Etiological Spectrum of Precocious Puberty: Data from Northwest India

We retrospectively analyzed clinic records of 55 children (36 girls) with precocious puberty. Majority (34, 62%) had central precocious puberty, out of which 19 were idiopathic. Peripheral precocious puberty was seen in 14 children. Congenital adrenal hyperplasia was the commonest cause of peripheral precocious puberty (6, 42.8%).

Keywords: *Congenital adrenal hyperplasia, Etiology, Idiopathic, Outcome*.

Precocious Puberty occurs due to premature activation of the hypothalamic-pituitary-gonadal axis, called central precocious puberty, or independent of it, called as peripheral precocious puberty. With the advancements in laboratory and radiological investigations, the etiological spectrum of precocious puberty has changed significantly in the past two decades with more cases of organic etiology being detected [1]. There is a limited data on etiology of precocious puberty from developing countries [2]. We retrospectively analyzed medical records of children with precocious puberty from a tertiary-care teaching hospital of Northern India between 2004 to 2018. Ethical clearance was obtained from institutional ethics committee.

Medical records of 55 children (19 boys) with complete information out of 80 children diagnosed as precocious puberty during the study period were analyzed. The mean (SD) age at onset of symptoms in boys and girls was 3.0 (3.2) y and 4.5 (2.5) y, respectively, There was a mean (SD) delay of 0.8 (1.4) y from onset to presentation to a health facility. The mean (SD) bone age was 8.2 (4.9) y in boys, and 7.8 (2.7) y in girls with mean (SD) advancement in bone age of 3.4 (2.9) y. The mean (SD) stimulated serum leutinizing hormone (LH) was 18.5 (1.9) IU/L in CPP group. The majority of patients (61.8%) had CPP, which was idiopathic in 56% (**Table *I***). Congenital adrenal hyperplasia (CAH) was seen in 42.8% of cases of PPP. Six patients with simple virilizing CAH had PPP at presentation and progressed to CPP in follow-up. Seven patients had incomplete PP variants.

The spectrum of diagnoses and patients' characteristics according to gender and type of precocious puberty are shown in ***Table* I**. Peripheral precocious puberty was less common in boys while incomplete variants were only diagnosed in girls. The delay in seeking medical attention and the consequent bone age advancement was more common in girls. Thirty-five out of 38 eligible patients were started on gonadotropin releasing hormone (GnRH) analogue therapy with leuprolide; remaining three had financial constraints. The mean change in height after 3 years of therapy was +0.6 SD score. Specific therapy for the underlying condition such as hydrocortisone and fludrocortisone for CAH, levothyroxine for hypothyroidism and surgery for adrenal tumor was provided. Four patients achieved final height during the study (mean height SDS -0.49) after mean (SD) duration of 6.7 (1.4) y of GnRH therapy. The worst height outcome (-2.72 SDS) was seen in a patient with central precocious puberty complicating CAH.

The spectrum of etiology in the present cohort of precocious puberty was similar to previous studies from developing countries [2,3]. Central precocious puberty was commoner than peripheral precocious puberty and was idiopathic in majority of the patients. Consistent with previous studies, central precocious puberty was more common than peripheral precocious puberty in boys indicating the critical role of neuroimaging in boys [4]. The female to male ratio of 1.9:1 in this study was lower than previous studies [4,5].

A significant finding was delay in seeking medical attention resulting in diagnostic delays, which was common amongst girls, especially those with peripheral precocious puberty and incomplete variants. Delayed medical attention resulted in significant advancement of bone age in the participants of present study. The late diagnoses and non-affordablility of treatment represent the challenges of managing precocious puberty in a developing country [6,7]. Bone age advancement at the initiation of therapy is associated with poor height prognosis [8]. The positive delta change in height SD score after of GnRH therapy indicated that GnRH therapy was unable to achieve the expected slowing of height velocity, if started late. In addition, the poor final height achieved in one of our patients also appears to be a consequence of delayed initiation of treatment.

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TABLE I PATIENT CHARACTERISTICS ACCORDING TO SEX AND TYPE OF PRECOCIOUS PUBERTY (*N*=55)

Characterisitics	*Males*		*Females*		
	Central (n=15)	*Peripheral (n=4)*	*Central (n=19)*	*Peripheral (n=10)*	*Incomplete (n=7)*
Age at onset, y	3.0 (3.2)	3.3 (3.7)	5.2 (2.5)	3.3 (1.9)	4.5 (3.2)
Age at diagnosis, y	3.6 (3.7)	3.4 (3.7)	5.8 (2.7)	4.3 (2.9)	6.4 (2.2)
Delay in diagnosis, y	0.6 (1.2)	0.2 (0.2)	0.7 (0.7	1.0 (1.6)	1.8 (2.8)
BA advancement, y	4.1 (4.0)	5.6 (2.2)	4 (2.6)	2.6 (2.6)	1.2 (1.7)
Height Z-scores	1.2 (1.9)	-0.03 (2.8)	1.5 (1.4)	0.3 (1.7)	0.6 (0.6)
Basal LH, IU/L	4.1 (4.3)	0.1 (0.0)	2.7 (2.5)	0.3 (0.4)	0.2 (0.2)
Basal FSH, IU/L	3.0 (5.7)	0.3 (0.2)	4.2 (2.0)	1.6 (2.1)	2.4 (0.8)
*Etiology	Idiopathic (7), Hypothalamic hamartoma (3), Hydrocephalus (3), Mega cisterna magna (1), Brain tumor (1)	Adrenal tumor (1), CAH (2), Hypo-thyroidism (1)	Idiopathic (12), Hypothalamic hamartoma (1), Hydrocephalus (2), Radiation-induced (2), Brain tumor (2)	CAH (4), Ovarian cyst (2), Hypothyroidism (2), McCune-Albright syndrome (1), Adrenal tumor (1)	Isolated thelarche (4), Isolated pubarche (3)

*All values in mean (SD); BA: bone age; CAH: Congenital adrenal hyperplasia; FSH: follicle stimulating hormones; LH: leutinizing hormone; *number of cases in parenthesis.*

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Nutritional Rickets with Severe Complications in Syrian and Iraqi Refugee Children

We investigated the presence of nutritional rickets in Syrian and Iraqi refugee infants who presented to hospital in Turkey in 2017. 25(OH)D levels were examined in 77 refugee children. Nutritional rickets was diagnosed in 22 (28.5%) children; 11 patients with rickets did not follow up.

Keywords: *Management, Prevalence, Vitamin D.*

The civil war in Syria in recent years has caused an enormous refugee crisis [1]. Nearly 4 million people have entered Turkey. Over 90% of whom are Syrian refugees. There are 142 thousand Iraqi refugees in Turkey [2]. In our country, routine use of a daily 400 IU vitamin D supplement is recommended for infants. Vitamin D has been provided free of charge to all infants during their first year since 2005 [3]. Syrians and Iraqi refugees benefit from health services free of charge if they register. This study aimed to investigate the presence of nutritional rickets in Syrian and Iraqi refugee infants who presented to our hospital.