Original research

The angiographic and clinical profile of patients with Takayasu aortoarteritis

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Abstract

Objective: Takayasu arteritis is a rare, chronic, inflammatory disease that primarily affects the aorta and its major branches. It mainly affects young females, and it can cause significant morbidity and mortality if untreated. The aim of this study was to evaluate the demographic profile, clinical manifestations, diagnostic features, angiographic findings in patients with aortoarteritis (Takayasu arteritis).

Methods: We enrolled prospectively 116 patients with Takayasu arteritis who came to Cardiology OPD at tertiary cardiac care hospital. We looked for constitutional symptoms, heart-related symptoms, systemic hypertension, neurological symptoms and upper & lower limb fatigue and claudication. We evaluated our patients using different diagnostic criteria: clinical, ACR criteria and Indian Takayasu Activity score. We also studied the angiographic profile and lesion characteristics in these patients, based on peripheral and coronary angiograms.

Results: We studied patients consisted of 14 male patients (12.1%) and 102 female patients (87.9%). Type V Takayasu arteritis was most common type (36.2%). Fatigue (60%) was most common cardinal symptom followed by myalgia (30%) and arthralgia (10%). About 43% of patients had neurological symptoms. Systemic hypertension (67%) was the most common manifestation of renal involvement. 110(95%) of the patients met clinical criteria and 105(91%) patients had American College of Rheumatology (ACR) score ≥3. Angiographic evidence of left renal artery stenosis was more (20%) than right renal artery stenosis (15%). bilateral renal artery involvement was found in 29% of patients.

Conclusion: Type V Takayasu arteritis was most common type (36.2%) of total study population. Hypertension and subclavian artery involvement both were seen in 2/3rd of population. Angiographic evidence of right and left renal artery stenosis was seen in 15% and 20% respectively, while bilateral renal artery involvement was found in 29% of patients.

Take home message: Takayasu arteritis rarely involves the coronary arteries. Angiographic evidence of right and left renal artery stenosis was observed in 15% and 20% of patients, respectively, with bilateral renal artery involvement found in 29% of patients.

Key words: Clinical presentation, aorta, renal artery, coronary artery, Takayasu aortoarteritis

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Introduction

Aortoarteritis (Takayasu arteritis) is a condition that affects people of all races and has an estimated incidence of 1.2-2.6/million per year in the Western population. It is more common in Southeast Asia, Central and South America, and Africa (1). Around 10% of Takayasu arteritis patients have no symptoms (2). Clinical manifestations of Takayasu arteritis are primarily determined by disease stages, which is divided into two phases, the first of which is pre-pulseless and the second of which is occlusive (3, 4)

The pulseless disease chronic inflammatory arteritis, mainly affects the coronary, carotid, pulmonary, and renal arteries in addition to aorta and its major branches (5, 6).

Takayasu's arteritis causes arterial media to be destroyed, which can occasionally result in aneurysm formation. It also causes increasing wall fibrosis and lumen constriction (6).

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Angiography can be performed to evaluate the extent and severity of arterial involvement. Angiography can help to assess the stenosis, occlusion, aneurysm formation, and collateral formation. The disease is classified into five types on the basis of angiographic findings (7). These systems are useful in comparison of patients and for planning management. The “disease extent index for Takayasu's arteritis (DEI.Tak)” is designed to document those features specific for Takayasu arteritis. These items were derived by consensus opinion from experts in the clinical management of Takayasu arteritis in India and in the U.K. It is an assessment tool in which items corresponding to large arterial disease carry greater weights than general items of the disease, and changes in the prior 3 months in the physical examination are the basis of evaluation (8). The Indian Takayasu's Arteritis Score (ITAS), a revised version of the DEI.TAK that takes disease activity and treatment response, was introduced (9).

Many biomarkers had been investigated to assess disease activity of Takaysu aortoarteritis; erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are the most commonly used biomarkers for the assessment of disease activity of Takaysu aortoarteritis.

The aim of this study was to evaluate the demographic profile, clinical manifestations, diagnostic features, angiographic findings in patients with aortoarteritis (Takayasu arteritis).

Methods

Study population and design

Prospective observational study was performed in 116 patients with Takayasu Arteritis satisfying the 1990 American College of Rheumatology (ACR), Ishikawa's, or Sharma's criteria were recruited from cardiology outpatient department at tertiary cardiac care hospital from September 2018 to February 2021. The study has been approved by the institutional ethics committee (UNMICRC/CARDIO/2018/15).Informed consent was obtained from all individual participants the manuscript.

Definitions

We studied 116 patients’ data related to clinical presentation, disease extent (DEI.Tak score), activity (Indian Takayasu arteritis clinical activity score), angiography and treatment variables were collected for all patients. ACR and Ishikawa's Criteria for Takayasu's Arteritis (Modified According to Sharma et al.)(10, 11) criteria include limb claudication, pulselessness or pulse differences in limbs, an unobtainable or significant blood pressure difference (>10 mmHg systolic blood pressure difference in limb), fever, neck pain, transient amaurosis, blurred vision, syncope, dyspnea or palpitations.

The American College of Rheumatology (ACR) has created Takayasu arteritis categorization criteria (3 of 6 are required) (10). When three or more criteria are present, the sensitivity of criteria in diagnosis of Takayasu arteritis is 90.5% and the specificity - 97.8%. The following are the criteria:

1. Age of 40 or less at disease beginning
2. Extensive claudication of the extremities
3. A reduction in the pulse of one or both brachial arteries
4. A difference in systolic blood pressure of at least 10 mm Hg between arms
5. A bruising of one or both of the subclavian arteries or the abdominal aorta
6. Arteriographic constriction or occlusion of the entire aorta, its principal branches, or big arteries in the upper or lower limbs caused by something other than arteriosclerosis, fibromuscular dysplasia, or other causes.

Data Collection

Based on peripheral and coronary angiograms, we collected data on the angiographic profile and lesion characteristics in these patients. We investigated these individuals' demographic, clinical, diagnostic, and angiographic profiles. We examined for constitutional symptoms, heart-related symptoms, systemic hypertension, neurological symptoms, and exhaustion and claudication in the upper and lower limbs.

Statistical analysis

Statistical analysis was performed using SPSS 26.0 software (IBM, Inc., Chicago, IL, USA). The categorical variables are expressed as number- percentages, and the continuous variables are expressed as the mean (standard deviation).

Results

Our study patients consisted of 14 male patients (12.1%) and 102 female patients (87.9%), with female to male ratio of 7.28:1. Demographic and symptoms of total population are mentioned in table 1. The mean age of total population was 30.16 (11) years with mean body mass index - 22 (5) Kg/m^2. Most common age of presentation was in age group 21 to 30 years (49%) followed by age group of 31 to 40 years (41%). The cardinal symptoms were - myalgia/arthralgia, neurological and mesenteric. Fatigue (60%) was most common cardinal symptom followed by myalgia (30%) and arthralgia (10%). Out of 116 patients 35(31%) had all cardinal symptoms. Cardiovascular system (CVS) (manifestations were seen in almost 52% of cases with exertional dyspnea being the most common symptom. Orthopnea and paroxysmal nocturnal dyspnea (PND) were least common symptoms (both less than 3%). About 43% of patients had neurological symptoms and of which giddiness was most common (39%), followed by syncope (21%), neck pain (16%) and stroke (12%), seizure and blurred vision (5%), TIA (2%) were least common symptoms. Mesenteric manifestations were sees less commonly, around 15% in all. Most common symptoms of this were weight loss (19%), followed by anorexia (16%) and postprandial abdominal pain (11%). Systemic hypertension (67%) was seen as the most common manifestation of renal involvement. Though, renal failure was rarely noticed (3% of patients). Upper limb claudication was seen in about 40% of the cases, with bilateral upper limb claudication in quarter of the patients. Lower limb claudication was seen in about 30% of the cases. Overall, 41% of the patients had miscellaneous complaints with headache as the most common complaint. About 1/5th of the patients had past history of tuberculosis (11%). Patients had increased sedimentation rate and C-reactive protein.

Table 1. Demographic and symptoms of total population (n=116)

Demographic data	**Number or mean**	**% or SD**
Age (years)	30.16	11
Gender		
Male	14	12.1%
Female	102	87.9%
Cardinal Symptoms		
Myalgia	35	30
Arthralgia	12	10
Neurological Symptoms		
Giddiness	45	39
Syncope	24	21
Neck pain	19	16
Stroke	14	12
Seizure	6	5
Blurred vision	6	5
Transient ischemic attack (TIA)	3	2
Mesenteric Symptoms		
Weight loss	22	19
Anorexia	18	16
Post prandial abdominal pain	13	11
Laboratory Tests		
Erythrocyte sedimentation rate	25.17	15.9
C-reactive protein	14.43	23.9

Clinical diagnostic criteria are mentioned in Table 2. Type V Takayasu arteritis was most common type in the present study and comprised 36.2% of total study population followed by type I (22.4%) and type II B (13.8%), type III (12.1%), type IV (8.6%) and type II A (6.9%). One hundred ten (95%) of the patients met clinical criteria and 105(91%) patients had ACR score ≥3. All of the study patients met at least one of the criteria (either clinical or ACR). At first visit 95% of patients showed ITAS score ≥ 3.

Table 2. Clinical diagnostic criteria

Clinical criteria	**n**	**%**
Major Criteria		
Typical sign and symptoms (>1/12 months)	75	65%
Imaging lesion in mid left subclavian artery	71	61%
Imaging lesion in mid right subclavian artery	54	47%
Minor Criteria		
ESR (>20 mm)	68	59%
Carotid artery tenderness	19	17%
Blood Pressure(Brachial BP>140/90, Popliteal BP >160/90)	45	39%
AR by auscultation, echo or angiography	18	16%
Pulmonary artery lesion	10	9%
Left common carotid artery lesion	52	45%
Distal brachiocephalic lesion	14	13%
Descending thoracic aorta lesion	29	25%
Abdominal aorta lesion	35	31%
Coronary artery lesion	19	17%

Angiographic profile of total population is mentioned in Table 3. The lesions of coronary and pulmonary artery were less commonly seen, in less than 20% of cases each. Angiographic evidence of right and left renal artery stenosis was seen in 15% and 20% respectively, while bilateral renal artery involvement was found in 29% of patients.

Discussion

The mean age of presentation of Takayasu arteritis in the present study was 30.16 (11) years. In the study of 88 patients by Subramanyam et al (12) from India, the mean age at symptom onset was 24 (9) years and mean age at diagnosis was 28 (10) years. In a large observational study done in Japan by Watanabe et al. (13) the median age at onset was 35 years, which was significantly higher in male patients (median, 43.5 years) than in female patients (median, 34 years; p<0.001). Previous studies have shown predilection for females though with a wide geographical variation. In the present study there were 14 male patients (12.1%) and 102 female patients (87.9%), with female: male ratio of 7.28:1. Panja et al. (14) reported female to male ratio as 6.4:1.14.

Type V Takayasu arteritis was most common type in the present study and comprised 37% of total study population followed by type I, type II, type III and type IV. However , there is a wide variation in the frequency of occurrence of types of arteritis. The genetic, regional and environmental factors may have a play in this varied spectrum.

Table 3. Angiographic profile		
Zone and vessel Involved	**N=116**	**(%)**
Aorta		
Ascending aorta	19	17%
Arch of aorta	8	7%
Descending aorta	30	26%
Abdominal aorta	26	23%
Arch Branches		
Innominate artery	18	16%
Rt. Subclavian artery	48	42%
Lt. subclavian artery	73	63%
Rt. Vertebral artery	11	9%
Lt. Vertebral artery	18	16%
Rt. Common carotid artery	33	29%
Lt. Common carotid artery	53	46%
Rt. Internal carotid artery	4	3%
Lt. Internal carotid artery	4	3%
Visceral Aortic Branches		
Celiac artery	54	47%
Superior mesenteric artery	33	29%
Inferior mesenteric artery	4	3%
Right renal artery	17	15%
Left renal artery	23	20%
Bilateral renal artery	33	29%
Iliac and Femoral artery		
Iliac artery	7	6%
Femoral artery	5	4%
Lt.-left, Rt-right		

Agarwal et al (15) reported type III (53%) is most common among north Indian patients and in a large series data of Panja et al showed type IV (36%) is most common type of Takayasu arteritis in patients belonging to Eastern India and Bangladesh (14).

Almost all patients (97%) had one or other cardinal symptoms. Fatigue was most common cardinal symptom in our patients followed by myalgia and weight loss. Of all the patients, 31% had all cardinal symptoms listed in the study. These findings correlate with other studies, in which symptoms like fever, night sweat, malaise, weight loss, arthralgia, myalgia and mild anemia were common symptoms, usually associated with the early or pre-pulseless phase (16).

CVS system manifestations were seen in almost 60% of cases with exertional dyspnea being the most common symptom. Orthopnea and paroxysmal nocturnal dyspnea were least common symptoms (both less than 3%) (17). Hoffman in his study found CVS symptoms in 38% of cases, most common being dyspnea followed by angina, palpitations (< 10%) and cardiac failure (<5%) (18).

About, 43% of our patients had neurological symptoms and of which giddiness was most common, followed by blurred vision and syncope. About 12% of our patients had a history of stroke. Hoffman found CNS symptoms in 57% of cases, most common being giddiness (18). Kim et al. (19) found headache in 50-70% of cases, vertigo and convulsions in 0-20% and stroke in 5-9% of cases.

According to Morwaki et al. (20)Japanese patients have higher rate of neurological complications, because of more frequent aortic arch involvement as compared to Indian patients in whom abdominal aorta and renal arteries are more commonly involved (21).

Mesenteric symptoms were less common, accounting for around 15% of all cases. Weight loss was the most prevalent, followed by anorexia and postprandial stomach pain. The most common sign of renal involvement was systemic hypertension (67%). Although renal failure was uncommon (seen in less than 3% of individuals). Approximately 60% of our study participants exhibited systemic hypertension, which was comparable to earlier studies in which approximately 33-83% of patients were found to be hypertensive (10, 22, 23).

A common cause of systemic hypertension in Takayasu arteritis patients is renal artery stenosis, other contributory factors being atypical coarctation, decreased baroreceptor reactivity and decreased aortic capacitance. In patients with Takayasu arteritis as the inflammatory process progresses and gradually leading to stenosis and occlusion, more characteristics clinical features appear but at the same time, the development of collateral circulation may ameliorate some features.

Upper limb claudication was observed in 50% of the cases in the current investigation, with a quarter of the patients experiencing bilateral upper limb claudication. Lower limb claudication was observed in 28.4% of the patients. The current investigation is consistent with the Panja et al series, which found intermittent limb claudication in 25% of Takayasu arteritis patients (14). Upper limb claudication (53%) was shown to be more prevalentin our patients than lower limb claudication (15%), 43% of the patients had a variety of problems, with headache being the most prevalent. Approximately one-fifth of the patients had a history of tuberculosis.

In this study, we applied clinical and ACR criteria to diagnose Takayasu arteritis (10). Overall, 95% of patients satisfied clinical criteria, and 91% had an ACR score of 3. All study participants met at least one of the criteria (clinical or ACR). This is equivalent to modified criteria by Sharma et al, which have a sensitivity of 92.5% and ACR score 3, which has a sensitivity of 91% previously assessed. In 95% of patients, the ITAS score was more than (3, 11).

All 116 patients underwent computed tomography or conventional angiography. The subclavian artery was the most often affected vessel; aortic involvement was largely seen at the abdomen level, with higher involvement of the left subclavian artery compared to the right subclavian artery and larger involvement of the left common carotid artery compared to the right common carotid artery.

Reno-vascular hypertension is a common finding in Takayasu arteritis, occurring in 50% of patients. The main cause of hypertension in Takayasu arteritis patients is renal artery stenosis, but other variables such as atypical coarctation and decreased arterial wall elasticity also play a role. Renal artery stenosis reduces renal perfusion, resulting in increased renin secretion and aldosterone levels, which leads to salt and water retention and higher blood pressure.

Takayasu arteritis rarely involves the coronary arteries. Angiographic evidence of right and left renal artery stenosis was observed in 15% and 20% of patients, respectively, with bilateral renal artery involvement found in 29% of patients.

In previous study, Kumar et al. (24) described that 9% to 11% coronary artery involvement in Takayasu arteritis presents as stenosis, occlusion or coronary artery aneurysm formation and mostly involving the ostia of the coronary arteries. In our cohort of 116 patients, the coronary and pulmonary artery lesions were less commonly seen, in less than 20% of cases each. Yamada et al. (25) found 70% pulmonary artery involvement in the small series of 30 patients and noticed that the extent of arteritis in the major branches of the aorta appear to correlate with pulmonary artery involvement. Johnston et al. (5) described 100% pulmonary artery involvement in Takayasu arteritis patients based upon method used to describe the pulmonary vasculature. Sharma et al. (26) studied pulmonary arterial anatomy in Takayasu arteritis patients using intravenous digital subtraction angiography) and found angiographically evident pulmonary arterial involvement in 14% patients and out of which 1/3rd of cases have abnormal chest radiographs. Takayasu pulmonary artery vasculopathy shows little correlation with the systemic pattern of arterial involvement.

Study limitations

Being a referral tertiary care center the population studied may not be perfect representative of actual incidence and prevalence of disease. The outpatients department visits, admission and follow-up may have been mostly constituted of the patients who underwent or had schedule for some kind of intervention.

Conclusion

Type V Takayasu arteritis was most common type (37%) of total study population. Hypertension and subclavian artery involvement both were seen in 2/3rd of population. Angiographic evidence of right and left renal artery stenosis was seen in 15% and 20% respectively, while bilateral renal artery involvement was found in 29% of patients.

Ethics: The study has been approved by the institutional ethics committee (UNMICRC/CARDIO/2018/15). Informed consent was obtained from all individual participants the manuscript

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Conflict of Interest: The authors declared that there is no conflict of interest with any financial organization regarding the material discussed

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References

1.Richards BL, March L, Gabriel SE. Epidemiology of large-vessel vasculidities. Best practice & research. Clin Rheumatol 2010; 24: 871-83.

2.Maffei S, Di Renzo M, Bova G, Auteri A, Pasqui AL. Takayasu's arteritis: a review of the literature. Intern Emerg Med 2006; 1: 105-12.

3.Uthman IW, Bizri AR, Shabb NS, Khury MY, Khalifeh MJ. Peritoneal sarcoidosis: case report and review of the literature. Semin Arthritis Rheum 1999; 28: 351.

4.Aluquin VP, Albano SA, Chan F, Sandborg C, Pitlick PT. Magnetic resonance imaging in the diagnosis and follow up of Takayasu's arteritis in children. Ann Rheum Dis 2002; 61: 526-9.

5.Johnston SL, Lock RJ, Gompels MM. Takaysau arteritis: a review. J Clin Pathol 2002; 55: 481–6. doi: 10.1136/jcp.55.7.481

6.Vaideeswar P, Deshpande JR. Pathology of Takayasu arteritis: a brief review. Ann Pediatr Cardiol 2013; 6: 52.

7.Hata A, Noda M, Moriwaki R, Numano F. Angiographic findings of Takayasu arteritis: new classification. Int J Cardiol 1996; 54: S155-63.

8.Sivakumar MR, Misra RN, Bacon PA. The Indian perspective of Takayasu arteritis and development of a Disease Extent Index (DEI. Tak) to assess Takayasu arteritis. Rheumatol 2005; 44(suppl_3): iii6-7.

9.Misra R, Danda D, Jayaseelan L, Sivakumar R, Lawrence A, Bacon P. ITAS and DEI. TAK-Scores for clinical disease activity and damage extent in Takayasu aortoarteritis (TA). Rheumatol 2008; 47: II101-II101.

10.Ishikawa K. Diagnostic approach and proposed criteria for the clinical diagnosis of Takayasu's arteriopathy. J Am Coll Cardiol 1988; 12: 964-72.

11.Sharma BK, Jain S, Suri S, Numano F. Diagnostic criteria for Takayasu arteritis. Int J Cardiol 1996; 54: S127-33.

12.Subramanyan R, Joy J, Balakrishnan KG. Natural history of aortoarteritis (Takayasu's disease). Circulation 1989; 80: 429-37.
13.Watanabe Y, Miyata T, Tanemoto K. Current clinical features of new patients with Takayasu arteritis observed from cross-country research in Japan: age and sex specificity. Circulation 2015; 132: 1701-9.
14.Panja M, Kar AK, Dutta AL, Chhetri M, Kumar S, Panja S. Cardiac involvement in non-specific aorto-arteritis. Int J Cardiol 1992; 34: 289-95.
15.Agrawal R, Tyagi S, Arora R, Khalilullah M. Clinical and angiographic profile of aorto-arteritis in India. Ind Heart J 1989; 12:964-72.
16.Alnabwani D, Patel P, Kata P, Patel V, Okere A, Cheriyath P. The epidemiology and clinical manifestations of Takayasu arteritis: a descriptive study of case reports. Cureus 2021; 15: 13.
17.Soto ME, Espinola N, Flores-Suarez LF, Reyes PA. Takayasu arteritis: clinical features in 110 Mexican Mestizo patients and cardiovascular impact on survival and prognosis. Clin Exp Rheumatol 2008; 26: S9.
18.Hoffman GS. Takayasu arteritis: lessons from the American National Institutes of Health experience. Int J Cardiol 1996; 54: S99-102.
19.Kim HJ, Suh DC, Kim JK, Kim SJ, Lee JH, Choi CG, et al. Correlation of neurological manifestations of Takayasu’s arteritis with cerebral angiographic findings. Clin Imaging 2005; 29: 79-85.
20.Moriwaki R, Noda M, Yajima M, Sharma BK, Numano F. Clinical manifestations of Takayasu arteritis in India and Japan--new classification of angiographic findings. Angiology 1997; 48: 369-79.
21.Krishna MV, Namrata RS. Takayasu arteritis – Stroke as an initial presentation. J Indian Acad Clinical Med 2004, 5: 274-76.
22.Kerr GS, Hallahan CW, Giordano J, Leavitt RY, Fauci AS, Rottem M, et al. Takayasu arteritis. Ann Intern Med 1994; 120: 919-29.
23. Jain S, Sharma N, Singh S, Bali HK, Kumar L, Sharma BK. Takaysu arteritis in children and young Indians. Int J Cardiol 2000:75: 163-6.
24.Kumar GV, Agarwal NB, Javali S, Patwardhan AM. Takayasu's arteritis with ostial and left main coronary artery stenosis. Tex Heart Inst J 2007; 34: 470-4.
25.Yamada I, Shibuya H, Matsubara O, Umehara I, Makino T, Numano F, et al. Pulmonary artery disease in Takayasu's arteritis: angiographic findings. Am J Roentgenol 1992; 159: 263-9.
27.Sharma S, Kamalakar T, Rajani M, Talwar KK. The incidence and patterns of pulmonary artery involvement in Takayasu's arteritis. Clin Radiol 1990; 42: 177- 81.