

BRIEF REPORTS

13. Eveleth PB, de Souza, Freitas JA. Tooth eruption and menarche of Brazilian born of Japanese ancestry. *Hum Biol* 1969; 41:176-184.
14. Eveleth PB. Eruption of permanent dentition and menarche of American children living in the tropics. *Hum Biol* 1966; 38: 60-70.
15. Kochar R, Richardson A. The chronology and sequence of eruption of human permanent teeth in Northern Ireland. *International J Pediatr Dentistry* 1998; 8: 243-252.

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## Uveitis and Anti Nuclear Antibody Positivity in Children with Juvenile Idiopathic Arthritis

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*This study was conducted to determine the frequency of antinuclear antibodies (ANA) positivity and uveitis in our newly diagnosed juvenile idiopathic arthritis (JIA) patients classified according to International League Against Rheumatology (ILAR) classification criteria. Ninety-two girls and 106 boys, totally 198 children were enrolled in the study. of them 36 (18.2%) were found to be ANA positive. Chronic anterior uveitis was detected in 20 (10.1%) patients. ANA positivity was determined in 4 of the systemic JIA patients, in whom no uveitis had been detected. Twenty-five of 37 patients with oligoarticular JIA were ANA positive, in 10 of them uveitis was also diagnosed. ANA were positive in 3 of 34 patients with RF positive polyarticular JIA, only one patient had positive ANA, and another one had uveitis. Nine patients were extended JIA and in none of them, ANA positivity or uveitis were present. Of 43 patients classified as enthesitis related arthritis (ERA), uveitis was diagnosed in 6 and there was no evidence of ANA positivity, but one had uveitis. We conclude that the incidence of ANA positivity and uveitis is low in Turkish children with JIA.*

**Key words:** Antinuclear antibody, Juvenile idiopathic arthritis, Uveitis.

Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease of joints with onset less than 16 years. The most commonly used descriptive markers for differentiation and classification of JIA are antinuclear antibodies (ANA), rheumatoid factor (RF), HLA B-27 marker and presence of anterior uveitis(1,2). The rates of ANA and uveitis positivity in patients with low socioeconomic

level and in developing countries are significantly lower than those in developed countries(3-5). For Turkey, the only reference study is our data that was collected ten years ago(3). Male preponderance, low rate of ANA positivity and uveitis presence with high amyloidosis incidence were the main differences between our cases and JIA patients in other countries The aim of this study was to

assess the relationship between the disease subgroups as per the new classification criteria suggested by the International league against rheumatism (ILAR) ANA positivity and uveitis, in newly diagnosed JIA patients.

### Subjects and Methods

Our study group consisted of the JIA patients followed by Cerrahpasa Medical Faculty Pediatric Rheumatology Division. The diagnosis was based on ILAR diagnostic criteria(2). The records of 198 JIA patients were investigated retrospectively. All patients had at least 6 months of disease duration. Age, gender, age of disease onset, age at the diagnosis and duration of follow-up were recorded. Positivity rates of ANA, RF, HLA B-27 and uveitis were determined in all patients. These parameters were evaluated according to subgroups. At the end of the study, ANA and uveitis positive groups were evaluated separately. ANA was determined by Hep-2 cell method and titers above 1/40 were considered positive. RF was studied with nephelometric method. HLA B-27 positivity was evaluated by histocompatibility antigen determination. ANA positive patients were

reclassified according to their JIA subgroups, gender, RF and HLA B-27 positivities.

### Uveitis evaluation

Slit lamp examination and detailed ophthalmologic examination for uveitis were performed by a well-trained ophthalmologist in all patients. Ophthalmologic exams were repeated every 3 months in uveitis or ANA positive patients. In addition to systemic treatment, local treatment was given in uveitis positive patients. In uveitis negative patients, ophthalmologic consultations were repeated with intervals of 6 or 12 months. Detection of uveitis in a single examination was considered sufficient for uveitis positivity. Uveitis positive patients were then reevaluated according to their JIA subgroups, gender, RF and HLA B-27 positivities.

### Results

Demographic features of the study group are shown in *Table I*. The mean age at diagnosis was 7.7 years (range 0.4-16 years), the mean duration of disease was 4.1 years (range 0.5-13 years) and the mean duration of follow-ups was 3.02 years (range 0-12 years)

**TABLE I**—Distribution of Juvenile Idiopathic Arthritis Patients According to ILAR Classification and Frequency of ANA Positivity and Uveitis..

JIA sub group	N	%	Female/ Male	Disease onset age (year)	ANA positivity (%)	Uveitis (%)
Systemic JIA	52	26.3	23/29	5.23 ± 4.01	4 (7.7%)	0
Oligoarticular JIA	37	18.7	22/15	3.48 ± 2.31	25 (67.6%)	10 (27%)
RF(-) polyarticular JIA	34	17.2	22/12	6.9 ± 3.8	3 (8.8%)	0
RF(+) polyarticular JIA	7	3.5	5/2	9.36 ± 3.06	1 (14.3%)	1 (14.2%)
Extended oligoarticular JIA	9	4.5	3/6	4.45 ± 3.59	0	0
Juvenile psoriatic arthritis	11	5.6	4/7	7.55 ± 4.62	3 (27.3%)	2 (18.2%)
Enthesitis related arthritis	43	21.7	12/31	10.45 ± 2.42	0	6 (14%)
Others	5	2.5	1/4	7.85 ± 1.84	0	1 (20%)
Total	198	100	92/106	6.62 ± 4.12	36 (18.2%)	20 (10.1%)

in all JIA patients. ANA and uveitis positivity with respect to different types of JIA is also shown in *Table I*.

Ten (27%) of ANA positive patients were male and 26 (73%) were females. Female gender was found as a significant risk factor for ANA positivity ( $\chi^2 = 11.74$ ,  $P = 0.0006$ ). Eight of ANA positive patients also had uveitis. Five (62.5%) of these patients were female. Seven (87.5%) of these cases had oligoarticular JIA and the other one had juvenile psoriatic arthritis (JPsA). Mean age of disease onset in antinuclear antibody positive patients was  $4.62 \pm 3.57$  years, whereas mean age of disease onset in 161 ANA negative patients was  $7.07 \pm 4.11$  years: When these data were compared, mean age of disease onset in antinuclear antibody positive patients was significantly lower than that of ANA negative patients ( $P < 0.001$ ).

Nine (45%) of uveitis positive patients were female and 11 (55%) were male. Uveitis distribution did not show gender difference ( $P = 0.88$ ). The risk of uveitis formation was significantly higher in ANA positive patients than that in ANA negative patients ( $\chi^2 = 7.12$ ,  $P = 0.007$ ). Mean age of disease onset was  $6.79 \pm 4.04$  and  $6.6 \pm 4.14$  years in uveitis positive and negative JIA patients, respectively ( $P = 0.84$ ). None of uveitis positive patients experienced progressive visual loss or blindness.

### Discussion

Many studies have been conducted to assess the definite geographic distribution of JIA and other chronic diseases(6,7). Most of the epidemiologic and descriptive studies concerning JIA are made in developed countries. Limited numbers of studies are from developing countries(3,8-10). High ratio of polyarticular JIA, low incidence of oligoarticular JIA, low rates of ANA and uveitis

positivity, gender differences, and high incidence of secondary amyloidosis were reported in studies conducted in developing countries(3,4,8-10). Similar findings were also reported in African Americans living in United States(5). Because of these observations, it was felt that socioeconomic environment might be a determining factor of disease clinical characteristics in addition to ethnic differences.

In our study, 36 of 198 patients had ANA positivity (18.2%). Twenty five percent of these patients were oligoarticular JIA. ANA positivity was lower in the previous studies performed in our country(3,11). In our study, ANA positivity ratio was significantly higher in oligoarticular JIA patients which was consistent with the classical knowledge. Similarly, ANA positivity ratio was significantly higher in our female patients than the male ones. The increment in the ANA positivity ratio in our recent study than that of 10 years ago could be explained by the assessment of ANA in all our subjects, the probable change in the progression of disease and changing socioeconomic factors. Ethnic differences could be another factor to explain the varying ANA positivity rates in juvenile idiopathic arthritis subjects(7). In a study performed in Greek JIA patients with whom we share similar geography, 41 of 69 patients (59.4%) had ANA positivity(12). In this study, ANA positivity ratios were found as 70% in pauciarticular type, 65% in polyarticular type and 37% in systemic subgroup. In the same study, ANA positivity ratio in healthy children was found to be 3% which was similar to the ratio in healthy Turkish children(12,13). High ANA positivity ratio of Greek JIA patient may be related to their high socio-economic level.

With studies conducted in different countries within different times, the uveitis

### Key Message

- The incidence of antinuclear antibody is low in Turkish children with juvenile idiopathic arthritis.

incidence in JIA patients was revealed as 2-34%(14-19). Comparing the results of our 1991 and 2001 studies; an insignificant increment from 7% to 10% in the uveitis incidence was detected. In another study conducted in Turkey, uveitis was detected in 11 of 90 JIA patients (12.2%)(18). In this study, frequency of uveitis was reported high in oligoarticular subgroup. This observation was concordant with our results. Kanski(14) reported the uveitis incidence as 1.6% in chronic disease, 7-14% in polyarticular JIA and 78-91% in oligoarticular JIA. Contrasting to Kanski's data, many of our uveitis positive patients were in the ERA subgroup. Although early onset of uveitis in JIA patients was reported in some studies, our data did not confirm this. This can be due to high frequency of ERA patients in our study group.

Kanski(14) and Dana, *et al.*(19) reported uveitis and ANA co-existence ratio as 71-93% and 93%, respectively and they found ANA positivity as an important risk factor for uveitis formation. In our uveitis positive patients, ANA positivity ratio was 40% and we also conclude that ANA positivity could be an important risk factor for uveitis.

In conclusion, low ratios of ANA and uveitis in our JIA patients persist, with an insignificant increment observed during 10 years.

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### REFERENCES

1. Schneider R, Passo MH. Juvenile rheumatoid arthritis. *Rheum Dis Clin N Amer* 2002; 28: 503-530.
2. Petty RE, Southwood T, Baum J, Bhattay E, Glass ON, Manners P, *et al.* Revision of the proposal classification criteria for juvenile idiopathic arthritis; 1997. *J Rheumatol* 1998; 25: 1991-1994.
3. Ozdogan H, Kasapcopur O, Dede H, Arlsoy N, Beceren T, Yurdakul S, *et al.* Juvenile chronic arthritis in a Turkish population. *Clin Exp Rheumatol* 1991; 9: 431-435.
4. Aggarwal A, Misra R. Juvenile rheumatoid arthritis in India: rarity of antinuclear antibodies and uveitis. *Indian J Pediatr* 1996; 63: 301-304.
5. Schwartz MM, Simpson P, Kerr KL, Jarvis IN. Juvenile rheumatoid arthritis in African Americans. *J Rheumatol* 1997; 24: 1826-1829.
6. Gare BA. Epidemiology. *Baillieres Clin Rheumatol* 1998; 12: 191-208.
7. Graham TB, Glass GN. Juvenile rheumatoid arthritis: ethnic differences in diagnostic types. *J Rheumatol* 1997; 24: 1677-1679.
8. Moe N, Rygg M. Epidemiology of juvenile chronic arthritis in northern Norway: A ten-year retrospective study. *Clin Exp Rheumatol* 1998; 16: 99-101.
9. Haffejee IE, Raga J, Coovadia HM. Juvenile chronic arthritis in black and Indian South African children. *S Afr Med J* 1984; 65: 510-514.
10. Arguedas O, Fasth A, Andersson-Gare B, Porras O. Juvenile chronic arthritis in Urban San Jose, Costa Rica: A 2 year prospective

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- study. *J Rheumatol* 1998; 25: 1844-1850.
11. Ozen S, Karaaslan Y, Ozdemir O, Saatci U, Bakaloglu A, Koroglu E, *et al.* Prevalence of JCA and familial Mediterranean fever in Turkey: A field study. *J Rheumatol* 1998; 25: 2445-2449.
  12. Siamopolou-Mavriidou A, Mavridis AK, Terzioglou AG, Filopoulou S, Athanasiadou S, Tzioufas AG. Autoantibodies in Greek juvenile chronic arthritis patients. *Clin Exp Rheumatol* 1991; 9: 647-652.
  13. Kasapcopur O, Ozbaklr F, Ingol H, Arlsoy N, Yazici H, Ozdogan H. The frequency of antinuclear antibodies and rheumatoid factors in healthy Turkish children. *Turk J Pediatr* 1999; 41: 67-71.
  14. Kanski JJ. Uveitis in juvenile chronic arthritis: incidence, clinical features and prognosis. *Eye* 1988; 2: 641-645.
  15. Candell Chalom E, Goldsmith DP, Koehler MA, Bittar B, Rose CD, Ostrov BE, *et al.* Prevalence and outcome of uveitis in a regional cohort of patients with juvenile rheumatoid arthritis. *J Rheumatol* 1997; 24: 2031-2034.
  16. Kotaniemi K, Kautiainen H, Karma BA, Aho K. Occurrence of uveitis in recently diagnosed juvenile chronic arthritis. *Ophthalmology* 2001; 108: 2071-2075.
  17. Tugal-Tutkun I, Havrlikova K, Pover WJ, Foster S. Changing patterns in uveitis of childhood. *Ophthalmology* 1996; 103: 365-374.
  18. Berk AT, Kocak N, Unsal E. Uveitis in juvenile arthritis. *Ocul Immunol Inflamm* 2001; 9: 243-251.
  19. Dana RM, Merayo-Lioves J, Schaumberg DA, Foster CS. Visual outcome prognostic indicators in juvenile rheumatoid arthritis associated uveitis. *Ophthalmology* 1997; 104: 236-244.
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