Takayasu’s Arteritis (TA) is an inflammatory vascular disease involving the aorta and its major branches as well as the pulmonary artery and its branches. It was introduced to the medical fraternity in 1827 by Dr. R. Adams who was the first physician to note absence of pulse in all four extremities. In 1856 Savory reported a case of young female with absence of pulses. In 1908, Dr. Mikito Takayasu, a Japanese Opthalmologist described a peculiar wreath like appearance of retinal blood vessels with absence of radial pulse. According to ICD-9 classification of diseases, NSAA is classified at 446.7.

Non-specific Aorto-arteritis is predominantly a disease of young females in their second and third decades. It occurs worldwide and no race seems to be immune. Age of onset may range from infancy to late middle age. Waern et. al. found a higher mean age of onset (41 yrs.) in an European study. In Japan mean age at presentation is quoted to be around 29 years. The disease has a predilection for females with wide geographical variations. In Japan it is 8 : 1, in Mexico 5 : 1, in India 4 : 1 and in Israel 1.2 : 1. In a recent series by Panja et. al. M : F ratio was 1 : 6.4.

There is also a geographical variation in the clinical presentations of NSAA vis-à-vis pattern of vascular involvement by the disease. In Japan, predominantly proximal aortic involvement with features of “reversed coarctation” is seen. In South East Asia and Africa, descending thoracic and abdominal aorta involvement with renovascular lesions, the so called “middle aortic syndrome” is found more commonly.

Concurrent geographical variation in genetic predisposition is also marked so far as HLA-association is concerned. In Japan high association with HLADR, MB, BW, DW, DQW (Dong et. al., Kasuya et. al.) Kasuya et. al. has shown that association with HLA Bw52 results in higher incidence of coronary artery and myocardial involvement and worse prognosis. In USA HLADR-MB3 is more commonly associated. In Koreans associations with HLA Bw52,Cw6,DRI & DQw2 are found. In Indians HLAB & B21 are more prevalent.

The disease is classified into different types according to the site of involvement of the aorta and its branches. Ueno et. al. in 1967 classified it into three types. In type-I, the inflammatory process is localized to the arch of aorta and its branches. In type-II, the lesions involve the Thoraco-abdominal aorta and its branches without involvement of the arch. Type-III is characterized by combined features...
of both Type-I & Type-II. Lupi Herrera et.al.\textsuperscript{5} in 1975 recommended an additional category (Type-IV) in which there is pulmonary involvement in addition to features of Type-I, II or III. Type-V disease has been proposed by Panja et. al.\textsuperscript{10} and it indicates involvement of coronary arteries. The distribution of various types is not uniform globally. As far as India is concerned – Agarwal et. al.\textsuperscript{19} reported among North Indian patients the incidence of various types as Type-I – 22%, Type-II – 25%, Type-III – 53% and Type-IV – 26%. Our study involving ‘650’ patients belonging to Eastern India and Bangladesh (largest Series from India) revealed somewhat contrasting data – Type-I – 16%; Type-II – 8%; Type-III – 76%; Type-IV – 36% and Type-V – 10%.

Aorto-arteritis is a Panarteritis involving all the three layers causing extensive intimal proliferation, in ammation of media and adventitia followed by marked fibrous scarring. Histologically there is round cell infiltration, cuffing of vasa vasorum and destruction of tunica media leading ultimately to gross fibrosis. In older cases, hyalinization of deeper layers of intima and dystrophic calcification can be seen. The appearance of aortic intima is closely related to the activity and duration of the disease. Circumferential intimal thickening, plaques and patches of raised intima are frequently seen on the inner surface of the aorta. In advanced cictricial stage, the aortic intima may have ‘tree-back’ appearance similar to that of luetic aortitis. Skipped areas of aortic involvement are quite characteristic of aorto-arteritis.

In the majority of cases, this disease is insidious in onset. However sudden onset is not very rare. Ishikawa\textsuperscript{20} reported insidious onset of symptomatology in 76% and sudden onset in 24%. Disease course is not uniform. In about 40% of cases the symptoms may follow Plateau-Crescendo course. In 36% of cases it is Plateau, in 19% of cases it is decrescendo and in about 5% it follows a decrescendo-Plateau-crescendo pattern. In the late chronic phase symptoms are due to the obliterative and in ammatory changes in blood vessels. Patients present with diminished or absent pulse (96%), bruits (94%), hypertension (72%), heart failure (28%), abnormal fundi secondary to hypertension (41%).\textsuperscript{5} In addition patients may present with dyspnoea on exertion, palpitation, intermittent claudication or angina pectoris. Neurologic symptoms include headache, syncope, hemiplegia and visual disturbances.

In this context, our study of 650 cases revealed unequal pulse (96%), hypertension (72%), oliguria due to renal failure (30%), intermittent cladication (25%) CNS symptoms (amaurosis fugax, syncope, TIA) (22.5%), eye changes (8.1%) and skin manifestations (Erythema Nodosum, Raynaud’s Phenomenon, leg ulcers) (3.8%).

Incidence of the various clinical features in children do not differ much from those of adults and in our series we observed congestive cardiac failure in 76%, hypertension in 70.5%, dilated cardiomyopathy in 20% and involvement of the thoracic aorta in 58.8% of cases.

Commonest aetiology for systemic hypertension is renal artery stenosis. Other causes are – atypical coarctation, reduced aortic capacitance as well as diminished baroreceptor reactivity.

Heart failure in ‘NSAA’ is related to Systemic hypertension or valvular regurgitant lesion. Isolated cardiomyopathy may be the underlying cause in about 5% of cases.\textsuperscript{21} Aortic regurgitation has been reported in 7.24%.\textsuperscript{22} Mitral regurgitation has been reported in 11.4%.\textsuperscript{23} Aortic dilatation with separation of the cusps is the predominant cause of Aortic regurgitation, however, thickening and puckering of aortic valve lea ets and thickening in the left atrial endocardium was also reported by Chhetri et.al.\textsuperscript{24}.

Incidence of aneurysms in aorto-arteritis varies from 2-26.7%. Aneurysmal form of aorto-arteritis is associated with a higher incidence of aortic regurgitation, hypertension and elevated ESR as compared to the non-aneurysmal form.\textsuperscript{25}

Study reports from Japan.\textsuperscript{26} and Mexico.\textsuperscript{27} revealed incidence of Pulmonary Artery involvement to be between 44% and 100%. This is much lower among Indians. Tyagi et.al.\textsuperscript{28} in their study with North
Indian patients reported this incidence as 26.3%. Our study (Panja et al.) on patients from Eastern India and Bangladesh revealed slightly higher incidence (36%) of pulmonary Arterial involvement. Both stenotic and occlusive lesions are seen and right upper lobe artery is most frequently involved. There is no relation between systemic and Pulmonary arterial systems as regards the extent and activity of the involvement.

Pulmonary hypertension in aorto arteritis can be due to three factors: Pulmonary Arterial involvement; left ventricular failure; combined Pulmonary Arterial and left ventricular origin. Coronary Artery involvement is mostly limited to coronary ostium and proximal coronary arteries but diffuse and triple vessel disease is also noted. Naturally patients may suffer from angina pectoris, Acute Myocardial infarction, congestive cardiac failure and even SCD.

Chronic reduction of the orbital and ocular blood produces hypoxic retinal vascular changes which have been classified into four stages by Uyama and Asayma. Stage – I, retinal veins become distended; Stage – 2, Microaneurysm formation – occurs at systolic retinal arterial pressure of 30 mmHg. Stage – 3; Arterio-venous anastomosis; Stage – 4 ocular complications – e.g. cataract, ruberosis, retinal ischaemia, neovascularization, proliferative retinopathy and vitreous haemorrhage.

Clinical diagnosis of aorto-arteritis is based on proposed diagnostic criteria by Ishikawa (1988). These consist of one obligatory criterion (age <40 years at diagnosis or onset of disease), two major criteria (left and right mid subclavian artery lesions) and nine minor criteria (high ESR, common Carotid artery tenderness, hypertension, Aortic regurgitation or annulo-aortic ecatisa, lesions of Pulmonary Artery, Left mid common Carotid artery, distal branchio-cephalic trunk, thoracic aorta and abdominal aorta). In addition to the obligatory criterion, the presence of two major criteria, or one major plus two or more minor criteria; or four or more minor criteria suggests a high probability of the presence of aorto-arteritis. These criteria have greater sensitivity for patients with active disease than for those with inactive disease. Geographic variation in pattern of arterial involvement may reduce sensitivity of these criteria.

Recently American College of Rheumatology (1990) has selected ‘6’ criteria for diagnosis of Aorto-arteritis. These include age of onset of disease< 40 years; claudication of extremities, decreased brachial artery pulse; BP difference > 10 mmHg between arms; bruit over subclavian arteries or aorta and Arteriogram abnormality. Presence of at least ‘3’ of these ‘6’ criteria suggests the diagnosis of Aorto-arteritis, which have a sensitivity of 90.5 % and a specificity of 97.8 %.

Specific treatment of the disease is not available in the absence of our knowledge of its exact aetiology. Treatment is mainly based on the clinical symptomatology and the possible immunologic basis of the disease. Medical therapy is recommended to patients with active disease, in whom surgery and balloon angioplasty are not feasible and in patients who refuse to undergo balloon angioplasty or surgery.

Glucocorticoids in high doses (prednisone, 1 mg/kg body weight per day) are well established as primary therapy of Takayasu Arteries and often dramatically improve the constitutional symptoms, halt disease progression in patients in the systemic in ammatory stage and lower the erythrocyte sedimentation rate (ESR) toward normal. Prednisone is tapered to an alternate day regimen after 3 months of daily therapy. Unlike giant cell (Temporal) arteritis, patients with aorto-arteritis may require treatment with low dose corticosteroid for extended periods of time. If prednisone cannot be tapered to an alternate day regimen after 3 months or if there is progression of disease on steroid therapy, cytotoxic drugs like Cyclophosphamide (2 mg/kg/day) or Azathioprin (100 mg/day) has been used in some studies with fair results. Alternatively low dose methotrexate (0.3 mg/kg/week) may enhance the efficacy of steroid therapy and facilitate steroid tapering. Methotrexate and dapsone appear to be useful steroid sparing agents and newer biological,
immunomodulatory agents may also become useful in clinical management.

Antihypertensive and decongestive therapy are given to patients with heart failure and systemic hypertension, usually with good response. Renovascular Hypertension responds poorly to drug therapy.

Efficacy of oral anti coagulants, antiplatelet agents and vasodilators for treatment of aorto-arteritis is not established. Sen et. al. instituted empirical antitubercular treatment demonstrating tubercular lesions, positive Mantoux’s test and increased erythrocyte sedimentation rate. But at present there is no role of empirical antitubercular treatment.

Spontaneous regression with steroid was noted in 4 cases in our series.

Major advancement in the treatment of this otherwise morbid condition has been brought by percutaneous transluminal angioplasty of stenotic vascular lesions. Lesions in Takayasu arteritis are purely stenotic in 85% of patients, purely dilatative in 2% and mixed in 13%. Stenotic lesions in aorta and its branches have been dilated with excellent immediate and long term follow up results.

We have performed balloon angioplasty of aorta in ‘52’ patients (58 lesions) since 1978, using 7-20 mm. balloon in ated at 4-17 atmospheric pressure. Deployment of stent was done in ‘12’ dilated lesions. Of the ‘58’ lesions – 28 lesions were in the thoracic aorta and ‘30’ lesions in the abdominal aorta. The mean diameter of stenosed segment increased from 5.1 +/- 2.7 mm to 10.6 +/- 5.2 mm with decrease in mean peak systolic pressure gradient from 68.8 +/- 21.6 mmHg to 28.4 +/- 19.6 mmHg. On follow up of 1-5 years, restenosis was noted in ‘3’ thoracic aortic lesions (25%) and ‘6’ abdominal aortic lesions (38%). Restenosis was noted in one stented case (11%). Minor dissection at the local dilated segment was very much frequent but this did not alter outcome. Stenotic lesions in aortoarteritis are often rigid and may require much higher in ation pressure for dilatation which should be done cautiously to avoid rupture of aorta and aneurysm formation. Post Balloon angioplasty aneurysm formation was noted in one case which was successfully treated by implantation of covered stent graft.

Balloon angioplasty of stenotic renal arteries was done in ‘120’ lesions in 102 pateints. ‘96’ lesion (80%) could be dilated with residual stenosis less than 50%. Stenting was done in ‘46’ lesions of which 22 lesions was stented directly without Balloon Predilatation. Renal stents have been used for ostial lesions, obstructive dissection, suboptimal dilatation or elastic recoil and restenotic lesions. Major complications was noted only in ‘2’ cases (one-death, one-dissection). On 1-5 years follow up (mean 1 year) restenosis was observed in 20 lesions (18%). Redilatation was attempted in all ‘20’ lesions and were successfully redilated. Restenosis was noted in ‘6’ stented lesions (2.76%). There was marked symptomatic improvement and decrease in blood pressure in hypertensive patients.

Balloon angioplasty of carotid arteries was attempted in ‘40’ lesions in ‘36’ patients with 70% (28 lesions) success rate. All the lesions were predilated with coronary angioplasty balloon (OMNIPASS – 2.5 mm-3.5 mm). Self expanding Wall Stent was deployed successfully in ‘4’ lesions. Major embolic event was noted in one case and transient neurologic deficit in ‘3’ cases. On follow up restenosis was noted in ‘7’ cases and stent deformation in one case.

Balloon angioplasty of stenosed subclavian arteries was attempted in ‘64’ lesions in ‘56’ patients. Lesions were dilated with HIGH-FIVE Peripheral angioplasty balloon. Stent was deployed in ‘14’ lesions. GLIDE GUIDE wire was used for total occlusion. Primary success rate was 80% (48 lesions). Stenosed segment less than 10 cms (40 lesions) have had higher success rate (90% - 36 lesions) than stenosed segment more than 10 cms (20 lesions – 60% success rate). Restenosis was noted in 6 lesions (12.5%) on 1-3 years follow up. Minor complication was noted only in one case.

Balloon angioplasty of iliac and sapheno-femoral systems were also highly successful and use of GLIDE guide wire resulted in high success rate in crossing the lesions. Lesion length is a very much determining
factor in success as in all other vessels.

Overall efficacy of Balloon angioplasty in aorto-arteritis was highly encouraging. Hypertension was controlled in 87% and claudication improved in 86%. Marked reduction in 5 years mortality was also noted – 9% after successful angioplasty. 42% after failed angioplasty and 25.8% in the control group.

The indications of surgery in the treatment of Takayasu Arteritis are not well established. Surgery is generally performed to correct renovascular hypertension, relieve cerebral ischaemia, repair aortic or arterial aneurysms, treat aortic regurgitation or by-pass coronary arteries. Surgery during the active phase of the disease carries significant risk of reocclusion and peri-procedural complications. This holds true for percutaneous procedure also.

Various modalities of surgical treatment are a) by pass of the obstructed arteries, b) resection of the narrowed segment and replacement with an interposition graft c) patch aortoplasty for short segmental lesion, d) endarterectomy, e) excision of sacular aneurysms f) aortic valve replacement.

The natural history of NSAA has two distinct phases; an active or Pre-pulseless phase and a chronic or pulseless phase. Active phase may remit spontaneously in three months or may progress insidiously into the chronic phase. There can be exacerbations of activity during the chronic illness. Not all patients have a manifest acute phase and may present in chronic phase only. In the chronic phase, the inflammation leads to either stenosis or occlusion (85%) of the affected vessel, aneurysm formation (2%) or both (13%). The best documented report on natural history of this disease from India is by Subramanyan et. al.23 in which they studied ‘88’ patients (54 women and 34 men) for a follow up period of 83.6 ± 74.4 months from the onset and 33.2 ± 37.0 months from the diagnosis. The survival rate at 5 years after diagnosis was 80.3% after which the survival curve attened out with no further mortality. As with the survival curve, the event free survival curve also attened out after the first 5 years of diagnosis. Ishikawa27 has reported higher rates of survival (89.7%) and event free survival (86.9%) at 5 years after established diagnosis. Cardiac failure was the single most common cause of death. Improvement in clinical condition, probably spontaneous can occur in young patients. Medical therapy is not much efficacious in altering the long term outcome of the disease. Childhood onset particularly when associated with a DCM like picture carries an ominous prognosis. Failed angioplasty also implicates high mortality. Early angioplasty of Stenosed vessels is a real hope in this otherwise morbid and potentially fatal disease.

Early angioplasty improves survival in all groups of aorto-arteritis, but we still have to go a long way to go for the proper clarification of aetiology of this disease and hence, the treatment and prevention also.

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