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Review Article

Medical and Dental Implications of Autism Spectrum Disorder: A Review

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Abstract

Globally 1 in every 68 child is diagnosed with Autism. Autism spectrum disorder (ASD) or Autism is a group of neurodevelopmental disorders, affecting the normal development and functioning of the brain in three core domains; reciprocal social interactions, verbal and non-verbal communication and the presence of restricted or repetitive behaviors. Typically it appears in the first three years of life and affects males four times more than females but females are more likely to show more signs of mental retardation. Other medical problems can co-exist along with Autism such as psychiatric illnesses, epilepsy; sleep disturbances, feeding problems, gastrointestinal problems and voiding problems. Autism cannot be cured, but the earlier the intervention the better the results. Medications, therapies and behavioral interventions can only alleviate Autism related symptoms and cause substantial improvement. Autism characteristics can have an impact on three different perspectives of dental care, which are oral care at home, oral care at the dentist and access to oral care. This paper aims to review and discuss the literature on the general and oral characteristics of children with Autism Spectrum Disorder in order to help the dental practitioners as well as the medical professionals in providing them with better oral and health services.

ABBREVIATIONS

%: Percentage; ASD: Autism Spectrum Disorder; USA: United States of America; WHO: World Health Organization; GABA: Gamma-Amino Butyric Acid; IQ: Intelligence Quotient;

DSM-V: 5th Edition of the Diagnostic and Statistical Manual of Mental Disorders; GI: Gastrointestinal; GERD: Gastroesophageal Reflux Disease; MMR: Measles, Mumps, and Rubella; MTHFR: Methylene tetrahydrofolate Reductase; DNA: Deoxyribonucleic Acid

INTRODUCTION

Developmental disorders are disorders of brain functions where there is an alteration in the growth and development of the central nervous system thus affecting the individuals emotion, learning ability, self control and memory which becomes apparent as the individual grows [1]. Disorders that are classified as developmental disorders are Intellectual disability, Fetal alcohol spectrum disorder, motor disorders, Down Syndrome and Schizophrenia. But the most commonly known developmental disorders are Autism and Attention deficit hyperactivity disorder.

Recently there has been an increase in the number of diagnosed Autism cases and due to the varying degrees of difficulties associated with this disorder, the aim of this paper is to review and discuss the literature on the general and oral characteristics of children with Autism Spectrum Disorder in order to help the dental practitioners and medical professionals in facilitating the provision of care to this group of individuals.

HISTORY

Leo Kanner was an Austrian scientist who founded the first child psychiatry clinic in Johns Hopkins University in the USA. In 1943 he published a paper entitled "Autistic Disturbances of Affective Contact" [2] which made him the first scientist to clearly define Autism as a distinct syndrome and put an end to naming the affected children as retarded or feeble-minded as was commonly used by people during that period.

DEFINITION

Autism was previously known as one of the pervasive developmental disorders. Pervasive developmental disorders are disturbances of the brain development with undermining genetic causes, these include: Autistic, Aspergers, childhood disintegrative, Rett's, and pervasive developmental disorders not otherwise specified disorders. But with the publication of the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders in May 2013, all Autism disorder subtypes were merged under one definition of Autism Spectrum Disorder (ASD) or Autism [3].

EPIDEMIOLOGY

Autism is four times more common in boys than in girls. According to the systematic review of epidemiological surveys of autistic disorder and pervasive developmental disorders worldwide conducted in 2011 by Mayada Elsabbagh et al under the commission and support of WHO, the Global prevalence estimate of Autism disorder since the year 2000 is a median of 17/10,000, in 2002 the prevalence estimate was 7 in 10,000 and in 2014 it has been estimated to be 1 in 68 [4]. The prevalence estimate in Europe is a median of 19/10,000, America 22/10,000, and Western Pacific 12/10,000 [5]. There were no estimates found for South East Asia, Eastern Mediterranean and Africa. Prevalence estimates for pervasive developmental disorders which can give an idea about Autistic disorders are available as follows: 100/10,000 in Sri Lanka [6], 6.3/10,000 in Iran [7], 1.4/10,000 in Oman [8], 20/10,000 in the United Arab Emirates [9].

This rise can be due to the improvement in the medical understanding of the disorder, broadening of the diagnostic criteria, improved diagnostic tools, increase in awareness leading to early screening and the increased exposure to environmental factors which might contribute to the development of autism such as food preservatives and environmental toxins. Furthermore, increase in the advanced maternal age and stress triggers during pregnancy such as trauma, illness and substance abuse have increased the fetal risk of developing autism. Advances in medical technology has led to decline in neonatal deaths and higher survival rates of those diagnosed with Autism [10].

Twin and family studies have strongly revealed that some people are more genetically predisposed to having Autism. Identical twin studies showed that "if one twin is affected, there is a 90% chance of the other twin having Autism also" [11]. Compared with a family with healthy children, a family with an autistic child is more at risk, with a 5% chance or 1 in 20, of having a second autistic child. This is greater than the risk for the general population. Researchers are currently trying to identify the specific genes that cause Autism and also the genes responsible for increased susceptibility in families with an autistic child. In some cases, parents and other relatives of a child with ASD show mild impairments in social and communicative skills and repetitive behaviors have been found in some families and relatives of an autistic child. Furthermore, there is evidence of the frequent occurrence of emotional disorders such as bipolar disorder in the families of autistic children [11].

AETIOLOGY

Results of neurochemical, neuro-pathological, neuroimaging and genetic studies all show that Autism spectrum disorders (Autism) are disorders of neuronal-cortical organization, connectivity and brain structure. These disorders are most probably influenced by genetic and environmental factors where the environmental factors affect the biological process in the body or modulate gene expression within the nervous system [4].

"Documented causes of Autism include genetic mutations and/or deletions, viral infections, and encephalitis following vaccination. Therefore, Autism is the result of genetic defects and/or inflammation of the brain" [12]. A defective placenta, undeveloped blood-brain barrier, and the immune response of the mother to infection while pregnant could cause the inflammation. Other risk factors can be advanced parental age, fetal exposure to valproate, a premature birth, and encephalitis in the child after birth, or a toxic environment [12].

Several studies have consistently revealed that the abnormal brain region in humans suffering from Autism compared to healthy humans is the cerebellum. The abnormalities were seen in the cerebellar size, morphology and function. The irregular cerebellar growth patterns begin from early infancy and continue into adolescence. 21 of 29 postmortem studies have found a reduction in the number of the primary cerebellar efferent neuron, the Purkinje neurons, which are responsible for most of the electrochemical signaling in the cerebellum. They release the neurotransmitter GABA that inhibits or reduces the firing rate of the neurons, which negatively affect body motor function. They are also necessary for coordinating late gestation

and postnatal cerebellar development, therefore any genetic or biochemical insults affecting early Purkinje neuron development could disrupt cerebellar growth and function, contributing to the development of autism [13].

ONSET AND PROGNOSIS

The onset of Autism can occur in three different ways, the congenital pattern where behavioral abnormalities are present within the first year of life; normal early development pattern which is followed by a developmental plateau and failure to reach developmental milestones; and the autistic regression pattern which is characterized by abrupt or gradual loss of previously acquired abilities.

The autistic child's IQ and language development level may predict outcome. Prognosis will be poor if the IQ level is less than 50, but even if the IQ is high the autistic child may still need substantial support from family and other support systems [14].

CLINICAL FEATURES AND DIAGNOSIS

Autistic children exhibit three clinically significant features, which are impairment in their social interactions, impairment in communication and restricted or repetitive actions or behaviors. The most noticeable feature is the impaired social interaction where they may resist cuddling in infancy, avoid making friends and engaging in social activities. In the preschool children the most noticeable features are delayed or total absence of development of spoken language and lack of pretend play which should normally be present in children by 12 to 15 months of age [15].

Wing [16] categorized children with Autism into three groups which are aloof and passive; reachable but socially alienated unless actively engaged; and active but odd and can initiate interactions but in an awkward and inappropriate ways.

The Diagnostic and Statistical Manual of Mental Disorders (DSM-V) [3] lists specific criteria for diagnosing Autism which are:

- A. Qualitative impairment in reciprocal social interaction
 1. Marked lack of awareness of the existence or feelings of others.
 2. No or abnormal seeking of comfort at times of distress.
 3. No or impaired imitation.
 4. No or abnormal social play.
 5. Gross impairment in ability to make peer friendships.
- B. Qualitative impairment in communication and imagination
 1. No mode of communication.
 2. Markedly abnormal nonverbal communication.
 3. Absence of imaginative activity.
 4. Marked abnormalities in the production of speech.
 5. Marked abnormalities in the form of content of speech.
 6. Marked impairment in the ability to initiate or sustain a

conversation, despite adequate speech.

- C. Markedly restricted repertoire or activities and interests
 1. Stereotyped body movements.
 2. Persistent preoccupation with parts of objects or attachment to unusual objects.
 3. Marked distress over changes in trivial aspects of the environment.
 4. Unreasonable insistence on following routines in precise detail.
 5. Markedly restricted range of interests.

DIFFERENTIAL DIAGNOSIS

There are several medical conditions similar to Autism and it is important to know the difference between them such as Attention-deficit/hyperactivity disorder; Stereotypic movement disorder where motor stereotypies can be one of the characteristics of autism, but when it starts to cause self-injury and become a focus of treatment then it can be diagnosed as a separate disorder not related to Autism; Rett syndrome where during the regressive phase of Rett syndrome (typically between 1-4 years of age) disruption of social interaction can be noticed; and Schizophrenia which can also develop in childhood after a period of normal or near normal development is associated with hallucinations and delusions which are not features of Autism. Furthermore, other differential diagnosis can be selective mutism which differs from Autism because the only clinical feature present is that the child doesn't speak; some forms of language disorder where there may be isolated problems of communication and some secondary social difficulties; and intellectual disability which might be difficult to differentiate it from autism in very young children.

MEDICAL PROBLEMS

Psychiatric illness

Psychiatric illnesses are commonly associated with Autism. It has been found in 72% of children diagnosed with autism, the most common being obsessive-compulsive disorder, attention-deficit hyperactivity disorder, separation anxiety, and specific phobias. Furthermore, 26-30% of autistic children suffer from mental retardation [14].

Epilepsy

The prevalence of epilepsy in Autism ranges from 8% to 42%. In Autism accompanied by severe intellectual disability and motor deficits the prevalence of seizures is 42% whereas in autistic children without these problems the prevalence of seizures is 6% to 8%. All types of epilepsy can occur in autism the most common is the partial complex seizures [17].

Sleep disturbances

The prevalence of sleep disturbances in Autism ranges from 44% to 83%. Their causes are due to abnormality of melatonin, which is elevated during daytime, and significantly lower nocturnal melatonin. The sleep disturbance usually starts at the age of 2 years with the most common types being sleep onset

insomnia, night awakenings and irregularities of the sleep wake cycle, including early morning awakenings [18].

Feeding problems

The prevalence of feeding problems and food intolerance in Autism ranges from 20% to 60%. Children with Autism breastfeed at the same rate as the healthy children, but the difference are in the slow feeding, difficulty in accepting solids and food selectivity. The slow feeding in infancy could be considered as early symptoms of an autistic child's difficulty in accepting change. The restriction in the type of foods eaten by the autistic child is apparent by 15 months of age and become progressively more apparent. It must be noted that these feeding problems do not impair the child's energy intake or growth and it doesn't lead to specific vitamin or mineral deficiencies. The causes of feeding problems in autism can be due to oral-motor dysfunction; medical conditions such as gastro oseo-pharangeal reflux, constipation, food allergies/intolerance, and colic disease; and the influence of medication on appetite such as psychotropic medications and anti-epileptic drugs [19].

Gastrointestinal problems

The prevalence of GI problems in autistic children is 9% to 70%, which is higher than in the healthy controls, and due to lack of prospective well-controlled studies the cause of this is not known yet but some clinical research suggests that some genes involved in autism can affect other systems in the body also. The most common GI symptoms in autistic children are chronic constipation, abdominal pain with or without diarrhea, GERD, abdominal bloating and disaccharidase deficiencies [20].

Voiding problems

The prevalence of voiding problems in Autism is 11% to 25%. It can be very difficult to toilet train an autistic child. Their bladder storage and emptying function is normal but their response to the bladder filling sensation is unpredictable. Some children have sensory issues and find the sensation of bladder contraction unbearable thus they might require anticholinergic medications to increase the interval between voiding. Others can completely ignore the signals from their full bladder and wet themselves because their attention is focused somewhere else. Voiding dysfunction and incontinence is higher in autistic children with intellectual disabilities [4].

TREATMENT OF AUTISM

Autism cannot be cured, but the earlier the intervention the better the results. Therapies and behavioral interventions can only alleviate symptoms and cause substantial improvement. The ideal treatment plan should be tailored around the specific needs of the individual child [11]. Therapists use individualized structured skill-oriented training sessions to help children develop social and language skills, such as Applied Behavioral Analysis. The therapists also provide family counseling to help the families adjust to living with an autistic child [11]. Medications are prescribed not to treat Autism but rather for treatment of Autism-related symptoms, such as anxiety, depression, or obsessive-compulsive disorder. Antipsychotic medications are used to treat severe behavioral problems. Anticonvulsant medications are

used to treat seizures. Attention deficit disorder medications can be used to decrease impulsivity and hyperactivity [11]. There still are no studies supporting the use of some medications or interventions said to treat or relieve the symptoms of Autism such as dietary interventions.

AUTISM MISCONCEPTIONS

Autism is a single condition

Autism was previously considered as one of 5 pervasive developmental disorders, but in 2013 the 5th edition of the Diagnostic and Statistical Manual of Mental disorders [3] redefined it and now Autism is a spectrum disorder that includes Autism, Asperger syndrome, pervasive developmental disorder not otherwise specified, childhood disintegrative disorder and Rett syndrome [3].

Only symptomatic children should be screened for autism

There are no specific universal guidelines yet but the American Academy of pediatric dentistry recommends universal screening [21]. This recommendation is due to the presence of early childhood interventions, which could be beneficial for the children who are identified early.

Since autism cannot be cured, early intervention offers no benefit

Randomized controlled trials results have indicated that early developmental and behavioral therapy can decrease symptoms associated with Autism and improve communication and social interactions. These therapies can improve the autistic child quality of life, adaptability to being enrolled in schools and eventual employability and independence [22].

Individuals with autism are intellectually disabled and cannot function independently

Less than one in five ASD children (19%) has an intellectual disability, but they do have difficulty living independently and they are more socially isolated compared to other disability groups. Only 53% of young adults with Autism have been employed and this is considered to be the lowest rate among disability groups [22].

Thimersol vaccines cause autism

The controversy and concern about a correlation between mercury and Autism began in 1999, when Wakefield published his study [12], and in 2002 strengthened by a further study by Uhlmann, to link Thimerosal containing vaccines to the increasing incidence of Autism [23]. The 1999 study by Wakefield AJ "identified associated gastrointestinal disease and developmental regression in a group of previously normal children, which was associated with possible environmental triggers such as MMR vaccine, measles infection and otitis media" [12]. Furthermore, the 2002 study by Uhlmann RV "confirmed the association between the presence of measles virus and gut pathology in children with developmental disorders" [23]. Since then the correlation has been disproven by a number of studies and further review of the initial studies proved their result to

be false. Despite the lack of evidence connecting Thimerosal to Autism, since July 1999 it has been removed from most childhood vaccines as a precautionary measure [24].

AUTISM FROM THE DENTAL PERSPECTIVE

Children with autism have a difficulty in maintaining good oral hygiene thus they are at an increased risk of developing caries and periodontal disease. This difficulty can be due to co-existing medical disorders like GERD and regurgitation; increased or decreased saliva secretion due to medications; poor dietary habits; damaging oral habits such as bruxism or pica; lack of proper oral care at home and the dental clinic due to behavioral and sensory difficulties [15].

Caries prevalence

Data on the incidence of dental caries among autistic children is inconclusive. Some studies show that they have a lower caries rate than their healthy counterparts, such as the study by Shapira and co-workers [25] where they concluded that institutionalized and non institutionalized autistic children had a lower caries rate than unaffected children. While other studies show that they have an increased caries rate, such as the study by Lowe and Lindermann [26], where they found the autistic patients had higher caries index but on recall there was no increase in caries rate compared to their control group.

Periodontal status

Autistic children and adolescents have more food accumulation around the teeth, larger amount of plaque accumulation and poorer periodontal health compared to their healthy counterparts [15]. A study by Klein and Nowak [27], reported that autistic patients had 39.5% healthy gingiva, 51.2% localized gingivitis and 9.2% had generalized gingivitis.

Controversial issues in treating the dental patient with autism

Robert E. Rada conducted a literature review in medical and alternative medical literature [28] to investigate the concerns that parents of autistic children may have when dental care is provided to their children. He identified six areas of concern that the parents have and some are considered as areas of controversy between the alternative medicine and dental perspective.

Mercury: Alternative medical literature suggests that children with Autism are genetically predisposed to an inability to clear the body of heavy metal contaminants such as aluminum and mercury due to their low level of glutathione which plays a part in the bodies detoxification system. Robert E. Rada found a 2007 study, which concluded the presence of excess mercury in the dental pulps of primary teeth of children with autism, which suggested their inability to clear mercury from their bodies.

Fluoride: It is suspected of inhibiting critical antioxidant enzymes and has been linked to excite toxic reactions within the brain, thus parents are trying to avoid its use [28]. Although from the dental perspective fluoride plays an important preventive role and can decrease the risk of caries in the medically compromised patients who are more prone to plaque accumulation and poor oral hygiene.

Gastrointestinal problems: Autistic patients suffer from gastrointestinal problems such as abdominal bloating, abdominal discomfort, diarrhea and gastro esophageal reflux. Thus many parents have started to remove from their child's diet any suspected GI irritants by putting them on gluten free or casein free diet. These parents have reported that when the GI problems were treated they noticed that their child's behavior also improved. The theory behind this from the alternative medicine perspective which states that when the body is unable to metabolize gluten and casein, the intestine will release peptides into the blood stream which will cross the blood brain barrier and bind to opioid receptors within the brain leading to abnormal behavior associated with Autism. But from the medical perspective there is not enough scientific evidence to support this theory [28]. This diet can affect the preventive dental treatment because parents will ask for gluten free prophylaxis paste and will not want to use products such as casein phosphopeptide amorphous calcium phosphate, which is recommended to enhance remineralization because its active ingredient is milk derived.

Antibiotics: The over usage of antibiotics has been related to an increase in the autistic symptoms due to change in the intestinal flora thus alternative medicine practitioners prescribe antifungal agents and probiotics [28].

Acetaminophen: One study results suggested that acetaminophen use after receiving the measles mumps rubella vaccine could be associated with autistic disorder, whereas this association was not found in children given ibuprofen. This can be due to the fact that some autistic children cannot metabolize acetaminophen due to deficient sulfation process, which will result in the accumulation of a toxic metabolite that can interfere with the immune system or have direct neurotoxic effects [28].

Nitrous oxide: Nitrous oxide inhibits the enzyme methylenetetrahydrofolate reductase (MTHFR), which is involved in the metabolism of folate; this can limit the synthesis of DNA severely causing megablastic changes in blood cells and bone marrow. There are no articles in the literature that specifically state against the use of nitrous oxide in autistic children. However, some autistic children's parents may be wary of sedating their children with nitrous oxide because some of these children may have biochemical abnormalities in folic acid metabolism, vitamin B12 deficiencies and the dysfunction of MTHFR [28].

Dental care: Autisms characteristics of impaired social interaction, abnormalities in communication, restricted interests, and repetitive and stereotyped behaviors have the ability to make oral care difficult in a variety of ways thus increasing the risk of dental caries, periodontal disease, delayed tooth eruption, bruxism and trauma to teeth [15].

Difficulties with social interactions could be challenging when parents or caregivers teach oral hygiene techniques to the autistic child. The child might get uncomfortable being in close proximity to someone else. If the brushing and flossing is not part of their daily routine, they might reject it due to their aversion to change. There might be lack of proper communication between the autistic child due to lack of eye contact between the autistic child and providers [29,30].

Impaired communication can make the autistic child unable to express his/herself if he/she is uncomfortable during treatment and also the dentist can't implement the basic behavioral guidance techniques during treatment [31]. Stereotypical and repetitive actions can also complicate dentist's ability to safely and effectively provide oral care due to the child's constant movement and inability to sit still during dental treatment [32]. Visiting a dental office for the first time can also be a challenge because children with Autism don't like change of their routine and can be oversensitive to the different sounds, tastes and smells they may experience due to their oversensitivity to sensory stimuli [30].

Other factors that can also influence their oral health is lack of necessary manual dexterity thus their inability to brush properly. "In general, children with Autism prefer soft and sweetened foods, and they tend to pouch food inside the mouth instead of swallowing it due to poor tongue coordination, thereby increasing their susceptibility to caries" [15]. Also some of the autistic children are prescribed psychoactive drugs or anticonvulsants, which can cause xerostomia and delayed tooth eruption [15].

Primary caregivers are the main supervisors of the autistic child's oral hygiene thus it is important for the dentist to provide them with the necessary information needed about oral hygiene and its implications and to understand the barriers to care from the perspective of the primary caregivers.

There have been several published articles globally addressing the issue of the presence of barriers to dental care for children with Autism. In the United states a 2012 case control research by Leah I. Stein concluded that "children with Autism experience great difficulties and barriers to care in both home and dental office settings than their typically developing peers" [33]. In addition to that in 2011 Leah I Stein also conducted a research which concluded that "compared with children with other disabilities, those with Autism had greater behavioral difficulties and sensory sensitivities that parents believed interfered with their children's oral care, the sensory sensitivities were associated with oral care difficulties in the home and dental office and with behavioral difficulties in the dental office" [34].

In the United Kingdom S. Barry published in 2014 a cross sectional case-control research which reported that difficulties exist for children with Autism in accessing dental care in the Hull and East Riding area [35].

In India, Richa published a research in 2014, which concluded that "the presence of functional limitations may have a negative impact on oral health status that might influence the child's oral health related quality of life" [36].

In the Middle East, a research published in 2005 in Saudi Arabia by Murshid et al concluded that in Riyadh 65% of autistic children have been to the dentist but half of these children had only minimal treatment done due to their difficult behavior in the dental office. The parents of the 35% of autistic children who have never visited a dentist attributed this to their children's difficult behavior and lack of compliance even during homecare [37].

CONCLUSION

Since the prevalence of Autism has increased in the recent years it is important for the medical and dental professionals to have a knowledge of the medical and oral health characteristics of the Autistic child, understand the experiences and challenges encountered by these children in order to be able to overcome these challenges and facilitate the provision of the best medical and dental care to them.

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