ABSTRACT
It is a rare neurogenic illness; because of its clinical characteristics it is important for dentists. PWS is first known human genomic imprinting disorder, microdeletion syndrome. It is caused by the absence of certain paternally inherited genes on long arm of chromosome 15. The clinical picture of Prader-Willi syndrome is complex and alters with age. It is mostly due to impaired hypothalamus function. The characteristic features include short stature; muscular hypotonia; hypopigmentation of the skin and hair; a triangular facies, frequently with a small mouth with a thin upper lip and down-turned corners; and diminished secretion of thick and sticky saliva. The article describes the phenotypic features of Prader-Willi syndrome (PWS) and their impact on the oral health status Primary care by pediatric dentist’s play an important role in children’s with PWS.

Keywords: Prader-Willi syndrome, Obesity, Oral findings, Management.

INTRODUCTION
Prader-Willi syndrome (PWS) is usually caused by chromosomal aberration, i.e. a partial deletion of long arm of the paternal chromosome 15 in loci 11 and 13.1 PWS is a complex multisystem genetic disorder characterized by hypothalamic-pituitary dysfunction.2 The clinical manifestations are complex and alter with age; features are neonatal hypotonia, distinctive facial features, delayed overall development with mental deficiency, behavioral abnormalities, poor growth in infancy followed by overeating with severe obesity, short stature and hypogonadism.3

PWS is now known to be one of the most common micro-deletion syndrome, first known human genomic imprinting disorder and leading known cause of genetic obesity. Thus, appropriate management of children with PWS requires collaborative efforts from geneticist, endocrinologist, pediatrician, nutritionist, psychologist, psychiatrist, educational specialist, pedodontist and family.

HISTORY
In 1956, Prader, Labhart and Willi published a report with a syndrome presenting extreme neonatal hypotonia and children were unable to cry and suck with weak, absent reflexes. Over a period of time hypotonia and lack of movement improved but progressed toward obesity, developed around 2 years of age along with growth deficiency, learning disabilities were delayed and incomplete during puberty.4 In 1976, Hawkey and Smithies described a abnormal karyotype showing a 15; 15 robertsonian translocation leading to loss of short arm of chromosome 15.5 In 1981 Ledbetter et al first used high resolution chromosome analysis to find interstitial deletions of long arm of chromosome15.6 Mean FJ and Butler MG in 1987 first presents the anthropometric parameters and second described craniometric variability of PWS patients. Cepahalometric parameters were analyzed in 1990,7 In 2007 oral phenotype with PWS was studied by Bailleul Forestier.8 Latest study by Saeves R et al analyzed orofacial dysfunction in 2011.9

GENETICS AND ETIOLOGY
Genetics findings was described by a term known as genetic imprinting, in which certain genes or groups of genes are expressed differently depending on the sex of the parent from which they were inherited. The maternally derived copy of chromosome 15 in the critical region for PWS is inactivated in unaffected individual. Mechanism of imprinting appears to be hypermethylation of the maternally contribute allele that interferes with the translation of those genes.10 PWS syndrome results when there is an absence of the normally active paternally inherited genes on the long arm of chromosome 15.11 It is also termed as maternal uniparental disomy12,13 because they have 2 maternal copies of chromosome 15 but no paternal chromosome 15. There is also translocation or other structural abnormality that involves chromosome 15. In 1% of cases there is micro deletion in imprinting center.14-16 Some clinical differences exist between individuals with PWS from 15q deletion and those arising from maternal uniparental disomy.

INCIDENCE AND PREVALENCE
It occurs with an incidence between 1:15000 and 1:50000 live births, occurs in both sexes and all races.17 Individuals with secondary complications owing to obesity such as cardio respiratory insufficiency, diabetes mellitus and obstructive sleep apnea have increased morbidity and mortality.18,19
DIAGNOSIS

Diagnostic criteria for PWS were developed in 1993 to aid in early recognition and diagnosis and have since been using molecular and cytogenetic techniques. Clinical features are believed to be secondary to hypothalamic insufficiency.

The diagnostic criteria are classified according to major and minor criteria (Table 1). Major criteria include neonatal hypotonia, feeding problems in infancy, characteristic facial features, excessive weight gain, hypogonadism, development delay and hyperphagia leading to obesity. Minor criteria are decreased fetal activity, behavioral and emotional problems (stubbornness, obsessive-compulsive behaviors, hyperactivity, aggressiveness), self-destructive behavior (e.g., picking of the skin), mental retardation, delayed speech, memory development, sleep disturbances, short stature, hypopigmentation of skin and hair, small hands and diminished secretion of thick and sticky saliva. Supportive findings are scoliosis, osteoporosis and high pain threshold.

The clinical features that should lead to diagnosis of PWS depend on the age of the patient. In infants the most characteristic feature is unexplained hypotonia and poor sucking skills. During childhood, a genetic test for PWS should be performed on obese children learning disabilities, specific dysmorphic features and a history of neonatal hypotonia. Finally genetic testing should be considered in adolescents and adults with behavioral problems in additional to obesity and hypothalamic hypogonadism.

ORAL MANIFESTATIONS

The syndrome is of interest to dentist because of its oral clinical features. The hypotonia reduces the mouth’s normal cleaning mechanisms, hindering sucking, swallowing and chewing and making a soft diet mandatory. The abnormal appetite increases carbohydrate intake, which together with the alteration in the quantity and quality of saliva, raises the risk of caries. The mental retardation adds to the difficulty of achieving optimal oral hygiene.

Thick viscous saliva has been reported to be a consistent finding in PWS and a diagnosis indicator of PWS in neonates. Decreased salivary flow rates and increased amounts of salivary ions and proteins have also been reported. Dental caries, enamel defects and poor oral hygiene have been described. Progressive dental tissue loss (tooth wear) gastroesophageal reflux, rampant caries, dental erosion and periodontal problems have also been reported.

MANAGEMENT

Children with PWS need early interventions. New born infants sucking problems and failure to thrive, developmental assessment should be done routinely.

Table 1: Diagnostic criteria for Prader-Willi syndrome

| Major criteria | Neonatal and infantile central hypotonia gradually improving with age | Feeding problems in infancy with need for special feeding techniques and poor weight gain/failure to thrive | Rapid weight gain between 1 and 6 years of age causing central obesity | Hyperphagia | Facial features: narrow bifrontal diameter, almond-shaped eyes, down-turned corners of the mouth | Hypogonadism |
| Minor criteria | Decreased fetal movement and infantile lethargy improving with age | Characteristic behavior problems, temper tantrums, obsessive/compulsive behavior; rigid, manipulative, steal an lie, picking of skin | Sleep disturbance or sleep apnea | Short stature for genetic background | Hypopigmentation | Small hands with straight ulnar border | Esotropia, myopia | Thick, viscous saliva |
| Supportive findings | High pain threshold | Decreased vomiting | Scoliosis and or kyphosis | Early adrenarche | Osteoporosis | Unusual skill with jigsaw puzzles | Normal neuromuscular studies |
| Scoring: major criteria at 1 point each. Minor criteria are weighed at 0.5 point. Requirements for diagnostic are: | Children 3 years of age or younger: 5 points (minimum 4 major criteria) | Children’s older than 3 years of age: 8 points (minimum 5 major criteria) |
Physical therapy should begin in infancy to facilitate development of motor milestones. Speech therapy for improving language skills. Appropriate educational interventions in schools are added, that addresses individual strengths and challenges as well as behavioral issues. Weight and dietary management involves consultation with a dietician as early in life. Most beneficial intervention is reduced calorie diet and increased physical activity, height, weight and BMI are monitored and daily food intake calculated. Low calorie diet consist of no more than 1000 to 1200 Kcal/daily and BMI below 30.\textsuperscript{17} Regular physical exercise is recommended for 30 minutes daily.

United States of Food in 2000, approved growth hormones for all children with PWS. Growth hormones in PWS children’s have shown significant benefit from infancy through adulthood,\textsuperscript{48} it increases rate of growth, allows adolescents growth spurts, may normalize height. GH enhances motor development in infancy.\textsuperscript{49} Pulmonary and sleep apnea are improved with GH therapy in infancy or at diagnosis, recommended dose is 1.0 or 1.5 mg/m\textsuperscript{2}.\textsuperscript{50,51} Consultation with pediatric endocrinologist is highly advised.

Sex hormone replacement is sometimes advised to help development of sex characteristics and may potentially increase bone mineral content and density. Low dose of 50 to 75 mg intramuscular depo-testosterone every 3 to 4 weeks, then slowly increasing dose of 150 mg every 3 to 4 weeks is offered in hypogonadism in boys around 17 to 18 years of age, whereas in girls it is low frequency administered.\textsuperscript{17}

Pharmacological management of behavior and psychiatric problems are often used, particularly in depression and obsessive compulsion symptoms. Selective serotonin reuptake inhibitors are particularly effective,\textsuperscript{52} fluoxetine is currently popularly used,\textsuperscript{53,54} risperidone is effective in treating psychosis.\textsuperscript{55}

Most dental problems with PWS are decreased salivary flow and mouth breathing, these promote to dental decay, periodontal disease, crowded arches, severe wear of tooth. First child/adult should have fluoridated water supply or fluoride tablets (1 mg/day) to fight decay, make them brush with fluoride toothpaste after each meal and before bedtime. Parents should check their teeth after food especially at night so they donot leave food along gum lines, this leads to decay and periodontal problems. Dry mouth is seen in individuals with PWS because of thick saliva, which leads to decay and periodontal disease. Normal saliva is thin and cleanses teeth while thick saliva harbors bacteria that cause decay and periodontal disease. As result of mouth breathing they will have narrow arches leading to crowding of teeth. Early orthodontic care at 6 to 9 years help to develop arches to normal shape, keep teeth clean; prevent decay and periodontal disease. Professional cleaning every 3 to 6 months is a big help in keeping teeth and gums clean and healthy. When there is wearing of teeth in some cases it can be restored with various restorative materials.

Once diagnosis of PWS is confirmed, multidisciplinary care is added to routine preventive health care from primary care physician. Early interventions include physical, occupational, speech therapy are essential for children with PWS. Therapeutic interventions to manage growth, dietary and behavioral concerns can enhance the child’s potential and significance impact on health. Early dietary management and regular exercise should be a part of daily life style.\textsuperscript{56,57}

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ABOUT THE AUTHORS

Umapathy T
Reader, Department of Pedodontics, Krishnadevaraya College of Dental Sciences, Bengaluru, Karnataka, India

Premkishore K (Corresponding Author)
Reader, Department of Pedodontics, New Horizon Dental College and Research Institute, Sakri, Bilaspur, Chhattisgarh, India, e-mail: dr_premkishore@yahoo.com

Mithesh D Kathariya
Senior Lecturer, Department of Pedodontics, Rural Dental College Pravara Institute of Medical Sciences, Loni, Maharashtra, India

Sridhara KS
Reader, Department of Endodontics, Krishnadevaraya College of Dental Sciences and Research Institute, Bengaluru, Karnataka, India

Ashwini CP
Dental Surgeon, Sri Vinayaka Dental Clinic, Vijayanagar, Bengaluru Karnataka, India