

**Original Article:****Adult onset Still's disease: 7 years experience at a tertiary care centre from South India****A. Krishna Prasad, A. Srujana, M.V.S. Subbalaxmi, M. Shetty, A.C. Upadhyay, M. Nageswar Rao***Department of General Medicine, Nizam's Institute of Medical Sciences, Hyderabad***ABSTRACT**

**Background:** Adult onset Still's disease (AOSD) is uncommon condition regarding which sparse published data are available from India.

**Methods:** Retrospective study of 6 patients, who presented with pyrexia of unknown origin (PUO) seen over a 7-year period who were diagnosed to have AOSD after a thorough work-up.

**Results:** Their mean age was 24.6 (range 18-38) years; there were four males. Mean duration of symptoms was 7.8 (range 3-5) weeks. In addition to prolonged fever, patients presented with rash, arthropathy, hepato-splenomegaly and peripheral lymphadenopathy. Laboratory evaluation revealed neutrophilic leukocytosis, hepatopathy, serositis, raised serum ferritin levels; anti-nuclear antibody and rheumatoid factor were negative in all. One patient developed acute respiratory distress syndrome and died. The remaining five patients were treated with non-steroidal anti-inflammatory drugs, oral corticosteroids, and hydroxy chloroquine and responded well to treatment.

**Conclusions:** Increased awareness and a high index of suspicion is required for the diagnosis of AOSD. Though mortality is rare, it may occur due to complications.

**Key words:** *Pyrexia of unknown origin, Adult onset Still's disease*

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**INTRODUCTION**

Pyrexia of unknown origin (PUO) is a common clinical problem in internal medicine. But adult onset Still's disease (AOSD) is a rare cause of PUO. Petersdorf et al<sup>1</sup> reported two cases of AOSD in their series of 100 cases in 1961.<sup>1</sup> But in another series<sup>2</sup> AOSD constituted 4 of 105 patients with PUO. In another report<sup>3</sup> 6 patients with AOSD were diagnosed over a period of 10 years. A few other studies<sup>4,5</sup> from India have attempted to document this disease earlier.<sup>4,5</sup>

Still's disease is named after the English physician Sir George Frederic Still (1861–1941). AOSD is a rare systemic inflammatory disorder of unknown aetiology, with a triad of symptoms characterized by quotidian or

double-quotidian spiking fever with an evanescent rash, arthritis and multi-organ involvement.<sup>6</sup>

Prevalence of AOSD is estimated to be 0.16 cases per 100,000 population; bimodal age distribution is evident with one peak incidence between 15-25 years and a second peak between 36-46 years.<sup>6</sup> Stress has been suggested as an important risk factor for all ages.

Although several sets of classification criteria have been developed from retrospectively analyze data,<sup>7</sup> most often used criteria for the diagnosis of AOSD are the Yamaguchi criteria.<sup>8</sup>

**MATERIAL AND METHODS**

We retrospectively studied the case records of patients, who presented with PUO to our

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**Corresponding author:** Dr A. Krishna Prasad, Additional Professor, Department of General Medicine, Nizam's Institute of Medical Sciences, Hyderabad, India.  
**e-mail:** drakpnims@gmail.com



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department during the period of April 2006 to March 2013. All these patients were admitted to our tertiary care teaching hospital for evaluation of PUO. In all of them a detailed history was taken and a thorough clinical examination was done. All of them underwent work-up for PUO which included haemogram, smear for malarial parasite, urine examination, blood and urine culture of chest radiograph, abdominal ultrasonography, biopsy of peripheral lymph node (where accessible) and bone marrow examination, including culture. Anti-nuclear antibody (ANA), rheumatoid factor (RF) and other relevant serological tests were also done in all patients. Other investigations were conducted wherever it was indicated. Common causes like infections, malignancy (lymphoma, leukaemia) and other common autoimmune rheumatic diseases were ruled out. AOSD was diagnosed as per Yamaguchi Criteria.<sup>8</sup> All patients were treated with non-steroidal antiinflammatory drugs (NSAIDs) and oral corticosteroids (0.5 mg/kg body weight and tapered over 6 to 8 weeks). Where ever necessary, oral hydroxy chloroquine (200 mg once a day) was added.

## RESULTS

Six cases of AOSD were diagnosed over a period of seven years. The clinical characteristics were shown in (Table 1).

All patients had spiking fever, arthralgias/ arthritis involving both large and small joints and a negative ANA and RF. No joint deformities were evident in any of them. Preceding sore throat was noted in 3 cases. Anti-streptolysin O (ASO) titres were not raised in these 3 cases. Salient laboratory abnormalities were as follows: mean leukocyte count 24,466 (range 5,800-61,300)/mm<sup>3</sup>, leukocytosis (n=5), neutrophilia (n=5), anaemia (n=6) hepatic dysfunction (n=4), mean serum ferritin 1704 (range 521-2000) ng/mL, raised

**Table 1: Clinical characteristics in 6 patients with adult onset Still's disease**

Variable	No. present
Males	4
Females	2
Age at onset (years)	
Mean	24.6
Range	18-38
Duration of illness before diagnosis (weeks)	
Mean	7.8
Range	3-20
Fever	6
Arthropathy	5
Rash	4
Sore throat	3
Lymphadenopathy	5
Splenomegaly	5
Hepatomegaly	5
Serositis	4

serum ferritin levels (>400 ng/mL) (n=6). Peripheral lymph node biopsy and culture were done in 3 cases. Bone marrow aspiration and biopsy including bone marrow aspirate culture were done in 4 cases. All cultures were negative for microbial growth. Both lymph node and bone marrow biopsies revealed reactive changes. Serositis with minimal fluid collection was noted in 4 cases (bilateral pleural effusion, pericardial and effusion ascites). All patients fulfilled the required Yamaguchi criteria<sup>8</sup> for the diagnosis of AOSD (Table 2). Five cases improved with management. One case developed acute respiratory distress syndrome (ARDS) and was treated with parenteral corticosteroids and mechanical ventilatory support. This patient died. Comparison of the results of our study with other studies<sup>3,9-11</sup> is shown in Table 3.

## DISCUSSION

So far most of the cases with AOSD have been reported from north India (Table 3). Awareness about the disease may be the cause for this rather than the incidence of the disease.

**Table 2: Confirmation of diagnosis of adult onset Still's disease**

Case	Major Criteria				Minor Criteria				No. of criteria <sup>8</sup> satisfied*
	Fever	Arthro-pathy	Rash	Leuko-cytosis	Sore Throat	L/S	Liver dysfunction	ANA/RF	
1	+	+	+	+	+	+/+	-	Neg	7/8
2	+	+	+	+	-	+/+	-	Neg	6/8
3	+	-	+	+	-	+/+	+	Neg	6/8
4	+	+	+	-	+	+/+	+	Neg	7/8
5	+	+	+	+	+	-/-	+	Neg	7/8
6	+	+	-	-	-	+/+	+	Neg	5/8

\* 5 or more criteria including 2 or more major criteria are required for diagnosis

L = peripheral lymphadenopathy; S = splenomegaly; ANA = anti-nuclear antibody; RF = rheumatoid factor; + = present; - = absent; Neg = negative

The age at onset of AOSD in the present study was 24.6 years. Our observations are similar to two other studies from India<sup>10,12</sup> where the mean age at onset was 28<sup>10</sup> and 26.2<sup>12</sup> years respectively (Table 3). In the study<sup>9</sup> from New Delhi, the mean age of onset (33.8 years) was

nearly a decade later. We observed a male preponderance (male: female = 2:1). A similar male preponderance has been reported in three other Indian studies (Table 3).<sup>3,9,11</sup> Only in one Indian study<sup>10</sup> a female preponderance was reported. The proportion of patients with fever

**Table 3: Comparison of results of present study with other published studies from India**

	Bambery et al <sup>3</sup> (n=6)	Singh et al <sup>9</sup> (n=27)	Reddy Munagala et al <sup>10</sup> (n=29)	Kakar et al <sup>11</sup> (n=8)	Present study (n=6)
Year of publication	1987	1992	2012	2004	-
Period of data collection (years)	10	5	17	0.5	7
Total number of patients	6	27	29	8	6
Male:Female	2:1	2.9:1	0.6:1	1.7:1	2:1
Age at onset (years)	-	33.8	28	26.2	24.6
Age range (years)	-	17-65	17-58	18-95	18-38
Average duration of fever (range) months	2 (0.7-4)	3.5 (1-6)	-	9 (4-16)	2 (0.75-5)
Fever	6/6	27/27	29/29	8/8	6/6
Arthropathy	6/6	27/27	26/29	8/8	5/6
Rash	3/6	23/27	13/29	1/8	5/6
Sore throat	-	12/27	8/29	3/8	3/6
Lymphadenopathy	-	22/27	15/29	5/8	5/6
Splenomegaly	3/6	16/27	13/29	3/8	5/6
Hepatomegaly	6/6	13/27	15/29	5/8	5/6
Serositis	2/6	2/27	5/29	2/8	4/6
Leukocytosis	5/6	27/27	28/29		5/6
Hepatic dysfunction	3/6		15/29		5/6
Mortality	1 death	1 death at 2.2 years follow-up	2 died due to infection at 23.7 months follow-up	No deaths 6 follow-up	1 death within hospital due to ARDS

ARDS = acute respiratory distress syndrome

and other systemic manifestations were similar in the present study and other published India studies (Table 3).<sup>3,9,11</sup>

Serositis in the form of mild pericardial effusion, bilateral pleural effusion and ascites was noted in four of the six cases in our study. But serositis was noted in only two out of 27 in another study.<sup>9</sup> Pericardial effusion was described in 8 out of 28 cases in a study from Iran.<sup>14</sup>

AOSD patients do well with NSAIDs and corticosteroids. However, occasionally organ failure associated with this disease or during its drug therapy have been described. In a study<sup>12</sup> of 23 patients, acute liver failure, respiratory insufficiency, myocarditis, progressive anemia due to bone marrow failure, paralytic ileus, peripheral facial nerve paralysis, retro-orbital myositis with a possible intra-orbital pseudo-tumor, increased intra-cranial pressure with mental confusion, glomerulonephritis, acute renal failure, rapidly destructive arthritis of hips and knees and septicemia have been described and have contributed to mortality. But mortality can also occur due to other serious complications like amyloidosis, pericarditis and macrophage activation syndrome (MAS).<sup>7</sup> ARDS is also reported in some cases.<sup>13</sup> One of our patients, developed ARDS and died.

A high index of suspicion is required for the diagnosis of AOSD. Prolonged fever with rash, arthropathy and systemic involvement should alert the treating physicians about the possibility of AOSD. Most of the patients improve with symptomatic management. Though mortality is rare, may occur due to complications.

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