteries on angiography during a prior hospitalization.⁸ In addition, compared with the baseline population, these patients are at increased risk for traditionally defined major cardiovascular events including premature death, myocardial infarction and stroke.⁹ In this study we intend to understand whether such adverse cardiovascular outcomes could be secondary to any change in the clinical characteristics of patients with CSX in the current era.

METHODS

This is a retrospective study which was conducted at a tertiary care hospital. Coronary angiograms of patients who underwent coronary angiography between November 2013 and October 2016, for suspected ischemic heart disease was reviewed. Patients with normal or non-obstructive coronaries (less than 50% stenosis) in angiography with chest pain were included in this study. Exclusion criteria were as follows: post-revascularisation status, structural heart disease, congenital heart disease, preoperative indications. Clinical profile and details of investigation such as electrocardiography, echocardiography and treadmill test were analyzed in all the patients included in this study. Further the study population was divided into 2 groups. Group 1 included all males satisfying inclusion and exclusion criteria, and group 2 included females who

satisfied inclusion and exclusion criteria. Clinical characteristics, ECG, echocardiography, treadmill test and CAG findings of the 2 groups were compared. Statistical analysis was performed using SPSS version 16 and two-tailed p value <0.05 was considered significant for all analyses. Continuous variables expressed as Mean ± SD. Categorical variables expressed in percentage. Continuous variables were analyzed with the unpaired t test and categorical variables were analyzed with Fisher Exact Test.

RESULTS

The total number of patients who underwent coronary angiogram for suspected ischemic heart disease was 2347. Out of which 410 (17.47%) patients satisfied the inclusion and exclusion criteria. There were 300 (73.2%) patients with normal CAG and 110 (26.8%) had non-obstructive lesion with <50% stenosis (P value <0.01). Table 1 shows the clinical characteristics of subjects included in the study.

Table 1: Clinical characteristics and risk factors of all patients included in the study.

| Parameter | N (%) |
|-------------------------------------|----------------------|
| Age | 54.28±9.898 in years |
| Gender | |
| Males | 198 (48.3%) |
| Females | 212 (51.7%) |
| Atherosclerotic risk factors | |
| Hypertension | 195 (47.6%) |
| Diabetes mellitus | 103 (25.1%) |
| Dyslipidemia | 57 (13.9%) |
| Symptoms | |
| Atypical chest pain | 290 (70.7%) |
| Typical chest pain | 120 (29.3%) |
| ECG ST-T changes | 260 (63.4%) |
| Abnormal echocardiography | 35 (8.1%) |
| TMT | |
| Positive | 125 (30.5%) |
| Negative | 285 (69.5%) |
| Cag | |
| Normal | 300 (73.2%) |
| Non-obstructive lesion | 110 (26.8%) |

n is the number of subjects; ECG-Electrocardiogram; TMT-Treadmill test; CAG- Coronary angiogram.

Table 2 shows the gender based clinical characteristics and risk factors for CSX. Of the total 410 subjects, 212 (51.7%) were females and 198 (48.3%) were males. Mean age of presentation was 53.46±10.5 years for males and 55.04±9.3 years for females (P value 0.11). Among the total number of subjects 290 (70.7%) patients had atypical chest pain, 120 (29.3%) patients had typical chest pain. The atherosclerotic risk factors among the study population. There were 195(47.6%) subjects with systemic hypertension and 215 (52.4%) without systemic hypertension. Among those with systemic hypertension,

102(52.3%) were females and 93(47.7%) were males (P value 0.817). There were 103 (25.1%) subjects with diabetes mellitus and 307 (74.9%) without diabetes mellitus. Among those with diabetes mellitus, 51(49.51%) were females and 52 (50.49%) were males (P value 0.607). Among 410 patients, 57 (13.9%) had dyslipidemia and 353 (86.1%) were not associated with dyslipidemia. Among them 25(43.9%) were females and 32 (56.1%) were males (P value 0.201). The number of subjects with ECG changes, abnormal echocardiography and TMT positivity. There were 260 (63.4%) patients

with ST-T changes on ECG, 150 (36.6%) patients had normal ECG. Out of 260 patients with ECG changes 155(59.62%) were females and 105 (40.38%) were males (P value <0.01). Echocardiography revealed regional wall motion abnormality with left ventricular systolic dysfunction in 35 (8.1%) patients, 375 (91.5%) patients had normal echocardiography.

TMT was positive in 125 (30.5%) and was negative in 285 (69.5%). Among them 73 (58.4%) were females and 52 (41.6%) were males (P value 0.072).

Table 2: Gender based clinical characteristics and risk factors for CSX.

| Variables | Total (n=410) | Females (n=212) | Males (n=198) | P value |
|----------------------------|---------------|-----------------|---------------|---------|
| Age | 54.28±9.898 | 55.04±9.298 | 53.46±10.466 | 0.11 |
| Hypertension | 195 | 102 | 93 | 0.817 |
| Diabetes mellitus | 103 | 51 | 52 | 0.607 |
| Dyslipidemia | 57 | 25 | 32 | 0.201 |
| ECG ST-T changes | 260 | 155 | 105 | <0.01* |
| TMT | 125 | 73 | 52 | 0.072 |
| CAG Non-obstructive lesion | 110 | 43 | 67 | <0.01* |

n is the number of subjects; * indicates significant at the 5% level of significance.

DISCUSSION

The prevalence of CSX reported as per earlier studies was 10–20%.¹ In a study conducted by Kaski JC, prevalence of CSX was found to be 20-30%.² Vermeltfoort et al, conducted a systematic review and found the incidence of CSX between 3-11%.¹⁰ The prevalence in the study was 17.47%. This difference in overall prevalence when compared to previous studies was probably due to lack of uniform definition for diagnosis of CSX. Some studies included patients with normal coronaries, some studies included those with normal as well as non-obstructive lesions. The study included patients with normal coronaries as well as non-obstructive lesions upto 50% stenosis. 300 (73.2%) patients had normal coronaries. Among them 169 (56.33%) were females and 131 (43.66%) were males. There was statistically significant difference among the group groups (P value <0.01). Among the total 410 subjects, 212 (51.7%) were females and 198 (48.3%) were males. There was no significant difference in prevalence of CSX among females and males. In contrast, prior studies have shown that CSX is more frequently seen in women.^{1,10} In a retrospective cohort study conducted by Humphries et al. which included 32,856 patients, 7.1% of men and 23.3% of women were angiographically normal (P <0.001).¹¹ Mean age of presentation was 53.46±10.5 years among males and 55.04±9.3 years among females. This difference was not statistically significant (P value 0.11). The lack of gender difference with CSX seen in the study, could be one of the contributing factors for the change in the occurrence of other clinical characteristics in patients with CSX. This

in turn may adversely affect the cardiovascular outcomes in CSX as it has been recently reported.¹²⁻¹⁴ Another reason for the worsening cardiovascular outcomes in patients with CSX would be the inclusion of non-obstructive coronaries in the definition of CSX. As per the literature, chest pain in CSX is more often atypical and it might resemble non-cardiac chest pain. However, chest pain in CSX may be severe enough to affect the quality of life of patients. Panic disorder and exaggerated preoccupation about health may contribute to chest pain in some patients with CSX.^{1,15} Findings in the study was consistent with the previous studies. 290 (70.7%) patients presented with atypical chest pain while 120 (29.3%) had typical chest pain. In the study, most 260 (63.4%) subjects had ST-T changes on ECG. Among them 155 (59.6%) were females while 105 (40.38%) were males. This difference was statistically significant with P value <0.01. Abnormal echocardiography revealing regional wall motion abnormality with left ventricular systolic dysfunction was seen in only 35 (8.1%) patients, 375 (91.5%) patients had normal echocardiography. These findings are similar to those observed in previous studies.^{1,10} 125 (30.5%) patients showed positive stress test for inducible ischemia. In a study conducted by Morrow et al. 20% of patients with CSX showed TMT positivity. Atherosclerotic risk factors including systemic hypertension, diabetes and dyslipidemia were quite prevalent in the study. However, there was no statistically significant difference among females and males with P value of 0.817, 0.607 and 0.201 respectively. Prevalence of systemic hypertension was highest (47.6%) followed by diabetes mellitus (25.1%) and dyslipidemia (13.9%). The effect of atherosclerosis in patients with CSX may be underestimated as there is outward enlargement in initial

stages of atherosclerosis and luminal narrowing occurs only later.¹⁶ Most of the studies including current study is based on angiogram which looks at the vessel lumen.

Limitation of the study was long term prospective studies are required to assess the prognosis of such patients including response to anti-platelets. In the study, intra-vascular ultrasound imaging and stress echocardiography were not performed.

CONCLUSION

CSX is prevalent in significant number of patients who present with symptoms of chest pain. It is important to recognize and treat them for microvascular angina. Unlike previous studies, there is no significant difference among males and females in prevalence and risk factors for this syndrome. Further non-obstructive lesions were found to be higher in females. Hence, need for anti-ischemic measures and control of risk factors becomes important among females. Prospective studies are required to assess long term prognosis in such patients.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Bhavya R, Suresh G, Subramanyam K. Clinical profile of patients with cardiac syndrome X in a tertiary care hospital. Int J Res Med Sci 2017;5:3231-4.