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Original Article

Takotsubo Cardiomyopathy-the Broken Heart Syndrome, an Indian Perspective

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ABSTRACT

Background: Takotsubo Cardiomyopathy (TTC) is a reversible cardiomyopathy which is precipitated by adrenergic stress. Trigerring factors, clinical features and mortality data from Indian subcontinent is absent. **Aims:** The present study was undertaken to determine the clinical features, type of emotional stress, mode of presentation, duration of improvement, cardiogenic shock, in hospital mortality,and the treatment given to the patients. **Methodology:** This is a single centre retrospective study,done on patients who presented with ACS and 2D Echocardiography showing Regional Wall Motion Abnormality (RWMA) from 2010 to 2015. The confirmation of TTC was based on 2D Echo findings and coronary angio graphy(CAG). Statistical analysis used- Chi square test was used to compare the categorical variables between different stresses. Fisher exact test was also used to compare the categorical variables. We used independent t test to compare the mean of the ejection fraction between 2 groups. **Results:** Among 43 patients with TTC, most were females, between age group 51 to 80 yrs (77%). Most patients were found to have stress, in form of medical stress(35%), emotional stress(33%) with equal percentage. Some patients had surgical stress(21%) and some patients(11%) did not have any stress at all. In the present study 56 % had hypertension (HTN), 44% had Diabetes Mellitus (DM), and 9% had dyslipidemia (DLP). ECG showed T wave inversion(54%), ST elevation(49%), Q wave(9%), ST depression(7%) and no ST-T changes(5%). Initial Echo showed Ejection Fraction (EF) ≤ 35% in 46.5 %, 36 – 45% in 46.5 % and 46–55% in 7 %. Cardiogenic shock (18.6%) occurred frequently in surgical group and associated with high mortality. In our study EF improved in most of the patients(86%) within 1 month of follow up. **Conclusions:** TTC, predominantly involves females and is precipitated by medical illness or emotional stress in most of the patients. Recovery of left ventricular function is complete in all patients and prognosis is good. But when it occurs in patients following major non cardiac surgery, there can be significant mortality and morbidity.

Key words: Transient Apical Balooning, Stress Cardiomyopaty.

Key Message: Not only emotional but even medical, surgical and even no stress contributes to it. Although recovery is good, mortality is seen in post surgical patients which should be managed aggressively.

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INTRODUCTION

Takotsubo Cardiomyopathy (TTC), transient apical ballooning, first reported in 1990 by Sato and colleagues, who described it as a reversible "takotsubo like left ventricular dysfunction.".[1] It distinguishes itself from an ACS in the fact that RWMA extend beyond a single coronary vascular bed and is reversible, and significant epicardial coronary occlusion is absent[1] It was in 1990 that Sato and colleagues described it as a reversible cardio myopathy as "takotsubo- like left ventricular dysfunction.[2]" TTC has female preponderance especially with elderly ones. The role of catecholamine excess in the pathogenesis of Takotsubo Cardiomyopathy is always debated.[3]

Mayo researchers have proposed diagnostic criteria which was modified in 2008.[4]

This condition accounts for approximately 1% to 2% cases of suspected ACS.[5] Majority of patients have apical involvement.[6]

As the incidence is quite low so we planned for a study in detail, the mode of presentation, various etiologies (pshychological, surgical) and also the mortality associated with it.

SUBJECTS AND METHODS

All the patients who were admitted in our hospital with chest pain fulfilling the inclusion criteria within a period of 2010 till 2015 were included in the study. When eligibility for inclusion was uncertain, cases were not included in our study.

MATERIAL AND METHODS

The Objectives in our study was to determine the Clinical features, type of emotional stress, mode of presentation, duration of improvement, in hospital mortality, and the treatment given in this retrospective study. In accordance to the Mayo clinic criteria our study also included patients with

1. Transient LV apical ballooning.
2. New ECG abnormalities (ST-segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin.
3. The absence of pheochromocytoma and myocarditis
4. Patients willing for coronary angiography.
5. No significant angiographic stenosis.

The patients having Cardiomyopathies, Significant coronary artery disease, Pheochromocytoma and Patients who were not willing for coronary angio graphy were excluded from the study.

OUTCOMES

We recorded all in-hospital complications, including cardiogenic shock, (the use of invasive or noninvasive ventilation or cardiopulmonary resuscitation), death from any cause. Retrospective analysis included

death from any cause and major adverse cardiac and cerebrovascular events (stroke or transient ischemic attack) on their regular follow up upto 6 months to 1 year. It was assessed retrospectively which medications (Angiotensin-converting–enzyme inhibitors, Angiotensin-receptor blockers, or Beta-blockers)were prescribed to these patients at the time of discharge.

STATISTICAL ANALYSIS

In this study we used proportions for variables like age, gender etc. Categorical variables are provided with percentages. Chi square test was used to compare the categorical variables between different stresses. Fisher exact test was also used to compare the categorical variables. We used independent t test to compare the mean of the ejection fraction between 2 groups. The statistical analysis was done with the help of SPSS 23 VERSION software.

RESULTS

We analyzed 43 patients which included 3 men and 40 women, aged between 29 to 78 years (Table 1). Of the 43 patients who were diagnosed to have Takotsubo Cardiomyopathy, 67% patients had some or the other risk factor like Diabetes Mellitus(DM), Hypertension(HTN), Dysliped-imea (DLP). Most of the patients, 77 % were of the age 51 – 80 yrs and 23 % of the patients were between 20 – 50 yrs of age (Table 2). In our study Hypertension was seen in 56%, Diabetes Mellitus was seen in 44% and Dyslipidemia was seen in 9 % of the patients. Among all these patients 5% were thrombolysed from outside before reaching our hospital.

Stress factor or a precipitating event, which is considered to be the major element was found in majority of the patients. 35% had Medical illness, 33% had Emotional stress, 21% had Surgical stress and 11% had no stress at all. The mode of presentation was such that 77% presented with chest pain, 40% had dyspnoea, 9% had Acute LVF, and 2.3% had fever (Table 3).

ECG showed T wave inversion in 54%, ST elevation in 49%, Q wave in 9%, ST depression in 7% and No ST or T wave changes in 5%. The Cardiac enzymes were raised in 56 % patients (Table 4).

Coronary angiogram was done in all the patients which showed normal coronaries in 93% and non flow limiting Coronaries in 7%.

2D Echo evaluation was done both initially and later on.

Initial Echo showed Ejection fraction ≤ 35% in 46.5%, 36–45% in 46.5% and 46–55% in 7% of the patients. Mean EF in no stress group was 40.923 ± 6.27% , emotional stress group was 36.524 ± 7.43%, medical illness group was 33.857 ± 7.01% and surgical stress group was 34.286 ± 6.72%. No stress group when compared to medical stress group had significantly better EF (p value : 0.0106).

Cardiogenic shock occurred in 2 patients in the medical group, 3 patients in emotional stress group and 3 patients in post surgical group. Intra aortic balloon pump was used for one patient in medical stress group and one patient in post surgical group. In hospital mortality was 7% (n = 3). All three patients were in surgical group and all of them had cardiogenic shock within 24 hrs of onset of symptoms. All of them had normal LV function by ECHO prior to surgery.

Follow up ECHO

Follow up echo was done in 70% of the patients. Most of the patients recovered within 4 weeks of follow up in which 23% recovered in first week and 33% in 2 weeks (Table 5).

DISCUSSION

It was Mayo Clinic who had formulated the criteria for diagnosing Takotsubo Cardiomyopathy which was revised later, which is as follows

1. Suspicion of AMI based on precordial pain and ST elevation observed on the acute-phase ECG Transient hypokinesia or akinesia of the middle and apical regions of the LV and functional hyperkinesia of the basal region, observed on ventriculography or echocardiography.
2. Normal coronary arteries confirmed by arteriography (luminal narrowing of less than 50% in all the coronary arteries) in the first 24 h after the onset of symptoms.
3. Absence of recent significant head injury, intracranial hemorrhage, suspicion of pheochromocytoma, myocarditis, or hypertrophic cardio myopathy[4,7]

Our study demonstrates that 67% patients had some or the other risk factors like Diabetes Mellitus, Hypertension, dyslipidemia. Majority of our patients like in other studies like Tsuchihashi *et al*,[8] Sharkey *et al*[9] are in the elderly age group. i.e 77% were in the age group of 51 to 80 yrs where as 23% were in the age group of 20–50 yrs. In Japan, takotsubo Cardiomyopathy is more prevalent among men,[10] for unclear reasons, but in our study it was females who dominated and which is also consistent with other studies like Kurowski *et al*.[11]

Previous studies have suggested that Takotsubo cardiomyopathy is predominantly preceded by emotional triggers.[3,12] Our data reveal that it is not only the emotional stress (33%) but also the medical stress (35%) like fever, acute gastroenteritis etc followed by surgical stress (21%) that plays the major role. Interestingly 11% of patients had no stress at all. As more and more studies are coming up it is becoming evident that along with the emotional stress there are other factors too which play an important part. One study has even shown that it's not only the tragedies or stress in one's life but it's also the happy emotions that can bring the same condition which is known as "happy heart syndrome".1[3] Though we did not get any such patients, but while elaborating the history one should be careful enough to exclude it too. Though chest pain was the most common mode of presentation in most of the studies in the past,[8,9] it has been consistent in our study too (77%). Along with it 40% patients also had dyspnoea. 18.6% had Cardiogenic Shock, 7% had Acute LVF. Takotsubo cardiomyopathy should be considered to be an acute heart failure syndrome, as reflected by the markedly increased levels of brain natriuretic peptide and left ventricular end-diastolic pressure.[6] These patients often present with cardiac symptoms in the emergency room and on evaluation of ECG are found to be abnormal. Thus the initial diagnosis of Takotsubo Cardiomyopathy is very difficult in the emergency room when the patient presents with typical symptoms. In our study ECG showed T wave inversion in 54%, ST elevation in 49%, Q wave in 9%, ST dep in 7% and No STT changes in 5% which is also consistent with studies done by Sharkey *et al*,[9] Sato *et al*.[14] The Cardiac enzymes were raised in 56% patients in ours study as well in the study conducted by Tsuchihashi *et al*[8]

Our study also supports that troponin levels and electrocardiographic changes on admission are not sufficient to differentiate between this disorder and Acute MI. Coronary Angigraphy was done in order to differentiate between Takotsubo Cardiomyopathy and ishchemic heart disease. After confirming the diagnosis the patients follow up was done to look for the time taken for improvement in the LV function. In our study follow up was available for 70% of patients. Most of the patients recovered with normal LV Systolic function within 4 weeks of follow up. In the study conducted by Sharkey *et al*[9] his patients recovered within 24 ± 29 days which is also consistent with our study. Most of the studies showed recovery after 3 weeks but in our study there was rapid recovery i.e. 56% recovered within1 to 2 weeks itself.[3,9,14,16] Coronary angiogram was done in all the patients in which 93% showed normal coronaries and 7% showed Non flow limiting coronary arteries. These results were consistent with other studies like Tsuchihashi *et al*,[8] Yoshida *et al*[15]

Table 1: Baseline Characteristics

Baseline characteristics	Mean Value	Percent
Gender		
Male	3	7%
Female	40	93%
Age	60.23 ± 12.1	
Hypertension	24	55.8%
Diabetes	19	44.2%
Total cholesterol	177 ± 44.8	
LDL	107 ±43.8	
HDL	48.2 ±15.1	
Stress Event	38	88.3%
Emotional stress	14	32.5%
Medical stress	15	34.8%
Surgical stress	9	20.9%
No stress	5	11.6%
Ejection Fraction	37.2 ±7.55	
Follow up EF	66.6 ±4.6	

Table 2: Age distribution

Age	Frequency	Percent(%)
20-50	10	23
51 - 80	33	77

Table 3: Presenting symptoms

	Number (%)
Fever	1(2.3)
Chest pain	33(76.7)
Dyspnoea	17(39.5)
Acute left ventricular failure	4(9.3)
Tachycardia	3(7.0)
Cardiogenic shock	8 (18.6)

Table 4: ECG changes on Admission

ECG changes	Number (%)
Deep T Inversion	23(53.5%)
ST elevation	21(48.8%)
ST Depression	3 (7%)
No ST/ T changes	2(4.7%)
Q wave	4(9.3%)

Table 5: Time taken for improvement in LV function (weeks)

No. of weeks	Percentage(%)
1	23
2	33
3	20
4	10
5 - 6	10
7 - 8	03

We had 2 patients in Medical illness group, 3 patients in Emotional stress group and 3 patients in the surgical stress group who developed cardiogenic shock. The patients in the non surgical group completely recovered, and it was these patients who took longer time to recover. Three patients in surgical group developed cardiogenic shock with in 24 hrs after surgery. All the other factors like hypovolemia or blood loss of any kind were ruled out. Ion tropic supports could be used only with caution as they are said to be contraindicated in Takotsubo Cardiomyopathy and they increase the catecholamines levels which are already increased in the body.[2] all three patients in surgical group who developed cardiogenic shock expired. Total in hospital mortality was found to be 7% in our study which was also consistent with Akashi *et al.*[16] Post surgical Takotsubo Cardiomyopathy is one of the most dreaded cardiovascular complication. The medical and emotional stress might not cause significant mortality which might be the reason why many studies did not show mortality.

According to Akashi *et al* though many studies have not reported any mortality, it does not convey that mortality in this condition is impossible. He further states that this cardiomyopathy should be considered a possible cause of sudden cardiac death resulting from arrhythmia or cardiac rupture in individuals without obvious heart disease. The prognosis is good in patients who survive the initial severe.

Insult without complications.[4] thus the patients with Takotsubo Cardiomyopathy should not be taken lightly but should be treated with utmost care especially the ones with acute left ventricular failure and cardiogenic shock.

CONCLUSION

Takotsubo Cardiomyopathy is a transient LV dysfunction which is precipitated by adrenergic stress. Pathophysiology and mechanism of distinctive wall motion abnormality are not yet clear. Majority of patients were elderly females. Most common precipitating factors were emotional stress, acute medical illness and surgical stress. Mortality in this condition is rare but when precipitated by surgical stress there was significant increase in mortality. Majority of patients showed recovery of LV function with 56% of the patients recovering within 2 weeks. We should do regular follow up of these patients in order to know the recurrence.

Limitation of this study is that it is a retrospective study with no comparison group. The follow up was done only up to the improvement of the LV function. Hence incidence of recurrence is unknown.

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CONFLICTS OF INTEREST

All authors have none to declare.

REFERENCES

1. Hurst RT, Prasad A, Askew JW 3rd, Sengupta PP, Tajik AJ. Takotsubo cardiomyopathy: a unique cardiomyopathy with variable ventricular morphology. JACC Cardiovasc Imaging. 2010;3(6):641-9. http://dx.doi.org/10.1016/j.jcmg.2010.01.009; PMid:20541719.
2. Sato H, Tateishi H, Uchida T. Takotsubo-type cardiomyopathy due to multivessel spasm. In: Kodama K, Haze K, Hon M, editors. Clinical Aspect of Myocardial Injury:From Ischemia to Heart Failure. Tokyo, Japan: Kagakuhyouronsha; 1990.

p. 56–64. PMid:2239249.

3. Wittstein IS, Thiemann DR, Lima JA, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. N Engl J Med 2005;352:539-48. http://dx.doi.org/10.1056/NEJMoa043046; PMid:15703419.
4. Yoshihiro J. Akashi, MD, PhD, Takotsubo Cardiomyopathy. A New Form of Acute, Reversible Heart Failure Prefecture, Circulation. 2008;118(25):2754-2762. http://dx.doi.org/10.1161/CIRCULATIONAHA.108.767012; PMid:19106400 PMCid:PMC4893309.
5. KurowskiV, Kaiser A, von Hof K, Killermann DP, Mayer B, Hartmann F et al. Apical and midventricular transient left ventricular dysfunction syndrome (tako-tsubo cardiomyopathy): frequency, mechanisms, and prognosis. Chest. 2007;132(3):809-16. http://dx.doi.org/10.1378/chest.07-0608; PMid:17573507.
6. C. Templin, JR, Ghadri J, Diekmann LC, Napp DR, Bataiosu M, Jaguszewski VL et al. Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy. N Engl J Med. 2015;373(10):929-38. DOI: 10.1056/NEJMoa1406761. http://dx.doi.org/10.1056/NEJMoa1406761.
7. Kazuo Komamura, Miho Fukui, Toshihiro Iwasaku, Shinichi Hirotani, Tohru Masuyama. World J Cardiol. 2014;6(7):602-9.
8. Tsuchihashi K, Ueshima K, Uchida T, Oh-Mura N, Kimura K, Owa M et al. Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction: Angina Pectoris–Myocardial Infarction Investigations in Japan. J Am Coll Cardiol. 2001;38(1): 11-8. http://dx.doi.org/10.1016/S0735-1097(01)01316-X.
9. Sharkey SW, Lesser JR, Zenovich AG, Maron MS, Lindberg J, Longe TF, et al. Acute and reversible Cardiomyopathy provoked by stress in women from the United States. Circulation. 2005;111(4):472– 9.http://dx.doi.org/10.1161/01.CIR.0000153801.51470.EB; PMid:15687136.
10. Aizawa K, Suzuki T. Takotsubo cardiomyopathy: Japanese perspective. Heart Fail Clin 2013;9(2):243-7. http://dx.doi.org/10.1016/j.hfc.2012.12.001; PMid:23562125.
11. Kurowski V, Kaiser A, von Hof K, Killermann DP, Mayer B, Hartmann F, Schunkert H, Radke PW. Apical and midventricular transient left ventricular dysfunction syndrome (tako-tsubo cardiomyopathy): frequency, mechanisms, and prognosis. Chest. 2007;132(3):809-16.http://dx.doi.org/10.1378/chest.07-0608; PMid:17573507.
12. Brandspiegel HZ, Marinchak RA, Rials SJ, Kowey PR. A broken heart. Circulation 1998;98(13):1349.http://dx.doi.org/10.1161/01.CIR.98.13.1349; PMid:9751687.
13. Ghadri, Jelena R., et al. Happy heart syndrome: role of positive emotional stress in takotsubo syndrome. European heart journal. 2016;ehv757. http://dx.doi.org/10.1093/eurheartj/ehv757; PMid:26935270.
14. Sato M, Fujita S, Saito A, Ikeda Y, Kitazawa H, Takahashi M *et al.* Increased incidence of transient left ventricular apical ballooning (so called "Takotsubo" cardiomyopathy) after the mid-Niigata Prefecture earthquake. Circ J. 2006;70(8):947-53. http://dx.doi.org/10.1253/circj.70.947; PMid:16864923.
15. Yoshida T, Hibino T, Kako N, Murai S, Oguri M, Kato K *et al.* A patho physiologic study of tako-tsubo cardiomyopathy with F-18 fluorodeoxyglucose positron emission tomography. Eur Heart J. 2007;28:2598 -604.http://dx.doi.org/10.1093/eurheartj/ehm401; PMid:17921529.
16. Akashi YJ, Musha H, Kida K, Itoh K, Inoue K, Kawasaki K *at al.* Reversible ventricular dysfunction takotsubo cardiomyopathy. Eur J Heart Fail. 2005;7(7):1171-6. http://dx.doi.org/10.1016/j.ejheart.2005.03.011; PMid:16397924.

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