Thyroid hormone mediates growth and development of the skeleton through its direct effects and through its permissive effects on growth hormone. The effect of hypothyroidism on bone is well described in congenital hypothyroidism, but the impact of thyroid hormone deficiency on a growing skeleton, as it happens with juvenile hypothyroidism, is less defined. In addition, the extent to which the skeletal defects of juvenile hypothyroidism revert on the replacement of thyroid hormone is not known. A study was undertaken in 29 juvenile autoimmune hypothyroid patients to study the skeletal manifestations of juvenile hypothyroidism and the impact of treatment of hypothyroidism on the skeletal system of juvenile patients. Hypothyroidism has a profound impact on the skeletal system and delayed bone age, dwarfism, and thickened bands at the metaphyseal ends being the most common findings. Post treatment, skeletal findings like delayed bone age and dwarfism improved significantly, but there were no significant changes in enlargement of sella, presence of wormian bones, ephyseal dysgenesis, vertebral changes and thickened band at the metaphyseal ends. With the treatment of hypothyroidism, there is an exuberant advancement of bone age, the catch up of bone age being approximately double of the chronological age advancement.

Key words: Advancement of bone age, juvenile hypothyroidism, skeletal manifestations


this study aims to fill in these lacunae in our understanding of impact of thyroid hormone deficiency on a growing skeleton and the effects of its treatment.

Aims and objectives

1. To study the skeletal manifestations of juvenile hypothyroidism
2. To study the impact of treatment of hypothyroidism on the skeletal system of juvenile patients.

Materials and Methods

Children between the age groups of 6 - 18 years (juvenile) who were diagnosed to have hypothyroidism were studied. Only patients with antithyroid antibody positivity or fine needle aspiration cytology (FNAC) thyroid suggestive of autoimmune thyroid disease were included in the study. Patients with mental retardation or anti thyroid peroxidase (TPO) negative patients were not included as they may be congenital hypothyroid patients who were diagnosed later. A total of 29 patients were studied, and the
skeletal X-rays, X-ray skull anterio posterior (AP) view, sellar view, X-ray left wrist with fingers AP view, X-ray spine AP and lateral views, X-ray pelvis AP view and X-ray left knee AP view were taken for all the patients to study for the effects of thyroid hormone deficiency on a growing skeleton. The X-ray were reported by two independent radiologists, and if both agreed on a finding, it was accepted as present. Bone age was assessed using the Tanner Whitehouse 2 system. Six months after starting of the treatment, and after ensuring compliance and a normal thyroid stimulating hormone (TSH) the same X-rays were repeated, and it was determined whether the previous X-ray findings were still present or not. The significance of change was calculated using a Fishers exact ‘t’ test using graph pad analytical software.

RESULTS
A total of 29 patients were studied, and the following were their baseline characteristics [Table 1].

Hypothyroidism has a profound impact on the skeletal system and delayed bone age, dwarfism, and thickened bands at the metaphyseal ends being the most common findings. The following were the skeletal findings in juvenile hypothyroid patients [Table 2].

Post treatment, skeletal findings like delayed bone age, dwarfism, improved significantly, but there were no significant changes in enlargement of sella, presence of wormian bones, epiphyseal dysgenesis, vertebral changes and thickened band at the metaphyseal ends [Table 3].

The most significant impact was on advancement of bone age. Six months of treatment of thyroid hormone resulted in an average increase of bone age by 11.3 months.

DISCUSSION
Thyroid hormone mediates the growth, development, and maturation of the skeleton by regulating chondrocyte proliferation, promoting differentiation of bone progenitor cells, mineralization and angiogenesis. It also has a permissive role on the action of GH by promoting GH secretion from pituitary, as well as GH dependent Insulin Like Growth Factor 1 (IGF 1) production in the bone.

When thyroid hormone is absent from birth, it leads to growth arrest, delayed bone age, and short stature. Ossification centers are defective, and they appear in an irregular and mottled pattern, with multiple foci that coalesce to give a porous or fragmented appearance known as stippled epiphyseal dysgenesis, most frequently noted in large cartilaginous centers, such as the head of the femur, head of humerus, and the tarsal navicular bone. When hypothyroidism is acquired during the growing ages, as in juvenile hypothyroidism, the manifestations are different. Skeletal maturation, defined as the appearance of secondary centers of ossification, is predominantly affected, with delayed fusion of epiphysis and delayed bone age. The epiphyseal centers are heterogeneous with irregular ossification. But the classical stippled epiphyseal dysgenesis, described with congenital hypothyroidism, does not occur. The metaphyseal end of long bones usually has a sclerotic band. The treatment of hypothyroidism results in improvement of skeletal defects especially improvement

| Table 1: Baseline characteristics |
|----------------------------------|
| Parameter                        | Value  |
| Mean age (years)                 | 11.4   |
| Male/female                      | 1: 2.22|
| Mean TSH (ïIU/ml)                | 132    |
| Mean T4 (ïg/dl)                  | 3.1    |
| Mean T3 (ng/ml)                  | 0.52   |
| Anti TPO antibody positivity     | 24     |
| FNAC-Autoimmune thyroid disease  | 5      |

| Table 2: Skeletal manifestations of juvenile hypothyroidism |
|------------------------------------------------------------|
| Finding                                      | Number of patients | Percentage (%) |
|----------------------------------------------|-------------------|----------------|
| Delayed bone age (more than 2 years less than chronological age) | 21                | 72             |
| Enlarged sella                                | 4                 | 14             |
| Wormian bones                                 | 8                 | 28             |
| Dwarfism (less than 3 standard deviation)     | 13                | 45             |
| Multicentric irregular epiphysis             | 3                 | 10             |
| Increased intervertebral distance             | 11                | 38             |
| Flattening of vertebrae                       | 7                 | 21             |
| Bullet-shaped vertebrae                       | 4                 | 14             |
| Narrow coxa vera                              | 9                 | 31             |
| Thickened band at the metaphyseal ends        | 18                | 62             |

| Table 3: Impact of treatment, comparing pre and post treatment findings |
|------------------------------------------------------------------------|
| Finding                                      | Number of patients pre treatment | Number of patients post treatment | P value  |
|----------------------------------------------|----------------------------------|----------------------------------|----------|
| Delayed bone age (more than 2 years less than chronological age)     | 21                               | 8                                | 0.0014   |
| Enlarged sella                                                               | 4                                | 4                                | -        |
| Wormian bones                                                                | 8                                | 8                                | -        |
| Dwarfism (less than 3 standard deviation)                                   | 13                               | 4                                | 0.0195   |
| Multicentre irregular epiphysis                                           | 3                                | 2                                | 0.98     |
| Increased intervertebral distance                                         | 11                               | 5                                | 0.14     |
| Flattening of vertebrae                                                     | 7                                | 4                                | 0.504    |
| Bullet-shaped vertebrae                                                     | 4                                | 2                                | 0.67     |
| Narrow coxa vera                                                            | 9                                | 7                                | 0.76     |
| Thickened band at the metaphyseal ends                                     | 18                               | 17                               | 0.99     |
in dwarfism. With treatment of hypothyroidism, there is an exuberant advancement of bone age, the catch up of bone age being approximately double of the chronological age advancement.

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