CHAPTER 17

INHERITED SKELETAL DYSPLASIAS AND COLLAGEN DISEASES

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1. INTRODUCTION

Inherited skeletal dysplasias are a heterogeneous group of genetic disorders associated with abnormalities in the skeletal system frequently presenting with limb abnormalities and disproportionate short stature. There are over 100 distinct skeletal dysplasias, which have been classified primarily on the basis of the clinical or radiographic characteristics (International Working Group, 1998). The management of these conditions require a combined effort involving various specialists including radiologists, orthopaedic surgeons, clinical geneticists, physiotherapists, rehabilitation clinicians and clinical psychologists.

Clinical geneticists play an important part in arriving at a diagnosis as genetic counselling is often required and is usually of concern for the family. Accurate estimate of the recurrence risks in future pregnancies is of paramount importance to facilitate informed reproductive decision making. In addition the parents can be given detailed information about natural history, management options and mode of genetic transmission of the skeletal dysplasia in consideration. The affected children are equally anxious to find out recurrence risks to their offspring when reaching the reproductive age.

The present chapter focuses on genetic disorders of the skeletal system with reference to the Indian subcontinent. However, majority of the data and information is based on reports and studies carried in other populations. In most of the skeletal dysplasias there is no clinical and radiological distinction in relation to the ethnic origin, but specific mutations might be more common in some ethnic groups. There are only a handful of clinical and radiological reports from the Indian subcontinent. Most of the published literature refers to patients and families with skeletal dysplasias living in the West.

2. EPIDEMIOLOGY

Individually most of the inherited disorders of the skeleton are uncommon, except for some conditions such as achondroplasia. There are no reliable figures to indicate prevalence of these disorders in any population or in a specific geographic region. Majority of the reports are part of the congenital anomaly registry system. There are, however, some hospital based surveys providing some prevalence figures. Whether
these are accurate would depend on method of collection, accuracy of clinical and radiological diagnosis, availability and interpretation of the family history and the classification system used.

The prevalence of short stature was estimated in a major Hospital in Bombay (now Mumbai) among 2500 children admitted for various medical and surgical problems (Colaco et al., 1991). 140 (5.6%) were considered to be of short stature (less than 5th percentile of an Indian standard). The causes of growth retardation were protein energy malnutrition [PEM] (42), chronic systemic disease (23), chronic anaemia (19), skeletal disorders (16), constitutional short stature (15), endocrine disorders (15), intrauterine growth retardation (5), chromosomal disorders (2), and miscellaneous (3). No specific clinical or radiological details are provided on the 16 cases classified as having a skeletal disorder. Some of these cases could be rickets or due to other metabolic causes. Congenital hypothyroidism and chronic malnutrition was attributed to large number of children presenting with short stature.

A hospital based study of skeletal dysplasias was conducted over a period of 2 years in Davangere, in the southern state of Karnataka, India (Kulkarni et al, 1995). A total of 169 cases of skeletal dysplasias were ascertained. One hundred were osteochondrodysplasias and were grouped according to international classification of skeletal dysplasias. Among the individual cases, osteogenesis imperfecta [OI] (13 cases) had the maximum representation. Several cases of rare disorders were also identified. Eighty eight cases of skeletal dysplasias were in the pediatric age group and of these 41 were newborns. The incidence of skeletal dysplasia among newborns was 19.6 per 10,000 deliveries and lethal dysplasias 5.2 per 10,000 deliveries. In 7 cases of skeletal dysplasia, an antenatal diagnosis was possible by ultrasonography.

Skeletal disorders were included in another survey from South India (Bhat and Babu, 1998). However, these were classified as musculo-skeletal (9.69 per 1000 live births), followed by cutaneous (6.33 per 1000), genitourinary (5.47 per 1000), gastrointestinal (5.47 per 1000), central nervous system (3.99 per 1000) and cardiac anomalies (2.03 per 1000). This study does not provide any data on a specific group of skeletal disorder such as OI or osteochondrodysplasias.

A significant number of genetic skeletal dysplasia disorders were ascertained in a study carried out at the Department of Pediatrics, Siriraj Hospital, Bangkok, Thailand (Wasant et al, 1995). Although, geographically this region is not included within the Indian subcontinent, the population is largely similar to that of Nepal, Bhutan and adjacent Himalayan states. The study includes cases of achondroplasia, hypochondroplasia, pseudoachondroplasia, atelosteogenesis, pyknodysostosis, spondyloepiphyseal dysplasia (SED) congenita, spondylometaphysial dysplasia (SMED), osteogenesis imperfecta type I, II and III, Ellis-van Creveld syndrome, cleidocranial dysostosis, thanatophoric dysplasia, rhizomelic chondrodysplasia punctata, trichorhinophalangeal syndrome, mucopolysaccharidosis I, II, IV and VI, mucolipidosis II, osteopetrosis, camptomelic dysplasia, metaphyseal dysplasia with spine involvement (Kozlowski type), Langer-Gideon syndrome and hypophosphatemic rickets. The hospital has a skeletal dysplasia registry system in operation. A Genetic Skeletal Dysplasia Clinic is established at Siriraj Hospital, Bangkok since 1992, and receives referrals from around the country. Genetic counselling is provided, including prenatal diagnosis and a multidisciplinary approach in management.