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Dentistry

DWARFISM AND ITS SIGNIFICANCE IN DENTISTRY –A LITERATURE REVIEW

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ABSTRACT Dwarfism is characterized by an adult with a height of 4'10"or less which may be due to hormonal deficiency or by mutation with a frequency of 1/26,000 to 1/ 40,000 birth in Achondroplasia and 1/10,000 birth in Diastrophic dysplasia among the world's total population. In India incidence is less than one million cases per year. Management includes both pharmacologic and non pharmacological intervention to optimize the function and independence. This review paper highlights the significance of dwarfism in dentistry with various diagnostic techniques, treatment options and surgical procedures.

KEYWORDS : Dwarfism, short stature, craniofacial management

INTRODUCTION:

Dwarfism is defined as height-vertex below two standard deviations (-2SD) or within third percentile for a given age and sex. [1] Advocacy groups Little People of the World Organization (LPOTW) and Little People of America (LPA) defined dwarfism as an adult with height of 4 feet 10 inches or under, owing to a medical or genetic condition. People with short stature identified as 'dwarf', 'little people' and have a community named 'Little people of America'. [1] Based on physical appearance dwarfism is categorized into proportionate short stature (PSS) and disproportionate short stature (DSS). [1] Proportionate short stature (PSS) denotes individual with proportionately small limbs and trunk and disproportionate short stature (DSS) implies an individual with average size torso and shorter limbs or a shortened trunk with longer limbs. In addition, DSS have significant difference in their sitting and standing height. [1]

Etiology: [2,3,4]

1. Disproportionate dwarfism - Skeletal dysplasia (most common)
2. Proportionate dwarfism- Metabolic and hormonal disorder.

- **Familial short stature**
- **Constitutional delay of growth and puberty (CDGP)**
- **Idiopathic Short Stature (ISS)**
- **Endocrine disorders**

i. Growth hormone deficiency [Most common]
ii. Hypothyroidism.
iii. Premature release of gonadotropins centrally or peripherally. [Precocious puberty]

- Genetic disorders

i. Down's syndrome
ii. Turner's syndrome
iii. Noonan's syndrome
iv. 3M syndrome
v. Prader-Willi syndrome
vi. Russell-Silver syndrome
vii. Aarskog syndrome and
viii. Short stature homeobox gene deficiency syndrome.

- Bone diseases [5]

i. Achondroplasia
ii. Spondyloepiphyseal dysplasia
iii. Diastrophic dysplasia
iv. Rickets

- Systemic disorders [Secondary effect on growth]

i. Juvenile idiopathic arthritis
ii. Malnutrition
iii. Inflammatory bowel disease [IBD]
iv. Celiac disease
v. Chronic kidney disease [CKD]
vi. Metabolic disorders
vii. Neoplasm and
viii. Glucocorticoid therapy. [6,7]

- Environmental pollutants: Lead, hexachlorobenzene (HCB), cadmium, polychlorinated biphenyl (PCB) etc. [8]

Epidemiology:

According to Allen's [1877] and Bergmann's rule [1847], stature of a person is determined by interaction between adaptation of gene and climatic condition. Individuals from extremely cold climate are generally short and round, whereas from hot climate are tall and thin. [9] Reported Frequency of dwarfism was 1/26,000 to 1/ 40,000 birth in Achondroplasia and 1/10,000 birth in Diastrophic dysplasia among the world's total population. 2.5% population in US was reported to have short stature.

In Saudi Arabia, reported frequency was 11.3% and 1.8% in children and adolescents with male predilection. [10] In developing countries, malnutrition was considered to be a causative factor for short stature. 1% of Galician population reported short stature due to malnutrition in children. In India, incidence was less than one million cases per year. Prevalence rate of 2.86% reported among south Indian school going children. [11] Velayutham et al in their study reported that short stature was mainly due to genetics and constitutional delay in growth [66.67%]; hormonal deficiency [22.99%] and malnutrition [6.69%] respectively. [11] According to gender, prevalence of short statue in males was due to social pressure [12] and in females due to age, weight and abdominal obesity. [13]

Pathogenesis: [1]

Growth is determined by equilibrium between proliferation and senescence of chondrocytes at the growth plate. Mechanisms involved in regulation of growth include:

- **Endocrine pathway**

i. **Hypothalamic-pituitary axis -** Growth hormone regulates linear growth of an individual directly or indirectly through insulin like Growth factor [IGF]-1. Lower levels of IGF-1 are associated with short stature. Stimulates elongation of bone and regulates growth of cartilage and soft tissues.
ii. **Gonadotropins –**Results in early maturation of the skeletal system resulting in short stature. [4]

- **Chronic inflammatory conditions –** Elevated pro-inflammatory cytokines negatively impact the growth.
- **Intracellular pathways –** Gene SHOX regulates chondrogenesis. Mutation of this particular gene results in non-specific short stature. [14]
- **Malnutrition –**Malnutrition in gestational period dampens the growth velocity and results in shunted growth. [15]

Clinical manifestation:

Proportionate dwarfism:

- Head, trunk and legs are small but all are in proportion.
- Small sized organs.
- Growth rate is slower than expected age.
- Delayed or no sexual development.
- Height is lower than 3 rd percentile for standard age.

Disproportionate dwarfism:
Individuals have average sized trunk and short limbs or vice versa. Intellectuals are not affected unless associated with hydrocephalus. Achondroplasia - Most common cause of disproportionate dwarfism occurring in 1 in 25,000 births. [16] Autosomal dominant condition with following manifestations: [17,18,19]

- Disproportionate short stature with medium height of 131±5.6 cm for males and 124 ± 5.9 cm for adult males and females respectively. [20]
- Cervico-medullary compression with stenosis of foramen magnum.
- Normal intelligence except in hydrocephalus or other central nervous system complications.
- Recurrent otitis media.
- Adenotonsillar hypertrophy. [21]
- Obstructive sleep apnea. [22]
- Rhizomelic shortening of extremities.
- Short stubby hand with increased space between the third and the fourth fingers.
- Lumbar spine stenosis.
- Lumbar lordosis.
- Thoracolumbar kyphosis.
- Flat chest.
- Knee Joint laxity.
- Limited elbow extension.
- Inferior dislocation of the shoulder.
- Bowleg deformity.
- Protuberant and prominent abdomen.
- Lower extremity deformities - genu varum, coxa vara and heel varus.

Orofacial manifestations:
Disproportionate dwarfism:
Achondroplasia [23,24,5,26]

- Frontal bossing.
- Short posterior cranial base.
- Enlarged calvarium with hydrocephaly.
- Depressed nasal bridge.
- Enlarged adenoids.
- Midface hypoplasia. [27]
- Retrognathic maxilla.
- Prognathic mandible.
- Retarded eruption of permanent teeth. [27]
- Skeletal and dental Class III malocclusion. [27]
- Crossbite. [27]
- Concave soft tissue profile.
- Protrusive maxillary incisor. [28]
- Anterior open bite. [28]
- Posterior open bite. [28]
- Macroglossia. [28]
- Migratory glossitis. [28]
- Class I malocclusion. [24,29]
- Class II division 1 malocclusion with protrusive maxillary incisors.
- Mouth breathing. [30]
- Cleft palate [Spondylo epithelia dysplasia].

Proportionate dwarfism: [31]

- Abnormalities of tooth development in pituitary dwarfism are:
- Delay in shedding of deciduous teeth.
- Delayed or absence of resorption of deciduous teeth root.
- Marked delay in eruption of the permanent teeth.
- Retention of permanent teeth in maxilla and mandible.
- Development of the apical roots of the retained permanent teeth and their growth toward the lower mandibular edge.
- Displacement of first molar from the mandibular shaft to rami.
- Smaller dimensions of teeth in comparison with control. [32]
- Incomplete eruption of teeth.
- Delay in root formation and closure of apical foramen.
- Tilting of retained teeth.
- Hypoplastic maxilla and mandible with crowding of dentition.
- Complete absence of wisdom teeth bud even in fourth decades.

Investigations:
Diagnosis has to be concluded after a detailed familial history and thorough physical examination, anthropometric assessment [body weight, trunk height, vertex height and limb length], medical history [Gestational period to birth, milestones], biochemical and radiological test. [1]

- Hematological disorders - Complete blood count
- Cystic fibrosis - Sweat chloride test
- Hypothyroidism - Serum thyrotropin (TSH) and free thyroxine (T4) levels
- Inflammatory bowel test - Wintrobe sedimentation rate
- Celiac sprue - Antibody testing

i. anti-endomysial immunoglobulin A (IgA) - more sensitive
ii. anti-endomysial immunoglobulin G (IgG) - more specific and
iii. anti-gliadin IgG titers.

- Malnutrition - Serum pre-albumin and transferrin
- Genetic disorders – Amniocentesis
- Growth hormone deficiency:

i. Insulin-like growth factor binding protein-3 (IGFBP-3) levels [more specific]
ii. Serum IGF-1 levels (somatomedin C) [33]

Other tests:

- Insulin tolerance test
- Levodopa-propanol HCL test
- Arginine HCL test
- Glucagon test.

Radiographic investigation:

- Ultrasound
- Magnetic Resonanace Imaging [MRI]
- Computed tomography [CT]
- Lateral Cephalogram
- Anterior Posterior view of skull
- Antero posterior view of left hand and wrist
- Dual-energy x-ray absorptiometry (DEXA) scan

According to Lawson Wilkin's there are four types of diagnostic patterns:

i. Rate of bone development is retarded to greater degree than rate of growth. [hypothyroid dwarfs and Some pituitary dwarfs]
ii. Rate of osseous development is retarded to a degree less than the rate of growth but nevertheless the bone age and falls progressively below the average. [Pituitary dwarfs]
iii. Osseous development remains consistently below the average over a number of years and although advances at a normal rate.
iv. Osseous development is within normal limits but growth is markedly retarded. [Primordial dwarfs]

Management:
Goal of management is to relieve the underlying cause, maximize function and independence of affected individual broadly divided into medical and surgical management.

Medical management: [34]

1) Hormonal therapy

- **Growth hormone**

Recombinant human growth hormone therapy [rHGH] [35] :subcutaneous dose of 0.2–0.375 mg/kg/week. [36]

- **Gonadotropin releasing hormone [GnRH]** [1,5]

GnRH agonist:
Triptorelin 3.75 mg intramuscularly
Deslorelin 4 mcg/kg/day [37]

2) Parathyroid hormone [PTH] [38]

3) Aromatase inhibitor – Delay bone maturation and improves adult height. [39]

i. Testolactone
ii. Fadrozole
iii. Letrozole -2.5 mg/day [Most potent and selective 3 rd generation inhibitor]
iv. Anastrozole

4) Low dose androgen therapy: [36]

i. Injectable testosterone
ii. Oral Oxandrolone – Preferred when skeletal age less than 11 years Dose: 1.25 -2.25 mg/day; increases growth rate by 3-5 cm per year.

5) Imatinib –Selective inhibitor of FGFR3 tyrosine kinase.

6) C-type natriuretic peptide [CNP]
CNP analogues: [25,40,41]

i. BMN-111 [Vosoritide] - Dose: Subcutaneous injection of

15mcg/kg. [42]
ii. TransCon CNP.
iii. Human VNP-53

7) Stem cells – Mesenchymal stem cells, statin treatment rescued stem cells. [25,41]

8) Meclizine [43]

9) Estrogen

10) Metformin [5]

11) Recombinant human insulin-like growth factor- 1 (RhIGF-1) [5,33,34]

Surgical management:

i. Thoracolumbar kyphosis and lumbar stenosis - Osteotomy.
ii. Spinal stenosis - Spinal canal decompression
iii. Hydrocephalus – Shunt placement.
iv. Limb lengthening - Distraction osteogenesis.

Craniofacial:

i. Selection of surgical procedures depends on severity of skeletal deformities
ii. Class III open bite deformity - Anterior mandibular body step osteotomy – Stable and versatile. [44]
iii. Mid-face advancement - Subcranial Le Fort III osteotomy. [45]
iv. Between age group of 6 to 10 years - Le Fort II and III type distraction is preferred.
v. Lefort III distraction osteogenesis - Indicated in patients with obstructive sleep apnea [45]
vi. Severe skeletal deformities cases - Front facial advancement, Le Fort I and vertical sub- sigmoid osteotomy preferred because of its optimized functional and esthetic result.

Dental management considerations:

Dental management requires special consideration in disproportionate type due to its short stature and disproportionate feature. [18, 23, 30] Presence of short limbs and chronic back ache makes hard for these patients to sit comfortably on a dental chair.

- Lowering the dental chair, use of step stool and placement of cushion behind reduces back pain and maintains the posture during treatment.
- Head control precautions like neck pillow, cuddle jackets and backrest can be employed due to presence of limited neck extension, craniocervical instability and foramen magnum stenosis. [24]

American Academy of Pediatrics recommends that any review for orthodontic problems should commence after 5 years of age. [18, 46] Antibiotic prophylaxis is mandatory before dental management due to placement of stunt, as in case of hydrocephalus. Management of malocclusion can be corrected by orthodontic means when skeletal discrepancy between maxilla and mandible is not severe or main concern. Rapid palatal expansion should be initiated to correct cross-bite and to gain space. Myo-functional therapy is used to correct tongue thrusting habits. Successful management of skeletal discrepancy is reported by orthondontic management alone or in combination with orthognathic surgery. [29,45]

General anesthesia (GA) poses greater complications and difficulty in intubation due to small nasopharynx, larynx and anteriorly placed epiglottis. In addition to this lumbar lordosis, small chest and narrowed of spinal cord poses a great risk. Evaluation of airway, radiographic evaluation of foramen magnum has to be done when dental management for a dwarf patient is planned to perform under GA /sedation. Use of appropriate sized endotracheal tube, oxygenation before intubation and after extubation to be done. In case of anticipated airway alternative intubation techniques should be employed [retrograde intubation, fiber-optic intubation]. [47]

CONCLUSION:

Management of patient with short stature involves multi-disciplinary approach including distinct medical management but also a tailored dental management. In addition to management, providing a psychological support will lead them have a normal life and overcome with their medical problem as well as social challenges of life. Dental professionals should be able to recognize the systemic and orofacial features and its associated complications. In addition to primary management, newer advancements like molecular genetics and pathway driven therapies develop in future which eventually would be more effective and optimized treatment.

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