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**Effectiveness of a 2 years individualized oral health preventive program
in preschool children with Neurodevelopmental Disorders**

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Preface

This thesis evaluated the effectiveness of an individualized oral health preventive program for preschool children with Neurodevelopmental Disorders (NDDs). These disorders affect not only the general health but also the orofacial area and the patient's quality of life. There are very few studies in the literature on the effectiveness of oral health preventive programs in children with NDDs. In this study, preschool children were selected because this age is particularly important for setting the basis for healthy oral habits and attitudes and prevent the initiation and development of oral health problems that may require costly and difficult to cope treatment. Completing this project was very challenging but it became possible with the help of people who stood by me and assisted me in every possible way.

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LIST OF ABBREVIATIONS

NDD - Neurodevelopmental Disorder

ASD - Autism Spectrum Disorder

ASDs - Autism Spectrum Disorders

PDD-NOS - Disorders-Not Otherwise Specified

CDC- Center for Disease Control

ADHD - Attention Deficit Hyperactivity Disorder

ID - Intellectual Disability

CD - Communication Disorder

SLD - Specific Learning Disorder

MD - Motor Disorder

MIH – Molar Incisor Hypomineralization

SHCN - Special Healthcare Needs

DS - Decayed Surfaces

CLD - Children with Learning Disabilities

CNLD - Children Without Learning Disabilities

GI - Gingival Inflammation

DDE - Developmental Defects of Enamel

YLDs - Years lived with disability: Metric seeks to provide a comparable measure of disease burden across diverse health conditions and impairment

ADLs- Activities of Daily Living

1. Neurodevelopmental disorders

1.1 Definition

The term neurodevelopmental disorder (NDD) is a relatively new term and includes a group of disorders in which the development of the central nervous system is disturbed (Cardoso et al., 2019). Typically occur in early development and are characterized by developmental deficits that produce impairments of personal, social, academic, or occupational functioning. Children with neurodevelopmental disorders can experience difficulties with language and speech, motor skills, behavior, memory, learning, or other neurological functions (Thapar et al. 2016, Cardoso et al., 2019).

According to diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), the most commonly diagnosed NDDs include cerebral palsy, autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), intellectual disability (ID), communication disorders (CD), specific learning disorders (SLD) and motor disorders (MD) (eg, develop mental coordination disorder and tic disorders) (Du et al. 2010, Abanto et al., 2012).

1.2 Prevalence

Globally, 52.9 million children younger than 5 years had developmental disorders in 2016 compared with 53.0 million in 1990. About 95% of these children lived in low-income and middle-income countries. YLDs among these children increased from 3.8 million in 1990 to 3.9 million in 2016. The global burden of developmental disabilities

has not significantly improved since 1990, suggesting inadequate global attention on the developmental potential of children who survived childhood as a result of child survival programs, particularly in sub-Saharan Africa and south Asia. (Global Research on Developmental Disabilities Collaborators 2018).

In Greece, there is no official record of people with NDD as a percentage of total population. Data from the Greek Foundation of Social Security (IKA) – the social security organization for 75% of the population – show that 218.129 people received disability benefits in the year 2010. (Anagnostopoulos et al., 2011)

1.3 Neurodevelopmental disorders (NDD)

1.3.1 Cerebral Palsy (CP)

Cerebral palsy (CP) is a term used to describe a group of permanent and progressive disorders affecting movement and posture that result from injury or insult to the developing brain (Lansdown et al., 2019, Rosenbaum et al., 2007). This insult can occur, anytime from during the prenatal period through the first few years of life (Dougherty, 2009). The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication and behavior, epilepsy and secondary musculoskeletal problems (Graham et al., 2016).

Cerebral palsy is the most common physical disability of childhood, occurring in 2:1000 live births in developed countries, and it is a lifelong condition (Smithers-Sheedy et al., 2016, Lansdown et al., 2019). Population-based registries of cerebral palsy, largely in Australia and Europe, have historically found prevalence ranging from 1.5 to 2.5 per 1,000 live births (Graham et al., 2016). In Greece, in a number of 100,000

thousand births per year, it is estimated that 300 children have CP of varying form and gravity (Angelopoulou 2004).

What links all people with cerebral palsy are the clinical and functional onset of symptoms in early development, the high probability that the symptoms have an effect on the whole life course and the current lack of a definitive cure (Graham et al., 2016). The exact etiology can be identified only in 40 to 50% of the cases. Approximately, 30% of cases have none of the known risk factors (Berker et al., 2008). The condition or risk factors associated with CP can be broken down into those occurring in the prenatal, perinatal or postnatal time period (Jones et al., 2007). It has been estimated that up to 70 to 80% of CP cases can be attributed to prenatal factors approximately 10% to birth asphyxia while the remaining cases are due to identifiable postnatal conditions (Dougherty, 2009).

The prenatal risk factors associated with CP included hypoxia, genetic and metabolic disorders, multiple gestation, intrauterine infections, thrombophilic disorders, teratogenic exposure, chorioamnionitis, maternal fever, exposure to toxins, malformations of brain structures, intrauterine growth restriction, abdominal trauma and vascular insults.

The perinatal risk factors associated with CP include asphyxia, premature birth (<32 weeks or <2500 gm), blood incompatibility, infection, abnormal fetal presentation, placental abruption and instrument delivery.

The postnatal risk factors associated with CP include asphyxia, seizures in postnatal period, cerebral infarction, hyperbilirubinemia, sepsis, respiratory distress syndrome, chronic lung disease, meningitis, postnatal steroids, intraventricular hemorrhage, periventricular leukomalacia, shaken baby syndrome and head injury (Berker et al., 2008, Jones et al., 2007, Dougherty, 2009).

CP is a heterogeneous condition in terms of etiology, motor type, and severity of impairments. Consequently, CP is described using different classifications primarily motor type, topography, and motor severity (Rosenbaum et al., 2006). Motor types of CP include spastic (85%), dyskinetic (7%) which includes dystonia and choreoathetosis, and ataxic (4%) (Cans et al., 2000). The spastic motor type is classified topographically as unilateral (hemiplegia 40%–60%) affecting one side of the body or bilateral affecting both sides of the body. Bilateral spastic CP includes: diplegia (10%–36%), with lower limbs more affected than upper limbs; and quadriplegia (24%–31%), with trunk and all four limbs affected. Dyskinetic, ataxic and hypotonic predominant motor types are not classified topographically (Guare et al., 2003).

The prediction of motor severity of CP over the age of two is well established using the Gross Motor Function Classification System (GMFCS), which indicates a child's level of gross motor function and mobility, and CP motor development curves. Both tools are recognized tools used to predict long term mobility (Miller et al., 2012).

Children with CP are at increased risk of developing dental problems as compared with healthy controls. This can create significant morbidity that can further affect the wellbeing of these compromised children and negatively impact their quality of life (*Jan et al, 2016*).

These challenges extremely influence their Activities of Daily Living (ADLs) and lead to a deteriorated oral health condition in the form of high caries rate, decreased number and rate of restored teeth and/or poor quality restorations, as well as intense periodontal inflammation (*Sedky et al., 2018*).

Neuromuscular dysfunction related to CP may affect oral health due to changes of orofacial structure, development of parafunctional habits, nutritional problems, and difficulties in observing oral hygiene. A large number of variables have been studied such as dental caries experience, gingival health, dental wear and trauma, developmental defects of enamel, malocclusions, and oral mucosal condition (Bensi et al., 2020).

1.3.2 Autism Spectrum Disorder (ASD)

Autism spectrum disorders (ASDs) is characterized by persistent deficits in social communication and social interaction across multiple contexts, including deficits in social reciprocity, nonverbal communicative behaviors used for social interaction, and skills in developing, maintaining, and understanding relationships (DSM5). The three core characteristics of ASDs are impairments of mutual social interactions, difficulties in communication, and limited ranges of behaviours and interests. The signs of autism can be evident early in life during the first 3 years of age, and ASDs can sometimes be detected at 18 months or younger (Lord et al., 2018, Sharma et al., 2018). ASD is broadly considered to be a multi-factorial disorder resulting from genetic and non-genetic risk factors and their interaction (Park HR et al., 2016, Sharma et al., 2018).

The Center for Disease Control (CDC) reports the prevalence of ASD to be 1 in 54 children. These estimates from the ADDM Network are based on data collected from health and special education records of children living in 11 communities across the United States during 2016. Studies in Asia, Europe, and North America have identified individuals with ASD with an average prevalence of between 1% and 2%.

In Greece, ASD prevalence in 10–11-year-old children was 1.15% (1.83% males, 0.44% females; ratio 4.14:1) (Thomaidis et al., 2020, CDC, 2020-<https://www.cdc.gov/ncbddd/autism/data.html>).

Many children with ASD have other co-existing conditions such as cognitive impairment, epilepsy, ADHD, depression/anxiety, bipolar disorder, schizophrenia, and sleep disorders (Mannion et al., 2016). Individuals with ASD demonstrate difficulties in social interaction, communication, and have repetitive behaviors or limited interests/activities (Landrigan et al., 2010). These symptoms can hurt the individual's ability to function socially, at school, work, or other areas of life.

The causes of ASD have not been fully explained although it is widely thought to be influenced by the interaction between genetic and environmental risk factors (Marshall et al., 2008, Herbert, 2010). Genetic causes including gene defects and chromosomal anomalies have been found in 10%~20% of individuals with ASD. Diverse environmental causative elements including pre-natal, peri-natal, and post-natal factors also contribute to ASD. Prenatal factors related with ASD include exposure to teratogens such as thalidomide, certain viral infections and maternal anticonvulsants such as valproic acid, increased paternal age. Low birth weight, abnormally short gestation length, and birth asphyxia are the peri-natal factors. Reported post-natal factors associated with ASD include autoimmune disease, viral infection, hypoxia, mercury toxicity, and others (Hye Ran Park et al. 2016).

Patients with AD do not present very specific oral disorders. They pose the greatest challenge for dentists, due to their complex and varied clinical manifestations (Udhya et al., 2014).

Literature suggests that the population with ASD presents with similar health problems as that of the typical population, but, due to factors including poor dietary preferences,

behaviours and specific aversions, like incapacity to take care of themselves independently, selfinjurious behaviour or drugs, this population is at a greater risk and more susceptible to developing chronic non-communicable oral health conditions. Thus, some of their characteristic behaviours or disorders, such as communication limitation, personal negligence, self-injurious behaviour, eating habits (uncontrolled and restrictive feeding), side effects of drugs, opposition to dental care, hyposensitivity to dental pain and hypersensitivity to external stimuli are often responsible for the deterioration of the oral health of children with ASD. These characteristics have an impact on oral health: children with ASD have a poor collaboration in practicing proper oral hygiene (Ferrazzano et al., 2020).

1.3.3 Attention Deficit Hyperactivity Disorder (ADHD)

Attention-deficit hyperactivity disorder (ADHD) is a neurobehavioral disorder characterized by pervasive inattention and/or hyperactivity-impulsivity, which can result in significant functional impairment (Bimstein et al., 2008). American Psychiatric Association, describes ADHD as a chronic, pervasive childhood disorder distinguished by developmentally inappropriate activity level, low frustration tolerance, impulsivity, poor organization of behavior, distractibility, and inability to sustain attention and concentration (American Psychiatric Association, 2000, Cormier, 2008).

The prevalence of ADHD ranges from 2 to 18%, with a prevalence below 5% in Europe. In Greece, prevalence of ADHD has not been adequately investigated. The greatest and the unique population study, to our knowledge, which was conducted in Crete by Skounti et al. (2006), concluded to a prevalence rate of 6.5% among 7-year-old schoolchildren. ADHD occurs more often in boys than in girls (Ehlers et al., 2019). The etiology of ADHD remains unclear, although it is known to be multifactorial, with

genetic, biological, environmental, and psychosocial factors . (Brassett-Harknett et al., 2007). About one fourth to one third of biological parents with an ADHD child are affected by ADHD themselves. A dopamine transmitter gene (DAT-1) and a dopamine receptor gene (DAT-4) have been linked to children with ADHD, and neuroimaging studies have identified abnormalities of brain structure and function (Faraone, 2006, Valera et al., 2006). Traumatic injuries to the brain have also been associated with behaviors characteristic of ADHD (Levin et al., 2007). Similarly, prenatal exposure to alcohol and/or cocaine, birth trauma, and exposure to lead or infections such as meningitis as a young child have been linked to the later development of ADHD (Brassett-Harknett et al., 2007).

There are three types of ADHD characterized by symptoms: predominantly inattentive, predominantly hyperactive-impulsive, and the combined form in which the two forms manifest themselves equally (Begnini et al., 2019). The core symptoms of ADHD are associated with impairments in several domains of functioning, including academic achievement and deportment at school, interactions with parents and siblings, and peer relationships (Cormier, 2008). Children diagnosed with ADHD also have a higher likelihood of coexisting psychiatric disorders (Brassett-Harknett et al., 2007) .

Children with ADHD need more support with regard to oral hygiene and eating habits. They must be examined more frequently, between dental examinations to prevent the progression of caries disease due to their oral health behavior.

Individuals from a group with ADHD showed higher prevalence of parents reporting toothache, bruxism, bleeding gums, and dental trauma as well as differences in the numbers of restored or decayed dental surfaces (Bimstein et al., 2008)

Children with ADHD, even when medicated, present a high risk for dental trauma due to their hyperactivity and impulsiveness (Begnini et al. 2019).

1.3.4 Intellectual Disability (ID)

Intellectual disability (ID) is a neurodevelopmental disorder that is characterized by deficits in both intellectual functioning (i.e., IQ below 75) and adaptive functioning, which comprises three skills types (conceptual skills, social skills and practical skills) whose onset is in the developmental period. A child with ID may present initially with receptive and expressive language delays, adaptive skills delays (eg, toileting, dressing), fine motor deficits, difficulties in problem-solving skills, social immaturity, and behavioral difficulties. ID is highly heterogeneous, encompassing syndromic and non syndromic forms. Different severity categories, ranging from mild to severe retardation, are defined on the basis of IQ scores (Purugganan, 2018).

ID affects approximately 1% to 3% of the population globally (Bouras et al., 2007). Among those with intellectual disability, mild, moderate, severe, and profound intellectual disability affects about 85, 10, 4, and 2% of the population, respectively. In Greece, there is no official record of people with intellectual disability as a percentage of total population. Madianos estimates that there were about 150 000 people with intellectual disability; this estimate, however, is based on 1991 data and cannot be considered representative today (Madianos, 1994).

There are many different etiologies for ID: genetic disorders (eg, chromosomal disorders, including X chromosome disorders, contiguous gene deletions, and single-gene disorders), environmental causes (eg, alcohol and other teratogens, prenatal infections), traumatic brain injury, neurologic/ brain disorders, nutritional deficiencies, and inborn errors of metabolism. A significant number of people with ID have no

identifiable cause. It is more likely to identify a biological cause in more significant forms of ID (such as moderate, severe, and profound ID) than in mild ID, which may be influenced by cultural, linguistic, and societal difficulties (*Purugganan, 2018*).

Limited access to dental care and compromised ability in self-care make oral health promotion particularly important for patients with intellectual disabilities. Children with ID have been reported to have more obstacles in daily tooth brushing than healthy children. This might be due to their difficulty in achieving the required manual dexterity for self-care and lack of awareness of the importance of oral hygiene practice (*Zhou et al., 2017*).

1.3.5 Communication Disorders (CD)

Communication disorders include language disorder, speech sound disorder, social (pragmatic) communication disorder, and childhood-onset fluency disorder (stuttering). The first three disorders are characterized by deficits in the development and use of language, speech, and social communication, respectively. Childhood-onset fluency disorder is characterized by disturbances of the normal fluency and motor production of speech, including repetitive sounds or syllables, prolongation of consonants or vowel sounds, broken words, blocking, or words produced with an excess of physical tension. Like other neurodevelopmental disorders, communication disorders begin early in life and may produce lifelong functional impairment (DSM-5).

The latest version of the DSM, the DSM-5, introduced Social Pragmatic Communication Disorder (SPCD) as a new subcategory of neurodevelopmental communication disorders. Pragmatic language difficulties can be part of a more general language disorder, ASD, or genetic/neurologic syndromes (eg, Williams syndrome, spina bifida/hydrocephalus). Research demonstrates that SPCD can present in the

absence of other conditions. Preliminary findings estimated the prevalence of SPCD to be around 0.5% (Simms et al., 2015, Visser et al., 2017).

1.3.6 Specific Learning Disorders (SLD)

According to the National Joint Committee on Learning Disabilities (NJCLD), specific learning disability (SLD) is a general term that refers to a heterogeneous group of disorders. They are neurobiological in origin and are characterized by difficulties with one's ability to process, organize, and retain verbal or nonverbal information. The main types of SLD are impairment in reading, written expression, and mathematics (Bonti et al., 2017).

The main factor attributed to learning disabilities is assumed to be neurobiological in origin, secondary to an identified brain pathology. Furthermore, both hereditary and environmental factors have been suggested. There is a possibility that these etiological factors together can intervene to precipitate the development of learning disabilities (Dominguez et al., 2020).

Learning disabilities are present in approximately 5% of school-aged children globally (Dominguez et al., 2020). In Greece prevalence rates ranged between 1.2% in 2004 and 1.6% in 2005 based on epidemiological studies and governmental reports. (Al-Yagon et al., 2012).

1.3.7 Motor Disorders (MD)

The neurodevelopmental motor disorders include developmental coordination disorder, stereotypic movement disorder, and tic disorders. Developmental coordination disorder is characterized by deficits in the acquisition and execution of coordinated motor skills

and is manifested by clumsiness and slowness or inaccuracy of performance of motor skills that cause interference with activities of daily living. Stereotypic movement disorder is diagnosed when an individual has repetitive, seemingly driven, and apparently purposeless motor behaviors, such as hand flapping, body rocking, head banging, selfbiting, or hitting. The movements interfere with social, academic, or other activities. If the behaviors cause self-injury, this should be specified as part of the diagnostic description. Tic disorders are characterized by the presence of motor or vocal tics, which are sudden, rapid, recurrent, nonrhythmic, stereotyped motor movements or vocalizations. The duration, presumed etiology, and clinical presentation define the specific tic disorder that is diagnosed: Tourette's disorder, persistent (chronic) motor or vocal tic disorder, provisional tic disorder, other specified tic disorder, and unspecified tic disorder (DSM-5).

2. Neurodevelopmental Disorders and oral health

Prevalence of certain NDDs, such as ASD and ADHD, has been increasing over the last four decades (CDC, 2009) CDC, 2010). Due to this increase in prevalence, dentists need to be more prepared to treat children with NDDs. The American Academy of Pediatric Dentistry classifies children with NDDs as children with special healthcare needs, which is defined as “any physical, developmental, mental, sensory, behavioral, cognitive, or emotional impairment or limiting condition that requires medical management, health care intervention, and/or use of specialized services or programs” (AAPD, 2016).

Poorer oral hygiene status has been shown to exist among preschool children with special health care needs (Zhou, Wong, & McGrath, 2019). These individuals may also be at increased risk for oral diseases throughout their lifetime. Oral diseases can have a direct and devastating impact on the health and quality of life of these individuals. Because of the unmet dental care needs emphasis on a dental home and comprehensive coordinated services should be established (AAPD, 2016). Patients with an established dental home are more likely to receive appropriate preventive and routine care that is individualized (AAPD, 2016). The most common oral diseases among children with NDDs are dental caries, gingivitis and periodontal disease.

2.1 Caries

Poor oral hygiene is frequently cited as a problem affecting the oral health status of individuals who have Cerebral Palsy. Several studies have demonstrated that the more severe the neurological damage is, the more frequent is the presence of the biting reflex and consequently, the higher is the risk of oral diseases in this population due to

the difficulty to perform an adequate oral hygiene (Guaré et al., 2003, *Dos Santos et al.*, 2005, Akhter et al., 2019). The incidence of caries among children and adolescents who have CP is high, also the factors associated with the incidence of caries were similar to those affecting the population at large (Ferreira de Camargo et.al., 2011). Dos Santos et al., discovered that the decayed, missing, and filled permanent surfaces (DMFS) of children with CP was 12.86 which was significantly higher than that of normal children were 2.87; likewise, the dental plaque index was higher in children with CP (Dos Santos et al., 2003). Dietary consistency and oromotor function had statistically significant influence on the DMF index, the youngest individuals, due to their oromotor dysfunctions, were fed a liquid diet and had a significantly higher total DMF score than those fed semisolid and solid diets (Santos et al., 2009) Guare et al., registered that children Brazilian children with CP had greater prevalence of dental caries in the primary dentition than healthy children (Guaré et al., 2003) On the contrary, Du et al., in their study, that was conducted in Special Child Care Centers in Hong Kong, revealed that children with and without CP had similar caries experiences (Du et al., 2010). Moreover, previous studies declared that CP would lead to abnormal movements of the tongue and facial muscles together with the low salivary flow, pH, as well as buffering capacity, which might intensify the risk for dental caries (De Camargo et al., 2008, Santos et al., 2010).

Conflicting results have emerged by the limited number of studies that carried out normative oral health assessment in children with Autism Spectrum Disorder. Some studies have shown that children with autism exhibit higher caries prevalence, poorer oral hygiene, and a higher extent of unmet needs of dental treatment compared to non-autistic healthy children (Jaber et al., 2011, Vishnu et al., 2012). Other studies have shown that children with ASD are more likely to be caries-free (Loo et al.,2008,

Orellana et al., 2012). However, in these studies, it was shown that children with ASD have other significant problems despite their decreased caries rate. More patients with ASD are uncooperative and required general anesthesia to complete dental treatment (Loo et al., 2008). A recent meta-analysis, conducted considering prevalence of dental caries in patients with ASD, showed that all the analyzed studies reported dental caries prevalence, and the pooled prevalence was 60.6% (95% CI: 44.0-75.1) (da Silva et al., 2017.) Furthermore, children with ASD exhibited a higher caries prevalence in primary teeth than in permanent ones with a ratio of 1:2.51 (Morales-Chávez, 2017). Children with ASD have eating habits that make them more prone to caries, many pouch food in their mouth for extended periods of time and have a preference for soft, sweet, or sticky foods (Klein et al., 1999).

Several studies have shown that children with ADHD have overall a poorer oral health status oral hygiene attitudes and higher plaque indices than those without ADHD (Aminabadi et al., 2016, Chau et al., 2017, Hidas et al., 2011). Higher caries prevalence in this group could be caused by their less effective tooth brushing due to their short attention span and difficulties to stay focused (Blomqvist et al., 2006). In addition, children with ADHD can have difficulties with performing various motor skills (Karatekin et al., 2003) Xerostomia is mentioned as one of the adverse orofacial side effects of most drugs, which are commonly used for pharmacological treatment of ADHD (Friedlander et al., 2003). Lower unstimulated salivary flow rates were found in participants with ADHD with or without medication (Hidas et al., 2011, Vafaei et al., 2018). Since saliva is important in the protection of teeth against dental caries, changes in salivary quantity and quality can have a negative impact on oral health. (Murray et al., 2012).

Regarding dental caries, Kohlboeck et al., reported a positive correlation of non-cavitated caries lesions with the presence of hyperactivity/ inattention in children (Kohlboeck et al., 2013). Children for whom their parents/guardians reported the presence of signs of inattention and hyperactivity had a higher risk for dental caries (Mota-Veloso et al., 2018). It was shown that children with ADHD had a significantly higher total enamel caries experience when compared to controls (Grooms et al., 2005). However, other studies did not find significant differences in DS/DMFS scores between children with or without ADHD (Chau et al., 2017, Blomqvist et al., 2006, Blomqvist et al., 2011, Ehlers et al. 2019).

Caries prevalence among children with Intellectual Disability was reported to be 86%, and children with severe intellectual impairment might have more carious lesions in the permanent dentition than their peers with moderate or mild intellectual impairment (Makkar et al., 2018). A systematic review of Zhou et al. evaluated the difference in dental caries experience between children with and without intellectual disabilities based on 32 studies. Diagnoses of caries in these studies were mainly performed in compliance with World Health Organization criteria. A total of 26 indices were used to indicate caries experience. The main findings of the systematic review showed that children and adolescent with or without ID had similar proximal carious lesions, but fewer decayed surfaces were treated among those with ID (Zhou et al., 2017). Another review confirmed that the rates of untreated caries were consistently higher among individuals with ID (Anders et al., 2010).

There is a lack of evidence around the impact that disability has on oral health and oral healthcare experience for children with Communication Disorders (Robertson et al., 2019). Inability to maintain proper oral hygiene is one of the primary factors influencing the prevalence of dental disease in special learning needs children. The

removal of plaque from teeth is a skill that can be mastered only when an individual has the dexterity to manipulate a toothbrush and an understanding of the objectives of this activity (Pinkham, 1975, Relwani et al., 2012).

(Relwani et al., 2012) In a recent systematic review and meta-analysis by Robertson et al., concluded that overall, there was no evidence that children with learning disabilities have different levels of dental caries in their permanent or primary dentition, to children without learning disabilities (Robertson et al., 2019). Evidence confirms that uptake of screening services for people with learning disabilities is lower and that they lack in oral health when compared with the general population (Ameer et al., 2012).

Generally, children with NDDs exhibit higher caries prevalence mainly because of poorer oral hygiene compared to the general population. Eating habits and reduced salivary flow caused by medication may also play a role. However, more studies are needed, since for some NDDs there is either not enough data in the literature or the results are conflicting.

2.2 Periodontal disease

Several studies have shown that gingival hyperplasia and associated bleeding occurs with higher frequency in children with CP (Minear, 1956, WHO 2010). This high frequency may be due to the same factors predisposing to dental caries and leading to biofilm buildup (Graham et al., 2004). Difficulties in conducting daily oral hygiene, intraoral sensitivity, and oro-facial motor dysfunction are the main contributing factors (Gunel et al., 2009). Another important factor is the use of antiepileptic drugs, particularly phenytoin (Jan, 2005). Gingival hyperplasia is predictive for periodontal

diseases. It tends to occur in children with spastic quadriplegic CP, particularly with advancing age. Choreoathetoid CP may also be associated with periodontal disease as a result of the continuous uncontrolled movements of the head making oral hygiene more difficult (Jan et al., 2016). In a cross-sectional study by Sedky (2018), who evaluated oral and dental health status in Egyptian children with CP, the predominant finding was poor oral hygiene, as well as severe gingival inflammation with 53.2% of the children having poor oral hygiene and 43.6% of them having severe gingival inflammation. Similarly, Guare Rde et al., registered higher values of gingival inflammation (GI) scores for Brazilian CP children with primary dentition in comparison to healthy children (Guare Rde et al., 2004).

The majority of ASD children have poor oral hygiene, and almost all of them have gingivitis (Fakroon et al., 2015). According to a recent meta-analysis, the pooled prevalence of periodontal disease in ASD children was 69.4% (95% CI: 47.6-85.0) (da Silva et al., 2017). Nevertheless, this is not always confirmed, as in the study by Fahlvik-Planefeldt et al., where there was no significant difference in the evaluation of the gingival status of children with ASD and the control group (Fahlvik-Planefeldt et al., 2001). Al-Maweri et al. and Fakroon et al. observed a higher gingival index for children with ASD, although they do not point out the significance. The latter study found that more than half of these children need scaling and 38.2% presented gingival inflammation (more than double that of the control group) (Al-Maweri et al., 2014, Fakroon et al., 2015). This worse periodontal status was seen to be statistically significant in two studies of the autism spectrum disorder (El Khabit et al., 2014, Luppanapornlarp et al., 2010)

The above findings could be related to irregular brushing habits, because of the difficulties the trainers and the parents encountered when they brushed the children's teeth. They could also be caused by lack of the necessary manual dexterity of ASD children, which may have resulted in inadequate tooth brushing (McKinney et al., 2014). Another possible explanation for the presence of generalised gingivitis might be the side effects of medications, which were used to control the manifestations of ASD, such as psychoactive drugs or anticonvulsants like phenytoin, correlated to an increasing of hypertrophic-hyperplastic gingivitis and an eruption delay. Other common drug classes used in these patients are antidepressants, stimulants, and antipsychotics that may have oral side effects (Alaluusua et al., 1994).

A meta-analysis that was performed for three studies (Hasan et al., 2004; Hidas et al., 2011, Kohlboeck et al., 2013). found significant effects of higher mean plaque index scores among children with ADHD (standardized mean difference = 0.758, 95% CI = 0.033, 1.483;) (Chau et al., 2017). Another study of Ehlers et al. found no statistically significant difference of plaque index between ADHD and non-ADHD children (Ehlers et al., 2019). More research is required to further clarify the periodontal status of children with ADHD. The generalized limited data on periodontal outcomes may be explained by the young ages of the study populations (Chau et al., 2017). Some studies have shown no statistically significant differences in gingival bleeding index GBI between ADHD and non-ADHD participants (Blomqvist et al., 2006, Aminabadi et al., 2016, Blomqvist et al., 2007) whereas in other studies statistically significant higher gingival bleeding in children using methylphenidate were found in children with ADHD (Chau et al., 2017, Blomqvist et al., 2012, Vafaei et al., 2018). Studies that included additional markers of periodontal disease also found no significant differences

in presence of calculus (Bimstein et al., 2008). One study observed significant levels of gingival enlargement in ADHD children who were medicated, which surprisingly could not be attributed to poor oral hygiene practices (Hasan et al., 2004).

In the systematic review Zhou et al. (2017, 2018) it was concluded that people with ID often had higher prevalence of periodontal diseases, when compared with the general population while the periodontal status of children and adolescents with ID was worse compared to their nonaffected counterparts (Zhou et al., 2017, Zhou et al., 2018). Furthermore, in a cross-sectional study, Roberts et al., (2016) reported that more than 69% of children with ID had gingival disease while Desai et al. reported that individuals with lower adaptive functioning were more likely to have poor periodontal status (Desai et al., 2001).

In conclusion, periodontal disease in children with NDDs appears to be more common than in general population. Poor oral hygiene and medication that cause gingival hyperplasia and generalized gingivitis are the main reasons for the worse periodontal status of these children. However, more research is needed in order to clarify the periodontal status of certain NDDs.

2.3 Developmental Defects of Enamel (DDE)

Children with CP are at an increased risk for having developmental enamel defects. Most of the enamel defects were located symmetrically in the primary incisors and first molars. The reported prevalence of enamel defects in CP children varies from 24-68% (Bhat et al., 1989, Bhat et al., 1992).

Lin et al., reported that around 42.4% of children with CP and enamel defects were born prematurely (< 37 weeks) whereas only 23.2% of them were born at normal

gestational age. in the same study, no statistically significant difference in the prevalence of enamel defects was found in relation to birth weight. (Lin et al., 2011). On the contrary, in two previous studies, enamel defects on children with CP were significantly more prevalent in low birth weight children (Seow, 1997, Seow et al., 1987).

There are limited data on the association between ASD and DDE. A study found that enamel defects of the primary teeth were found in 43% of the control groups but hardly any in the autistic group. Even when prenatal etiology was suggested (infectious conditions), no enamel defects were found in the autistic children. According to the researchers, either the insult was too subtle or the effect was minute and microscopic similar to the neo-natal line and other traumatic lines (Sarnat et al., 2016).

Similarly, there are not adequate data in the literature on the association of ADHD with enamel defects. Kohlboeck et al. found no significant differences in children with enamel defects with regard to ADHD in a study population of 1126 children among which 161 had ADHD. However the authors stated that severe levels of ADHD may contribute to a higher risk for enamel defects in school age children (Kohlboeck et al., 2012).

Scientific data show that children with genetic syndromes or other diagnoses that are known to be associated with ID have a relatively high incidence of enamel hypoplasia (Bhat et al., 1989) Enamel defects associated with various degrees of intellectual disability are typical of several genetically determined diseases, such as velocardiofacial syndrome (22q11.2 deletion syndrome), the Kenny Caffey syndrome, as well as Kohlschütter-Tönz syndrome (Moussaid et al., 2012, González-Arriagada et al., 2013). The risk of acquired enamel defects has also been discussed in the context of brain development. Cohen and Diner noticed that enamel defects occurred with higher

frequency in children with IQ deficits compared to neurologically healthy children (Cohen et al., 1970). Their study and further reports suggested that affected enamel may give information concerning the timing of insults, possibly influencing other structures of ectodermal origin, such as the brain (Martínez et al., 2002, Modrić et al., 2016, Bhat et al., 1989, Jindal et al. 2011). However, there are speculations in the literature that the chronologically distributed developmental defects of enamel (DDE) might be a significant aid in the neurological diagnosis, especially since many cases of intellectual disability are of unknown etiology (Bhat et al., 1989, Jindal et al. 2011, Opydo-Szymaczek et al., 2012).

There are few studies that provide data concerning the prevalence of enamel defects in the population of children and adolescents with ID. According to Gereth et al., who examined enamel defects in special-care students, the highest number of students (24.66%) with DDE was observed in the group of individuals with mild intellectual disability, whereas the lowest (11.11%) in those with profound disability. Interestingly, defects of early developing teeth appeared more frequently in subjects with moderate to profound forms of intellectual disability, which suggests that factors affecting the development of ectodermal structures during the prenatal and perinatal period and early childhood may lead to more serious neurological problems (Gereth et al., 2020).

In another study Modrić et al., found that children with intellectual disabilities had more developmental defects of enamel than children in the control group, which was considered statistically significant ($p = 0.021$).

The most common types of developmental defects of enamel were demarcated enamel opacities. Isolated demarcated opacities were noticed in 19 (26.39%) children with intellectual disabilities (Modrić et al., 2016).

Finally, Jindal et al. carried out the examination concerning developmental enamel lesions in 496 students, aged 8–15 years old, with various developmental disabilities, including ID). They discovered that 40.90% of special needs children had developmental defects of enamel, whereas in the control group of healthy children the changes were observed in 5.40% of individuals (Jindal et al., 2011).

Although there is data in the literature that show a correlation between some NDDs and DDE, more studies are needed. It also seems that DDE are more common in more profound forms of NDDs.

2.4 Malocclusion /Bruxism/Oral Habits

Prevalence rate of malocclusion in patients with CP has been reported between 59 and 92% with vast majority of malocclusion classified as Angle's Class II (Dougherty 2009, Winter et al., 2008, Franklin et al., 1996, Carmagnani et al., 2007) with increased overjet and overbite (Rosenbaum et al., 1969, Miamoto et al., 2010).

Oliveira et al., found that patients with CP have a three-fold greater chance of developing anterior open bite (Oliveira et al., 2011) while distribution of open bite was found to decrease with increased age (Rosenbaum et al., 1969). Spastic patients presented with an increased incidence of open bite (Carmagnani et al., 2007). High rate of Class II malocclusion and anterior open bite can be attributed to hypotonia of the orofacial muscles with resultant forward tongue posture, a poor swallow reflex and frequent mouth breathing (Dougherty, 2009).

Miamoto et al., (2011) concluded that children with CP had a significantly greater chance of developing signs and symptoms of temporomandibular disorders. The presence of CP, male gender, severity of the malocclusion, mouth breathing and mixed

dentition were identified as risk indicators for signs and symptoms of temporomandibular disorders.

A high prevalence of bruxism in individuals who have CP has been reported in several articles (Ortega et al., 2007, Lindqvist et al., 1974). In extreme cases, bruxism leads to tooth abrasion and flat biting surfaces (Ferreira et al., 2011). Ortega et al. found that along with bruxism there were habits like pacifier-sucking, finger sucking, habit of biting objects and tongue inter positioning (Ortega et al., 2007).

The absence of proprioception in the periodontium is discussed as a possible cause of bruxism (Lindqvist et al., 1974). Minear et al. have hypothesized that bruxism habits in these population are related to problems with dopamine function and not regulated by local factors, such as malocclusion. It was shown that abnormal dental wear is more closely related to a low level of mental development than to the degree of severity of CP (Minear et al., 1956).

According to studies concerning children with ASD, these populations exhibit oral habits such as oral breathing, daytime and nighttime bruxism or atypical swallowing patterns which may give rise to facial and buccodental alterations as well as malocclusions (Al-Sehaibany, 2017, da Silva et al., 2017, Fontaine-Sylvestre et al., 2017, Sarnat et al., 2015). Such habits could contribute to significant dental problems such as soft tissue damage, dental loss and wear, anterior open bite and posterior crossbite (Du et al., 2018, Fontaine-Sylvestre et al., 2017; Luppapornlarp et al., 2010; Orellana et al, 2012).

Bruxism is reported to be the most common habit in children with ASD (Schreck et al., 2000). This is consistent with the observations of Al-Sehaibany et al., who found that preschool children with ASD had a bruxism prevalence of 54.7%. (Al-Sehaibany et al., 2017).

Moreover Leiva-García et al., found that the children with ASD that yielded higher food rejection scores also had more bruxism than the controls. In the same study occlusion problems (specifically class II malocclusion and open bite) were seen to be directly associated to food rejection ($p = 0.042$) (Leiva-García et al., 2019). In line with the sensory processing difficulties, these patients may exhibit hyposensitivity, with diminished muscle tone, chewing problems and atypical chewing patterns that may explain the observed association between mealtime behavioral disorders and malocclusion (Ben-Sasson et al., 2008; Dunn et al., 2008; Nadon et al., 2011).

Several studies have investigated the relation between parafunctional oral habits and ADHD. Chau et al. found a statistically significant higher percentage of bruxism in children with ADHD (Chau et al., 2017). In addition, Roy et al., found that patients with ADHD had significantly more parafunctional oral habits including bruxism, nail biting and non-nutritive sucking habits than the control group (Roy et al., 2020). However, other studies found that the presence of bruxism was similar between ADHD and non-ADHD children (Hidas et al., 2011, Ehlers et al., 2019).

Atmetlla et al., state that oral habits (such as nail biting, bruxism and frequent biting of different objects) and their significant association with the presence of ADHD could be explained as an expression of a high level of anxiety displayed by these children in a controlled environment (Atmetlla et al., 2006). In addition, Malki et al. suggests that there could be an association between ADHD medications and parafunctional activity, especially focusing on the use of CNS stimulants (e.g. methylphenidate or amphetamines) (Malki et al., 2005).

Although parafunctional oral habits can be related to dental malocclusion, few studies have looked at the prevalence and severity of malocclusion in children with

ADHD. Atmetlla et al., found no difference in malocclusion in children with ADHD when compared to the control group (Atmetlla et al., 2006). On the contrary Roy et al., found that patients with ADHD had significantly higher severity of malocclusion and dental rotation than the control group (Roy et al., 2020).

The general poor muscle development, physiological abnormalities such as under development of orofacial musculature, habits such as mouth breathing, finger sucking and tongue thrusting may facilitate the development of malocclusion in individuals with ID (Akinwonmi et al., 2019). Akinwonmi et al., found that the oral health of individuals with ID had consistently shown that they are more likely to have malocclusion than the general population and when compared to the other groups with special healthcare needs and that these correlate with the severity of the impairment (Akinwonmi et al., 2019).

Cabrita *et al.* strengthen the connection between malocclusion and intellectual disability. In their study of 123 patients with intellectual disability and 79 with no impairment, they showed that Class III cases were present almost exclusively in the intellectual disability group (91.7%). Linear regression indicated that having an intellectual disability seem to have a tendency to severe or very severe malocclusion (Cabrita et al., 2017).

In conclusion, children with NDDs exhibit malocclusion problems caused either by dysfunctional orofacial muscles or by oral habits such as nonnutritional sucking habits, tongue interpositioning etc. In addition, bruxism seems to be the most common parafunctional habit among children with NDDs.

3. **ELEPAP**

ELEPAP is the first non-profit charitable association in Greece to provide rehabilitation services to children since 1937. Specifically, the program of early educational and therapeutic intervention in the special pre-school education unit of ELEPAP is addressed to children from 18 months to 6 years old who show mobility, sensory and developmental disorders. The intervention is based on the design and implementation of individualized programs tailored to the needs of each child. ELEPAP has rehabilitation center in our country with branches in 6 different cities in Greece (Athens, Thessaloniki, Ioannina, Chania, Volos and Agrinio). (<https://elepap.gr/en/>).

Many reports show that people with NDDs have more dental disease, more missing teeth, and more difficulty obtaining dental care than other members of the general population. Studies report that persons with developmental disabilities who reside in community settings have significant unmet medical and dental needs (Glassman et al., 2003).

A cross sectional study conducted in Greece by Tzouanaki et al, 2019 recorded the oral health status of preschool children with NDD with movement limitations, attending the centers of “ELEPAP—Rehabilitation for The Disabled” and compare it to the oral health status of healthy children. Results showed that the children in the NDD group had fewer dental problems and better oral hygiene than the control group; however, the prevalence of precavitated lesions was higher in the NDD group.

An important issue related to the oral health of children with NDDs is the degree to which these children are able to cooperate and perform daily oral hygiene procedures and also to cooperate during dental treatment. In addition, the family, therapists and the

environment in which the child lives further affect oral care as well as his or her ability to receive proper dental care (Mitsea et al. 2001).

The time and financial requirements associated with caring for a child with NDDs are the burden usually placed on parents and limit their social role (occupation, household, social life). This in turn has negative effects on the provision of both medical and dental care to these children (Chi DL et al. 2014).

Also, the additional mobility problems of these children, their lack of insurance, as well as the low socio-economic and educational level of the parents further aggravate the situation (Chi DL et al. 2014).

Therefore, every effort made to provide medical and dental care for children with NDDs should also aim to reduce the burden on the people who have taken care of them. This is more common in socio-economically vulnerable families and therefore early intervention programs provided free of charge, such as ELEPAP's, are particularly important.

4. Aim

The aim of this study was to evaluate the effectiveness of an individualized preventive oral health program for preschool children with NDD in ELEPAP Athens and identify factors that affect it.

More specifically:

The effectiveness of the preventive program was evaluated for:

- a) Caries (prevention of new caries lesions, inhibition of the development of manifested lesions)
- b) Oral hygiene (improvement of oral hygiene index)

Factors that may affect effectiveness of individualized preventive oral health program will include:

- a) The age, sex and medical condition of the child
- b) The socio-economic and educational level of the parents
- c) Marital status of parents, maternal age
- d) Distance from the place of residence to the rehabilitation center of ELEPAP
- e) Attendance of daily intervention program in the facilities of ELEPAP
- f) Compliance with follow up examinations
- g) The existence of enamel hypoplasia, gingival hyperplasia

5. Material and Methods

5.1 Study design

In this prospective longitudinal, clinical study, children with neurodevelopmental disorders (NDD) received an individualized preventive program and were followed for two years. The collection of data took place between September 2017 and November 2020 at the Dental Clinic of the rehabilitation center for children with NDDs (ELEPAP, Rehabilitation for the Disabled) in Athens, Greece. The study protocol was approved by the Ethics Committee of the Dental School of the National and Kapodistrian University of Athens (N.K.U.A.) Greece, and the Scientific Committee of ELEPAP (Protocol number 413 /5.4.2019).

5.2 Participants

Parents from all children with NDD attending the early intervention program of ELEPAP, received an information letter explaining the purpose of the study and were invited to participate.

Inclusion criteria

- Children 1-5 years old
- Attendance of the early intervention program for the two following years
- Having signed an informed consent

5.3 Data collection

All parents were requested to sign a consent form and accompany the children at the baseline dental examination to receive the information about the individualized

preventive program. Data on the diagnosis, child's medical history, medications, birth-weight, full-term/preterm pregnancy and, and demographic information (child's age, gender, parent's age and employment status, area of residency), were obtained from the medical records of the ELEPAP.

Parents provided information through a structured interview by the dentist on dental history (previous dental treatment and topical fluoride application, oral pain, gingival bleeding, frequency and supervision of tooth brushing, use of fluoridated toothpaste and dental floss, habitual mouth breathing, frequency of consumption of sweetened snacks and drinks and bottle feeding at night), consumption of processed food, use of nasogastric catheter. Children were categorized, according to the principal NDD, in two main disorders, cerebral palsy (CP) and syndromes (epileptic syndromes, Trisomy 21, nonmosaicism, arthrogryposis multiplex congenita) or other NDDs (epilepsy, brachial plexus disorders, nontraumatic intracerebral hemorrhage in hemisphere). Diagnosis was based on the ICD10 10 code in their medical record. All children had movement limitations.

Each participant was examined at the dental clinic of the ELEPAP Center. Two experienced and calibrated pediatric dentists, working with assistants, performed the examinations, decided the individual preventive program for each child and provided all the relevant information. Furthermore, they provided all the necessary treatment in following visits.

The clinical examination included registration of: a) oral hygiene status, b) dental caries and restorations and c) developmental defects as follows:

Dental plaque was recorded using the modified Green and Vermilion Plaque Index (VPI) in 6 teeth (#55, #51, #65, #75, #71, and #85). On each tooth surface the extent of

plaque was recorded as 0: absence of plaque, 1: plaque on the gingival third of the surface, 2: plaque on more the half of the surface and 3: plaque covering all the surface. The average of the sum of the plaque scores divided by the number of examined surfaces resulted in the index registration.

The presence of *dental caries and/or restorations* were determined with the use of periodontal probe and mirror, after the teeth were cleaned and dried with air-syringe using the ICDAS II. The index was then converted to dmft. The ‘d’ parameter was evaluated at the level of initial lesions (ICDAS 1,2) and advanced/cavitated lesions (ICDAS 3-6). Missing teeth were recorded as (m) only if it was known that they were lost due to caries, and dental restorations were recorded as (f). The dmft index was calculated using both incipient and cavitated lesions according to the definition of ECC by Tinanoff et al (2019). No radiographical examination was conducted.

Dental developmental defects were recorded as presence or absence of: (a) demarcated or diffuse opacities, (b) post eruptive breakdown or hypoplasia. Each child received a positive code if there was at least one defect present in the mouth.

The *individualized preventive program* was planned according to each child’s individual needs, as follows: Detailed instructions on oral health, including a demonstration on oral hygiene (tooth-brushing and flossing), to the parent, with the use of fluoridated toothpaste 1000ppm, performed by the caregiver twice a day. Also, instructions on restriction of consumption of carbohydrates between meals were given to the parents. In order to achieve better oral hygiene, special care was given to children with reduced chewing function.

The follow-up visits for each child were planned by the dentist and a reminder for each appointment was sent to the parent by the secretariat of ELEPAP. The parent was responsible to schedule and keep the appointment.

In the first visit, each child received professional tooth-cleaning and application of topical fluoride varnish. The intervals of the follow-up examinations and topical fluoride application were determined based on the presence of dental developmental defects (DDD) and caries risk assessment using CAMBRA (Ramos-Gomez et al., 2011) as follows: a) 2 times / year for children without DDD and low caries risk, b) 3 times / year for children without DDD and moderate caries risk and c) 4 times / year for children with DDD, regardless of caries risk, as well as for children at high caries risk. The total number of follow-ups for two years were calculated for each child and the number of performed follow-up visits were recorded. The preventive protocol was applied at baseline and to all follow-up visits, while full clinical examination was performed at baseline and then after the first and after the second year. The 2-years preventive program was free of charge. Teeth were restored if needed and sealants were applied to high-risk caries patients with deep occlusal grooves on posterior teeth.

The two paediatric dentists were calibrated for caries examination. Intra-examiner reliability was assessed by examining 10 children twice, one week apart and inter examiner reliability was assessed by examination of 10 children by both examiners after completing the online course on ICDAS II. The intra examiner reliability was found to be $k=0.89$ and the inter examiner $k=0.84$

5.4 Outcome variables

The main outcome variables were: a) the dmft and b) the binary outcome (increase/not increased) of the dmft change after two years (Δ dmft). Secondary outcomes were d1-2, d3-6, d1-6, prevalence of dental caries and VPI after one and two years.

Factors related to the effectiveness of the preventive program were: child's age, gender and diagnosis, parental age and employment status, distance between area of residence and the ELEPAL Center, number of follow ups, presence of dental defects, number of performed follow ups and number of lost follow ups.

5.5 Power of the study

The sample size was determined by the number of eligible children attending the early intervention program of ELEPAP. A post hoc power analysis, based on the dmft mean values for the 3 time points included in the repeated measurements one-way ANOVA used, was conducted using SPSS, v.22 and revealed a power value of 0.96 for the specific test.

5.6 Statistical analysis

Analysis of the data was performed using IBM SPSS Statistics v.22. The data collected were analyzed using descriptive statistics (% , mean and standard deviation (SD) or median and inter quartile width (IQW), one-way ANOVA for repeated measurements, χ^2 and Kruskal Wallis tests, bivariate correlations (Spearman correlation coefficient rho), as well as logistic regression analysis. The level of statistical significance was set at $p \leq 0.05$.

6. Results

From the 102 children examined at baseline, 99 were followed for two years, while 3 children moved in another city before the 1st year examination. The mean age of the children was 3.03 yo (SD:1.3), of the mothers 39 yo (SD:5,6) and of the fathers 41 yo (SD:6.04), while 55% of the children were boys. Regarding employment, 15% of the mothers and 6% of the fathers were unemployed while all families had public health insurance. The median distance between area of residence and ELEPAP was 7.9km (IQW:3.7 – 13.95)

Most children were born prematurely (67%) with a mean number of gestation weeks 32 (SD:5.3) and with a mean weight 1967gr (SD:968). All children had movement impairment. More precisely 59% of them had cerebral palsy while the rest had various syndromes or other NDDs. Only 9 children were on medication (mainly antiepileptic).

The baseline dental visit was the first for 88% of the children, oral pain was reported for 4% and gingival bleeding during brushing for 7%. and for 5% of the participants. One third of the children never brushed (figure 1), 67% of the parents supervised oral hygiene at home and in only 4% of them dental floss was used. Finally, only 5% of the children had professional topical fluoride application. Regarding feeding ability and habits, 32% were eating processed food and were not able to chew while 2 children were using nasogastric catheter and only 10% consumed more than 3 sweetened snacks or drinks daily. Habitual mouth breathing was reported for 37% of the children.

Table 1 summarizes the clinical data at baseline and of the 1st and of the 2nd year examinations. Four (4) children had abscess/fistula, this was due to trauma (3 cases) and to caries (1 case). Developmental dental defects were found in 24% of the children. The percentage of caries-free children at baseline was 78%. Caries risk distribution at baseline was 24% low, 53% moderate and 23% high. The incidence rate for developing caries

(incipient/cavitated lesions) was 17,6% while 47% were caries-free after two years. Follow up examinations that should have been performed according to the study protocol ranged between 4 and 12 visits (median 6) while performed follow ups ranged between 1 and 10 visits (median 2) indicating that most parents did not follow the suggested protocol. From the total sample, 4 children came 1 or 2 more times than assigned by the protocol.

After 2 years the increase of the $\Delta dmft$ was statistically significant correlated with younger age of the child ($\rho = 0.325$, $p=0.005$), older maternal age ($\rho=0.361$, $p=0.005$) and unemployment ($\rho = 0.271$, $p=0.038$), increased number of performed follow ups ($\rho=0.414$, $p<0.001$), the presence of dental defects ($\rho=0.289$, $p=0.013$) and consumption of more than 3 sugary snacks/day ($\rho = 0.353$, $p=0.003$). At the same point of time, change of VPI didn't have any significant correlations with the examined factors. Table 2 presents the results of the logistic regression analysis where the full model containing all predictors was statistically significant ($\chi^2= 27,5$, $p<0.0001$) indicating that the model could distinguish between children who developed caries and those who didn't and classified correctly 92.2% of the cases. In the multifactorial logistic regression analysis, the factors that retained statistical significance in the model were maternal age ($p=0.02$) and consumption of more than 3 sugary snacks/day (0.04).

When comparing the clinical parameters change, there was a significant increase of the percentage of children in the moderate caries risk group but mainly in the high-risk group compared to the low risk group as regards GVPI, dmft and incipient caries (Table 3). Moreover, children in moderate and high-risk group missed more appointments, while in the low-risk groups some children came for more follow ups than the ones they needed.

Table 1. Clinical data (caries, dental plaque) at baseline of the 1st and of the 2nd year and statistical differences between time points (N=99) differences between time points (N=99)

	Mean (SD) or %			Test	P value
	Baseline (N = 102)	1st year (N=87)	2nd year (N=73)		
GVPI	1.8 (0.9)	1.6 (0.9)	1.4 (0.9)	Wilks' Lambda = 0.792 ^a	0.003* ^b
dmft	1.1 (2.7)	1.36 (3.03)	2.04 (3.6)	Wilks' Lambda = 0.881 ^a	0.02* ^c
d ₁₋₂	0.47 (1.5)	0.10 (0.6)	0.18 (0.8)	Wilks' Lambda = 0.961 ^a	0.3
d ₃₋₆	0.52 (1.7)	0.4 (1.7)	0.32 (1.3)	Wilks' Lambda = 0.920 ^a	0.08
d ₁₋₆	0.99 (2.4)	0.53 (1.9)	0.49(1.7)	Wilks' Lambda = 0.890 ^a	0.03* ^d
<i>Caries prevalence (d1-6)</i>	19	22	36	-	-
<i>Caries prevalence (dmft)</i>	22	35	53	-	-

*statistically significant

^a repeated measurements ANOVA

Bonferroni post hoc test indicated statistically significant difference: ^b between baseline and 2nd yr and 1st and 2nd yrs

^{c,d} between baseline and 2nd year

Table 2. Logistic regression analysis of factors explaining the increase of dental caries (Δ dmft)

	B	p-value	Odds Ratio	95% C.I.for Odds Ratio	
				Lower	Upper
Gender (male)	0.661	0.597	.516	0.044	5.999
Child age	0.735	0.184	.480	0.162	1.417
Maternal age	0.324	0.018*	1.382	1.057	1.808
Maternal unemployment	1.357	0.337	.258	0.016	4.101
No of performed follow ups	0.317	0.315	.729	0.393	1.351
Presence of development dental defects	2.304	0.078	.100	0.008	1.298
Consumption of more than 3 sugary snacks/day	5.347	0.041*	.005	0.000	0.794
Constant	4.873	0.267	.008		

*statistically significant

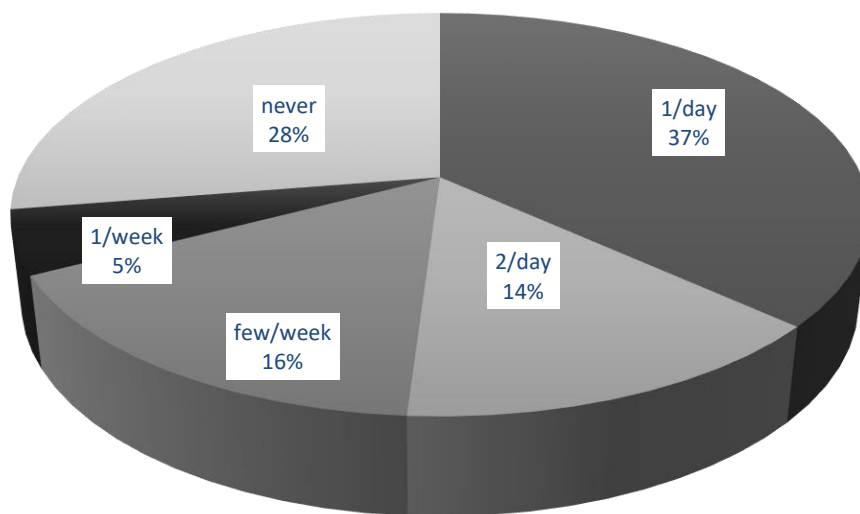
Table 3. Table 3. Prevalence of children in the three caries risk categories with increase of clinical parameters (caries prevalence, dental plaque) between the second year follow-up and baseline and the number of missed appointments (N=99)

	% or median (IQW)			χ^2	P value
	Low (N = 22)	Moderate (N=54)	High (N=23)		
Δ GVPI	8	40.7	43.5		0.008*
Δ dmft	7.7	14.6	47.4		0.007*
Δ d ₁₋₂	0	0	43.5		<0.001*
<i>Missed follow ups</i>	1 (-0.25, 3.25)	5 (2-7)	6(2-9)		<0.001**

* χ^2 , statistically significant

**Kruskal Wallis Test, statistically

Graph 1. Distribution of brushing frequency (N=99)



7. Discussion

This was a prospective longitudinal clinical study carried out to evaluate the effectiveness of an oral health preventive program in a rehabilitation center for children with NDDs and to identify factors that may affect it.

The preventive program was part of the holistic approach that is applied in ELEPAP and aims in improving the health and function of the participants and supports its families. Inclusion of the oral health in the holistic management is fundamental due to the specific characteristics of these children and the increased risk for oral health problems.

Results showed that the applied oral health preventive program was effective in improving significantly oral hygiene but not dental caries status of preschool children with NDD. Increased maternal age was correlated with worst caries status while children that consumed more than 3 sugary snacks per day had higher probability to develop caries. We also found that families with high caries risk children were more difficult to comply with oral health habit changes (brushing, appointment keeping).

In this study, preschool children were selected because this age is very important for setting the basis for healthy oral habits and attitudes throughout life and is more crucial in children with NDDs since, in their case, there are additional limitations regarding oral care. To our knowledge, there is no other study in the literature that assesses the effectiveness of an oral health preventive program for individuals with NDDs in this age group. In the few studies that evaluate preventive interventions in individuals with NDDs there is a wide range of diagnoses, interventions and age groups so that the study populations have different characteristics and cannot be directly compared (Hartwig et al, 2017, Bizarra et al, 2019, AbdAllah et al, 2018).

Collection of baseline data regarding dental history and dietary habits was carried out by a structured interview of the parents by two pediatric dentists. However, data on the diagnosis, child's medical history, medications, birth-weight, full-term/preterm pregnancy and demographic information were obtained from the medical records of the ELEPAP in order to be more accurate. The parent's interview was not repeated at the end of the preventive program, 2 years after the baseline examination, since the parents could have given biased answers if the interview was repeated. Therefore, objective findings such as caries and plaque indices were used as more objective measurements. Children were examined at the dental clinic of the ELEPAP Center by two experienced and calibrated pediatric dentists, working with assistants increasing the accuracy of data recording compared to studies performed in none-dental settings (eg classrooms) (Hartwig et al, 2017, Bizarra et al, 2019). In longitudinal studies, loss of participants during follow ups is a usual limitation. Hence a major strength of this study was that almost all of the children examined initially followed the program and were re-evaluated after one and two years.

A major component of the program was the individualized oral health instructions and demonstrations given to the parents in how to provide effective oral hygiene for their children. As a result there was a significant decrease of the VPI, indicating improvement of oral hygiene after the two years of implementing the program. This finding is in accordance with other studies that evaluated interventions for individuals with NDDs involving their caregivers. Hartwig et al. (2017) reported on the effect of supervised toothbrushing and educational activities to students and verbal oral health instructions to their caregivers and found a significant decrease in dental debris and gingival indices after 4 weeks compared with baseline. Similarly, AbdAllah et al. (2018) found a significant reduction in plaque mean values one year after an oral

health educational and preventive program in improving oral health knowledge and oral hygiene practices for a group of autistic Egyptian children. Although there is a variability in the duration of the studies, the type of preventive intervention, the type of NDD and the age of the participants, the reduction of dental plaque indices at the end of the interventions was consistent and is also seen in adult patients when caregivers apply the oral health routines (Bizarra et al. 2019). This strongly indicates that parents and caregivers should be motivated and trained accordingly in order to provide adequate care because individuals with NDDs have physical and mental limitations together with oral characteristics that make oral hygiene a challenging task. Furthermore frequent motivation is necessary in order to keep the long term results as it seems that oral hygiene routines show a decline overtime (Bizarra et al. 2019)

Assessing caries risk in preschool children is a challenge since most systems show poor performance in predicting caries development in this age group. CAMBRA has been shown to have a superior performance compared to other systems (Agouropoulos et al, 2020), but in the population of this study a major issue was the presence of DDD, which increases substantially the risk for developing caries and have detrimental effect on caries process. (Alaluusua et al 2012, Corrêa-Faria et al, 2020). Cerebral palsy, which was the most frequent health problem in the study population, is the NDD that is mostly related with DDDs with a reported prevalence ranging between 24-68% (Bhat et al., 1989, Bhat et al., 1992) and being more frequent in prematurely born infants (Lin et al., 2011). Considering that most of the children in the study group were prematurely born, more than half had CP and 24% had obvious DDDs, it was reasonable to include the presence of DDD as one of the major components, together with caries risk assessment, in determining the follow up visits and increasing the number of follow-up visits when DDDs were present.

Use of fluoride in the dental office and at home (fluoridated toothpaste) is the basis of any caries preventive program and fluoride application should be more frequent as caries risk increases. In this study the preventive program resulted in an overall decrease of both incipient and progressed caries lesions although not significant, suggesting a limited efficacy of the preventive program on caries. This finding should be interpreted with caution since there are two important factors involved. The first is the presence of DDD. As discussed above, teeth with DDD are more prone to develop caries and also to present post-eruptive breakdown that requires restoration or extraction. This explains partly the increase of the “m” and “f” components and the subsequent increase of the dmft index. The second factor is the compliance with the suggested preventive protocol as far as appointment-keeping is concerned. Moreover, high and moderate caries risk children missed significantly more follow-up visits than the low-risk ones and this has probably affected the effectiveness of the program. Research suggests that patients who are least likely to access dental care are the ones who are in most need of that care. In healthy children, higher caries scores are positively correlated with underutilization of free dental services (Maserejian et al., 2008) and a tendency toward missing more appointments (Casaverde et al., 2006). In this study, although a reminder for each appointment was sent to the parents who were responsible to schedule and keep the appointment, a lot of appointments were missed in the higher caries risk categories, despite the fact that the service was free. This finding that has been reported before (Nelson et al., 2012) and shows that, for some parents, dental care is generally regarded as a low priority aspect especially when, as in this study, severe health issues coexist. Also, the motivation to attend a dental appointment can be low, particularly if the value of preventive care is poorly understood. Providing parents with information on the importance of oral health can motivate them to have the appropriate

level of priority to dental visits (Primosch et al., 2000), but in our study this was not proven to be effective except for the low-risk children, that came for more follow up appointments than the needed ones.

We have found in a previous report (Tzouanaki et al, 2019) that children with NDD are of increased risk for caries development compared to healthy children of the same age, mainly due to the presence of high levels of MS and the poor quality of oral hygiene. Another significant caries risk factor was identified in the multifactorial logistic regression analysis of the present study, i.e. the consumption of more than 3 sugary snacks/day. Obviously, frequent exposure to carbohydrates leads to sustained acid production and to the increase of acidic species in the dental plaque, which is higher in the high-risk individuals (Tinanoff et al., 2019) leading to the demineralization of the tooth structure. Although dietary advice was part of the information given to the parents, this was not enough to improve daily habits.

The other significant factor affecting caries status was older maternal age. Mothers of children with physical and mental disabilities exhibit a significantly greater amount of stress and family burden compared to mothers of children without disabilities (Shyam et al., 2014). This may include stress related to the child's characteristics, specific behavioural problems, inadequate support and long-term care. Furthermore, mothers with increased age may also have poorer general health which also increases anxiety (Pinho et al., 2017). Therefore, older maternal age is probably combined with increased physical and emotional burden which in turn compromised the ability to maintain proper habits, including oral hygiene and appointment keeping.

In this study the medical condition was not a significant factor predicting the effectiveness of the preventive program. This is not surprising, since in this young age group, it is the parents who are responsible for maintaining good oral health. Children

with NDD is a very diverse group with different levels of physical and mental conditions. Engaging the parents in developing proper diet and hygiene routines early in their child's life is important and should be modified according to the child's specific needs. Keels et al (2019) state that "children with special health care needs comprise a heterogeneous group that must be treated in a precise, diagnosis-specific manner in caries risk assessment". However our results suggest that there are other factors that might be more important than the medical condition. According to the International Classification of Functioning, Disability and Health (ICF), the medical condition is secondary to assessing a person's disability as this can be strongly modified by environmental factors, and this also applies to oral health (Faulks et al, 2013). Therefore, future research should focus on individual caries risk assessment and also on the improvement of motivation and engagement of the family, as this can make a great difference in the oral health of children with NDD.

The sample of children with NDDs for this study was drawn from a well-organized rehabilitation center and may not be representative of the general population. In addition, the preventive program was free of charge and care was provided by paediatric dentists with experience in children with NDDs. These are limitations to the generalization of the results, especially in countries like Greece where dental treatment is self-paid and mainly offered by private dentists and only a small number of children are covered by dental health insurance (Mantonaki et al.,2013). Another limitation of the study is the absence of a control group. Since the aim of the study was to assess a full preventive protocol, it would be unethical to randomize the children in groups where intervention would not be offered at all, or would be offered in part.

In conclusion, the individualized preventive program for preschool children with NDDs was effective in significantly improving oral hygiene but not dental caries

status, while families with high caries risk children complied less with oral health habit changes (brushing, appointment keeping). Frequency of sugary snacks consumption and maternal age were factors that predicted the development of dental caries over the two years, suggesting the need for support and motivation of these families to cope with the physical and emotional burden and maintain proper oral health habits.

8. Summary

The term neurodevelopmental disorder (NDD) includes a group of disorders, in which the development of the central nervous system is disturbed and can have direct and indirect effects on oral health status. There are very few studies in the literature on the effectiveness of preventive programs in children with NDDs. The aim of this study was to evaluate the effectiveness of an individualized preventive oral health program for preschool children with NDD at a rehabilitation center (ELEPAP Athens), over a two years period.

Material and Methods

In this follow up clinical study, children with neurodevelopmental disorders received an individualized preventive program and were followed for two years. Demographic and health related information was obtained from the medical records in the Athens ELEPAP Center (ELEPAP). Parents provided information related to dental history. Children were categorized, according to the principal NDD, in two main disorders, cerebral palsy (CP) and syndromes or other NDDs. All children had movement limitations. Two experienced and calibrated pediatric dentists, working with assistants, performed the examinations, registered all the information and provided appropriate training on the individualized preventive program . The clinical examination included registration of a) oral hygiene status (modified Green and Vermilion Plaque Index (GVPI), b) dental caries using the ICDAS II converted to dmft and c) presence or absence of developmental dental defects (DDD) (demarcated or diffuse opacities or hypoplasia or post eruptive breakdown on teeth)

The individualized preventive program was planned according to each child's individual needs and included: a) tooth-brushing with toothpaste 1000ppm F twice a day, by the parent/caregiver and flossing (if needed), b) instructions on restriction of consumption of carbohydrates between meals, c) professional tooth-cleaning and

topical fluoride varnish application. The follow-up visits for each child were planned by the dentist and a reminder for each appointment was sent to the parent by the secretariat of ELEPAP. The parent was responsible to schedule and keep the appointment. The intervals of follow ups were determined by the presence of dental developmental defects and caries risk assessment using CAMBRA as follows: a) 2 times / year: no DDD and low caries risk, b) 3 times/year: no DDD and moderate caries risk, c) 4 times / year: DDD and any caries risk as well as children at high caries risk. The total number of follow ups for two years were calculated for each child and the number of performed follow ups were recorded.

The data collected were analyzed using descriptive statistics (% , mean (standard deviation), median (inter quartile width), one-way ANOVA for repeated measurements, Spearman correlation coefficient rho and logistic regression analysis. Statistical significance level was set at $p \leq 0.05$.

Results

From the 102 children examined at baseline, 99 were followed for two years, while 3 children moved in another city before the 1st year examination. The mean age of the children was 3.03 yo (SD:1.3), of the mothers 39 yo (SD:5,6) and of the fathers 41 yo (SD:6.04), while 55% of the children were boys. Regarding employment, 15% of the mothers and 6% of the fathers were unemployed while all families had public health insurance. The median distance between area of residence and ELEPAP was 7.9 km (IQW:3.7 – 13.95). Most children were born prematurely (67%) with a mean number of gestation weeks 32 (SD:5.3) and with a mean weight 1967gr (SD:968). And 59% had cerebral palsy. The baseline dental visit was the first for 88% of the children. One third of the children never brushed, 4% used dental floss and 67% of the parents supervised oral hygiene at home, 32% were eating processed food and were not able to

chew while 10% consumed more than 2 sweetened snacks or drinks daily. Developmental dental defects were found in 24% of the children. Caries free children at baseline were 78%. Caries risk distribution at baseline was 24% low, 53% moderate and 23% high. The incidence rate for developing caries (incipient of cavitated lesions) was 17,6% while 47% were caries free after two years. Follow up examinations that should have been performed according to the study protocol ranged between 4 and 12 (median 6) while performed follow ups ranged between 1 and 10 (median 2). Children in the moderate and high caries risk groups missed significantly more follow up compared to the low caries risk group ($p < 0.001$). After 2 years the increase of the $\Delta dmft$ was statistically significant correlated with younger age of the child ($\rho = 0.325$, $p = 0.005$), older maternal age ($\rho = 0.361$, $p = 0.005$) and unemployment ($\rho = 0.271$, $p = 0.038$), increased number of performed follow ups ($\rho = 0.414$, $p < 0.001$) the presence of dental defects ($\rho = 0.289$, $p = 0.013$) and consumption of more than 3 sugary snacks/day ($\rho = 0.353$, $p = 0.003$). In the multifactorial logistic regression analysis, the factors that retained statistical significance in the model were maternal age ($p = 0.02$) and consumption of more than 3 sugary snacks/day (0.04). Change of GVPI didn't have any significant correlations with the examined factors.

Conclusions

The individualized preventive program improved oral hygiene but was not as effective for dental caries, probably because the moderate and high-risk children missed their follow up dental visits. Individual characteristics of children with NDDs and the presence of developmental dental defects dictate the need for more frequent dental visits and intensive preventive programs. Family characteristics are of paramount importance for daily oral health care and maintenance of dental appointments as it seems that the increased physical and emotional burden compromise the ability to

maintain proper oral health habits. Families with caries high risk children need more support and motivation in order to improve the oral health status of their children.

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ΚΛΙΝΙΚΗ ΕΞΕΤΑΣΗ											
ΕΞΩΣΤΟΜΑΤΙΚΗ ΕΞΕΤΑΣΗ											
ΠΡΟΣΩΠΟ: Τύπος, κατατομή, αναλογίες, συμμετρία				ΜΥΤΗ: Σχήμα, μέγεθος, άνοιγμα και συμμετρία ρωθώνων, εκκρίσεις							
ΚΡΑΝΙΟ: Μέγεθος, συμμετρία, στάση				ΤΡΑΧΗΛΟΣ: Λεμφαδένες, ύπαρξη μαζών							
ΜΑΛΛΙΑ: Ποιότητα, ποσότητα, χρώμα				ΧΕΙΛΗ: Χρώμα, μορφολογία, κατάσταση δέρματος, λειτουργία							
ΑΥΤΙΑ: Διάπλαση, θέση				Στοματική αναπνοή							
ΜΑΤΙΑ: Σχήμα, μέγεθος, θέση, βλεν. βλεφάρων, δράση				Βρεφική κατάποση							
ΕΝΔΟΣΤΟΜΑΤΙΚΗ ΕΞΕΤΑΣΗ											
ΒΛΕΝΝΟΓΟΝΟΣ:				ΥΠΕΡΩΔΑ:							
ΟΥΛΑ:				ΓΛΩΣΣΑ:							
ΦΑΡΥΓΓΑΣ:				ΧΑΛΙΝΟΙ ΑΝΩ:							
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ΠΑΡΑΤΗΡΗΣΕΙΣ:											
ΟΔΟΝΤΙΚΗ ΣΥΓΚΛΕΙΣΗ											
Προσθιοπίσθια σχέση γομφίων:					Πρόταξη Τομέων (χλ.):						
Νεογιοί:					Κατά το οριζόντιο επίπεδο:						
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Προσθιοπίσθια Σχέση Κυνόδοντων:					Σταυροειδής Σύγκλειση:						
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	ΗΜΕΡ.	16/55	11/51	26/65	36/75	46/85	31/71	ΕΠΙΦΑΝΕΙΑ	ΑΘΡΟΙΣΜΑ	Μ.Ο.	
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Κλινική εξέταση

Α.Δ.	ΤΕΡΗΔΟΝΑ					ΟΔΟΝΤΙΚΟ ΤΡΑΥΜΑ	ΣΥΡΙΓΓΙΟ ΑΠΟΣΤΗΜΑ	ΔΥΣΠΛΑΣΙΕΣ		Επεξηγήσεις κωδικών καταγραφής
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