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Original Work

Does the clinical profile of Gujarati patients with Takayasu's aortoarteritis differ from other Indians?

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ABSTRACT: Takayasu's aortoarteritis is a well-known yet rare form of large vessel vasculitis. It is a chronic inflammatory diseas, which has remained an enigma since it was first described a century ago. The present study was done to document the demographic profile, clinical course, complications and survival of 30 consecutive patients with aortoarteritis in the Gujarati population of western India. The study used non-invasive (color doppler, CT and MR angiography) and invasive techniques (conventional angiography) to document the vessels involved. The study showed almost equal incidence of disease in males and females in the Gujarati population unlike in other studied populations. Incidence of type-III aortoarteritis was the most common and left renal involvement was found to be significantly more common than right renal involvement in the present study. There was no mortality during the study period.

KEY WORDS: ***Vasculitis; Takayasu's aortoarteritis; Clinical profile; Gujarati population***

INTRODUCTION

Takayasu's aortoarteritis or pulseless disease is an inflammatory vascular disease of unknown etiology with varied natural history, clinical presentation and prognosis. Adams[1] first described nonspecific aortoarteritis in 1827, when he noted absence of pulse in all four extremities in his patient. In 1908, Takayasu[2], a professor of ophthalmology in Japan, presented a case of a 21-years-old woman with characteristic fundal arteriovenous anastomoses with absent radial pulse. Subsequently, this nonspecific panarteritis that affects the intima and the adventitia of the aorta and its major branches was called Takayasu's arteritis.

The inflammation leads to stenosis, occlusion, aneurysm formation or combinations of these. Takayasu's aortoarteritis mainly involves the aorta and its major branches. The arterial lesions can lead to secondary hypertension, retinopathy, cardiac involvement, cerebrovascular accident or premature death, depending on the artery involved. While the etiology of aortoarteritis remains unknown, various modes of treatment including steroids, vascular surgery and balloon angioplasty have been employed for management of this disease. To make a decision about elective intervention, we must have data on the natural history, clinical course, complications and prognosis of this disease. Although a lot of work has been done in the past to understand the various aspects of this disease, many things regarding etiology, natural history and clinical course still needs to be understood. The disease manifests with great variation in clinical profile in India as compared to Japan and western countries.[3] The present study is an effort to study the clinical profile of Takayasu's arteritis in the Gujarati population in an attempt to solve some of the various challenges posed by this disease in our part of the world. This study documents the demographic profile, clinical course, complication and survival of 30 consecutive patients with aortoarteritis, who underwent systematic follow-up at our centre in a prospective manner.

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METHODOLOGY

Study population

The study is a prospective, single centre observational study carried out in the Department of Cardiology, UN Mehta Institute of Cardiology and Research, from January 2009 to December 2010. UN Mehta Institute is a tertiary level cardiac care centre situated in Ahmedabad, Gujarat, India. Thirty consecutive patients residenting inGujarat, diagnosed with Takayasu's arteritis were enrolled in the study. The diagnosis of Takayasu's aortoarteritis was based on the American Rheumatology Association criteria.[4]

Methods

After taking approval from the ethical committee of the institute, all enrolled patients underwent detailed history, physical examination, noninvasive and invasive testing after due consent. Data were collected for the symptoms which brought the patients to the physician's attention, signs and symptoms of organ ischemia (arm or leg claudication, visual disturbances, syncopal attacks, TIA, stroke, angina, hemoptysis, congestive heart failure, subclavian steal syndrome), and the cardiac symptoms with their staging. All the patients underwent carotid artery doppler, bilateral upper limb arterial doppler, abdominal aorta doppler and renal artery doppler study. All patients had detailed echocardiography to assess LV function, aortic regurgitation, involvement of proximal coronaries and involvement of pulmonary artery as manifested by development of pulmonary artery hypertension. This was followed by noninvasive imaging with CT or MR angiography for ascending aorta, arch vessels, descending thoracic aorta and abdominal aorta with its branches. Twenty-five patients out of 30 patients had conventional catheterization done either with angiography or with digital subtraction angiography.

All patients were followed for two years for the development of new signs or symptoms, neurological events, development of renal failure or other evidence of organ ischemia. Data for the treatment received were also collected.

Statistical analysis

All collected data were analyzed by using statistical software SPSS v20; Medcalc and Microsoft Excel 2007. Quantitative data was expressed as median and range while qualitative data was expressed as a percentage. Chi-square test and Fisher's exact test had been performed to find out comparisons among qualitative data. P value of <0.05 has been considered as significant.

RESULT

Out of total 30 patients, 14 were males and 16 were females (p=NS). The median age of patients in the study was 30.5±4.6years; ranging from 12 to 39 years. Twenty-five out of 30 patients had hypertension documented in one of the central vessels. Headache was the most common presenting symptom with 25 (83.3%) out of 30 patients having Takayasu's aortoarteritis. Pulselessness, the major sign of aortoarteritis was found in 20 patients (66.6%)whereas five patients (18.8%) had congestive heart failure according to the Framingham criteria for the diagnosis of heart failure, with 4 patients (13.3%) having hypertensive heart failure. None of the patient had valvular regurgitation. Five patients (18.8%) had neurological event in the form of hemiplegia, and retinopathy was seen in 16 patients. Ten patients (37.3%) had normocytic normochromic anemia. (**Table 1**).

Elevated ESR>20mm in the first hour was seen in 12 (40%) patients. Nine (30%) patients, including 5 men had strongly positive Mantoux test. A careful search revealed active tuberculosis in only 3 (10%) patients; with all of them having pulmonary tuberculosis.

Table 1: The incidence of various signs and symptoms at presentation

Clinical Features	Percentage
Hypertension	83.3%
Headache	83.3%
Dyspnoea	53.3%
Syncope / Giddiness	20%
Nausea / Vomiting	16.6%
Stroke	16.6%
Palpitation	16.6%
Visual Complaints	13.3%
Weight Loss	13.3%
Arthralgia	3.3%
Fever	3.3%

Distribution of various subtypes of aortoarteritis

The distribution of various subtypes of aortoarteritis showed some similarity with previous studies. However some differences were also seen. These include similar incidence of type I and type II but higher incidence of type III (61%) and type IV (25%) aortoarteritis in the Gujarati population compared to other Indian populations. (**Table 2**)

Angiographic findings

Twenty-five out of thirty patients underwent invasive angiography. The remaining 5 patients were subjected to MR angiography and/or color Doppler study of involved vessels, as there was difficulty in vascular access with conventional angiography in these patients. (**Table 3**)
The abdominal aorta was the most common site of involvement (P<0.01). Renal arteries were highly involved in the subgroup with involvement of the right renal artery in 26.6%, the left renal artery in 46.6% and both vessels in 6.6% of the patients. Ascending aorta and arch involvement was seen in fewer patients in the study. This may be one of the reasons for lesser incidence of hemiplegia and aortic regurgitation seen in the present study.
During 24 months of follow up, out of 30 patients, 5 patients (16.6%) developed a neurological event in the form of hemiplegia, 5 (16.6%) developed congestive heart failure and one patient presented with hemoptysis.

Table 2: Comparison of distribution of various subtypes of aortoarteritis

Type	Mexican study[5] N=40	Sharma et al[6] N=83	Korean study[7] N=61	Present study N=30	P-value
Type I	8%	10%	31.1%	2(6.66%)	<0.01
Type II	11 %	30%	18.1 %	3 (10%)	<0.01
Type III	65 %	55%	9.8%	18 (60 %)	<0.01
Type IV	16 %	5%	11.5%	7 (23.33 %)	<0.04
Type V	-		29.5%	-	

Table 3: Incidence of vessels involved on angiography

Clinical Features		Percentage	P-value
Ascending Aorta		3.33%	
Arch of Aorta		3.33%	<0.01
Thoracic Aorta		20%	
Abdominal Aorta		70%	
Subclavian	Rt	8 (26.6%)	0.76
	Lt	8 (26.6%)	
Carotid	Rt	3 (10%)	1.00
	Lt	4 (13.3%)	
Renal	Rt	26.6%	0.24
	Lt	46.6%	
	Both	6.6%	
Celiac		3.33%	
Superior Mesenteric		3.33%	
Inferior Mesenteric		0%	
Iliac		12%	

DISCUSSION

Takayasu's aortoarteritis is a disease of young people. Most of the patients in the present study were in the age group 20 to 40 years except for 2 patients, one of them being 12 years and another 15 years of age. According to Sharma et al[8], the age of onset may range from infancy to late middle age. Kerr et al[9] in his study found 1/3rd of his cases comprising of childhood onset of nonspecific aortoarteritis (NSAA). While in another study by Panja et al[10], some patients were as young as 5 years.

Takayasu's aortoarteritis has strong predilection for females as shown by various studies[10-12]. According to Panja et al[10], Male: Female ratio was 1:6.4 in eastern Indian and Bangladeshi patients. However in the present study the males and females are almost equally affected.

The most common presentations of Takayasu's arteritis include symptoms resulting from arterial occlusive disease of the aorta, aortic arch, and large vessels. Nearly all patients with Takayasu's arteritis either present initially with or ultimately develop large-vessel manifestations of the disease, including hypertension caused by suprarenal aortic or renal artery occlusive disease, pulse deficits and/or vascular bruits, and upper and/or lower extremity claudication.[13] However variable disease presentation between different populations is well illustrated by Moriwaki et al[3] in their study of Indian and Japanese patients.

Hypertension was the most common mode of presentation in the present study with 83% patients having hypertension and only 66% patients having pulselessness. While Wilkinson et al[14] found the most common mode of presentation to be pulselessness. Another study, by Lupi – Herrera et al[15], demonstrated diminished or absent pulse in 96% of patients, bruits in 94% and hypertension in 72% of patients. The commonest etiology for systemic hypertension in Takayasu's arteritis is renal artery stenosis, while other less common causes include atypical coarctation, reduced aortic capacitance and diminished baroreceptor reactivity. These findings highlight that a comprehensive vascular examination, including measurement of blood pressure in both arms, palpation and auscultation of pulses in all major vascular regions are critical components of the clinical evaluation of patients with suspected Takayasu's arteritis.

There is wide variation in the pattern of vascular involvement according to geographical region. According to Agrawal et al[16], the incidence of type-III and type-IV aortoarteritis is greater in the north Indian population. In the present study also, the incidence of type-III and type-IV aortoarteritis is found to be commoner than type-I and type-II. Similarly, Panja et al[10] found type-III and IV to be the more common types in eastern India and Bangladesh. In Japan, the proximal aorta is predominantly involved, with features of "reversed coarctation"[17,18]. In southeast Asia and Africa "middle aortic syndrome" is found more commonly i.e. involvement of the descending thoracic aorta and abdominal aorta[19]. Similarly, in the present study, thoracic and abdominal aorta involvement was found to be much more common than other vessel involvement. There was no case of coronary artery involvement (Type-V) in the present study.

Although the most frequent pattern of disease varies geographically[6,20,21], stenotic lesions were found predominantly in more than 90% of patients, whereas aneurysms were reported in approximately 25% of patients[9,19,22,23]. Pulmonary arteries were involved in up to 50% of patients[24,25].

Different natural history studies report different survival rates[25,26]. Subramanyan et al[26] in his study has reported 5 years survival rate of 80.3% after diagnosis beyond which the survival curve flattened out with no further mortality. Similar to the survival curve, the event-free survival curve also flattened out after the first 5 years of diagnosis. Ishikawa et al[25] has reported higher rates of survival (89.7%) and event-free survival (86.9%) at 5 years after patients were diagnosed. Five-year survival rate in combined groups IIB and III was 70%, compared with 100% in-group I. No acute event occurred in patients from group I compared to 5 events in other categories[25]. In the present study, no mortality was reported possibly because of the brief period of study (2 years) and lesser incidence of type I and type II arteritis possibly contributing to lesser strokes and aortic regurgitation, an important contributor to mortality.

Limitations of study

Takayasu's aortoarteritis is not an uncommon disease in this part of the world with significant morbidity and long term complications. However the true nature of Takayasu's aortoarteritis in the Gujarati population may be under-represented in the present study due to these being tertiary hospital statistics and because patients with moderate severity of disease may not have sought medical consultation. Other reasons for underestimation of the true incidence of the disease may be small sample size, shorter inclusion period and relatively shorter follow-up period.

CONCLUSION

This study provides epidemiological data on Takayasu's aortoarteritis for the Gujarati population. The important conclusions from this study are as follows:

- The study shows that there is no difference in incidence of Takayasu's aortoarteritis between males and females in Gujarati populations unlike many other studies where female preponderance has been encountered.[10,11,12]
- The study found that involvement of the left renal artery was significantly more common than the right renal artery, a phenomenon that needs to be evaluated further.
- Type III Takayasu's aortoarteritis is more common than other types of Takayasu's aortoarteritis unlike the Korean Study where Type I and Type IV are commonest.
- There was no mortality throughout the study period thus showing a relatively benign short

course probably due to lesser involvement of arch vessels.

There is need for further research regarding the pattern of disease in the Gujarati population to find out effective preventive and treatment strategies to reduce complications and mortality for this chronic disease affecting young people of our society.

REFERENCES

1. Adams R. Cases of diseases of the heart accompanied with pathological observations. *Medical Classics*. 1939;3:633-96. (Originalausgabe in: *Dublin Hospital Reports*. 1827;4:S353-453).
2. Takayasu M. A case of peculiar changes in the central retinal vessels. *Acta Soc Ophthalmol Jpn*. 1908;12:554-5.
3. Moriwaki R, Noda M, Yajima M, Sharma BK, et al. Clinical manifestations of Takayasu arteritis in India and Japan: new classification of angiographic findings. *Angiology*. 1997;48:369-79.
4. Arend WP, Michel BA, Bloch DA, Hunder GG, et al. The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. *Arthritis Rheum*. 1990;33(8):1129-34.
5. Dabague J, Reyes PA. Takayasu arteritis in Mexico: a 38-year clinical perspective through literature review. *Int J Cardiol*. 1996;54 Suppl:S103-9
6. Sharma BK, Sagar S, Singh AP, Suri S. Takayasu arteritis in India. *Heart Vessels Suppl*. 1992;7:37-43.
7. Park MH, Park YB. HLA typing of Takayasu arteritis in Korea. *Heart Vessels Suppl*. 1992;7:81-4.
8. Sharma S, Rajani M, Shrivastava S, Kaul U, et al. Non-specific aorto-arteritis (Takayasu's disease) in children. *Br J Radiol*. 1991;64(764):690-8.
9. Kerr GS, Hallahan CW, Giordano J, Leavitt RY, et al. Takayasu arteritis. *Ann Intern Med*. 1994;120(11):919-29.
10. Panja M, Kumar S, Sarkar C, Sinha DP, et al. Long term follow up of Takayasu's disease. *J Am Coll Cardiol*. 1997;29:P-218A.
11. Numano F, Okawara M, Inomata H, Kobayashi Y. Takayasu's arteritis. *Lancet*. 2000;356(9234):1023-5.
12. Dillon MJ. Childhood vasculitis. *Lupus*. 1998;7(4):259-65.
13. Mwipatayi BP, Jeffery PC, Beningfield SJ, Matley PJ, et al. Takayasu arteritis: clinical features and management: report of 272 cases. *ANZ J Surg*. 2005;75(3):110-7.
14. Wilkinson NM, Page J, Uribe AG, Espinosa V, et al. Establishment of a pilot pediatric registry for chronic vasculitis is both essential and feasible: a Childhood Arthritis and Rheumatology Alliance (CARRA) survey. *J Rheumatol*. 2007;34(1):224-6.
15. Lupi-Herrera E, Sánchez-Torres G, Marcushamer J, Mispireta J, et al. Takayasu's arteritis. Clinical study of 107 cases. *Am Heart J*. 1977;93(1):94-103..
16. Agarwal R, Tyagi S, Aroa R, Khalilullah M. Clinical and angiographic profile of aorto-arteritis in India. *Ind Heart J*. 1989;41:390-3
17. Shimizu K, Sano K. Pulseless disease. *J Neuropath clin Neurol*. 1951;1:37.
18. Inada K, Shimizu H, Kolayashi J. Pulseless disease and atypical coarctation of aorta, with special reference to their genesis. *Surgery*. 1962;52:433.
19. Sen PK, Kinare SG, Engineer SD, Parukar GB. The middle aortic syndrome. Br Heart J. 1963;35:610.
20. Ishikawa K1, Maetani S. Long-term outcome for 120 Japanese patients with Takayasu's disease. Clinical and statistical analyses of related prognostic factors. *Circulation*. 1994;90(4):1855-60.
21. Park MC, Lee SW, Park YB, Chung NS, et al. Clinical characteristics and outcomes of Takayasu's arteritis: analysis of 108 patients using standardized criteria for diagnosis, activity assessment, and angiographic classification. *Scand J Rheumatol*. 2005;34(4):284-92.
22. Maksimowicz-McKinnon K1, Clark TM, Hoffman GS. Limitations of therapy and a guarded prognosis in an American cohort of Takayasu arteritis patients. *Arthritis Rheum*. 2007;56(3):1000-9.
23. Lupi E, Sánchez G, Horwitz S, Gutierrez E. Pulmonary artery involvement in Takayasu's arteritis. *Chest*. 1975;67(1):69-74.
24. Yamada I, Shibuya H, Matsubara O, Umehara I, et al. Pulmonary artery disease in Takayasu's arteritis: angiographic findings. *AJR Am J Roentgenol*. 1992;159(2):263-9.
25. Ishikawa K. Survival and morbidity after diagnosis of occlusive thromboaortopathy (Takayasu's disease). *Am J Cardiol*. 1981;47(5):1026-32.
26. Subramanyan R, Joy J, Balakrishnan KG. Natural history of aortoarteritis (Takayasu's disease). *Circulation*. 1989;80(3):429-37