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Review Article

DIETARY RISK FACTORS ASSOCIATED WITH AUTISM – A REVIEW

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A R T I C L E I N F O

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A B S T R A C T

Autism is the fastest growing developmental disorder that affects children particularly prior to the age of three in the areas of verbal & non-verbal communication, social interaction & cognitive function. Autism prevalence statistics are growing rapidly in India affecting 1 in 68 children & among boys, it is 1 in 42(30% rise). The etiology of autism is unknown as there is no single cause for the development of autism, but it is expected that both environment and genetics play a crucial role. Currently there is no known cure to treat autism, however children with the disorder do progress & the diverse symptoms related to it can be improved with primary intervention & treatments. Professionals researching on autism have clearly indicated that early diagnosis &intervention programs including the pharmacological & non-conventional methods viz; occupational, pragmatic skills along with dietary modifications may lead to significant improvement outcomes & better levels of functioning for children with autism, as they reach adulthood. The present review summarizes on the findings of the dietary related risk factors & how food plays a major role in reducing the symptoms of autism.

INTRODUCTION

Autism is one of five developmental disorders included under the umbrella of the Pervasive Developmental Disorders (PDDs). In addition to autism, other disorders in this family are Asperger's Syndrome, Rett's Disorder, and Childhood Disintegrative Disorder. These conditions lead on to disabilities in virtually all the psychological and behavioral sectors with protuberant disturbances in social, communicative and cognitive ranges. Autism spectrum disorders are neuro-developmental disorders characterized by series of impairments in socialization, communication and repetitive behavior (APA, DSM, 2013). Historically, autism was considered a "mysterious" brain disorder, entailing that it begins and ends in the brain. Though autism had existed much early, it was only described & named in the 1950's as evident by its special & specific characteristics. The word 'autism' was first used by Bleuler, a Swiss psychiatrist in 1911 to refer to schizophrenia. The historical perspective of autism in India was first described by Leo Kanner in 1943 in his classic report of 11 children with "autistic disturbances of affective contact".Another pediatrician Ronald observed similar characteristics of autistic children in Darjeeling to that made by Kanner & made a fact that the difficulties experienced by autistic children can have an overall lifelong impact on their mental personality (Purkayastha & Girimaji *et al*; 1997).

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Center for Autism, India (Action for Autism) the current statistics (2010 data) on prevalence of autism & its spectrum disorders is 1 out of 80 children. According to (Autism Society of America), it is four times more prevalent in boys than girls in the United States. Incidence extrapolations for India for Autism: 11,914 per year, 250 per month, 57 per week, 8 per day, 1.4 per hour. Autism is more common than Down syndrome, which occurs in 1 out of 800 births. Estimates of 15 per 10,000 are now typical rising to 64 per 10,000 or even higher if the entire spectrum is included. This steep rise in the occurrence of the disorder could be attributed to the diagnostic tools & treatment strategies employed to correct the conditions (ADDM & CDC, 2012).

Diagnosis

Autism can be diagnosed in infants as young as 1 year old by observation using proper questionnaires & screening tools. A developmental pediatrician, psychologist, neurologist or psychiatrist familiar with developmental disorders can make a diagnosis. At first glance, some autistic children may appear to have an intellectual frailty, sensory processing issues, or problems with hearing or vision; therefore, it is very important to differentiate autism from other disorders, as suitable treatment programs (interventions) can be provided based on the accuracy and early diagnosis (Srinath & Choudhary *et al*; 1989). Autism cannot be managed by single therapist; it requires multi-dimensional approach of various disciplines to focus on the issues and to bring about positive outcomes. Therefore, the management team for autism is as shown in the figure-1.

Fig 1 Management Team for Autism

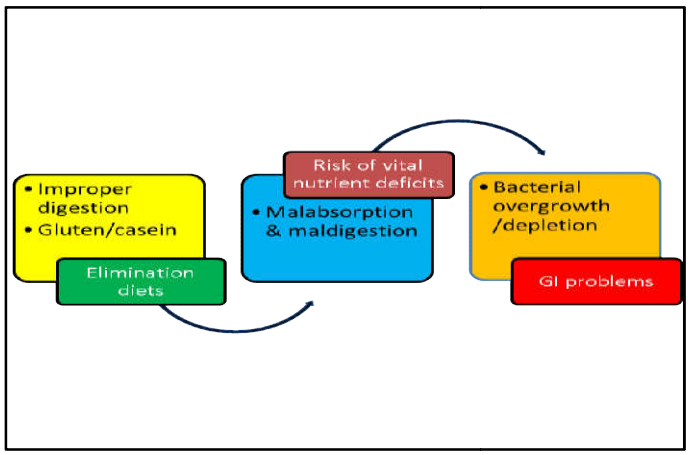

Fig 2 Sequence of Nutritional related problems in Autism

There is no medical test existing to diagnose autism because many of the behaviors allied with autism are common to other disorders, therefore an accurate diagnosis must be based on observation of the individual's communication, social interaction, and his or her activities and interests. Wide ranges of screening and diagnostic instrument for diagnosis of autism have been devised during the last decades. It is also observed that clinical based screening is the most common reported method to diagnose autism (Howlin & Moore; 1997). In India, in the recent years, Indian Scale for Assessment of Autism (ISSA) was developed at NIMH (National Institute for Mental Health, Secunderabad). It is a standardized tool with high degree of reliability and validity for issuance of disability certificate for persons with autism in India (Russell & Daniel *et al*; 2010).

However, an initial medical assessment typically includes; a medical history of the mother's pregnancy, developmental milestones, eating and sleeping habits, coordination issues, stomach and bowel functioning, sensory challenges, allergies, medical illnesses, including ear infections and seizures, any family history of developmental disorders,etc.

Causative factors

Despite recent advances in the diagnostic tools& knowledge of pivotal factors, the exact etiology of autism remains unidentified, but it is assumed to be due to exposure to genetic susceptibility, medical co-morbidities & other environmental factors. Researchers claim that there is no known single cause for autism spectrum disorder, but it is generally accepted that it is caused by abnormalities in brain structure or function. However, there is every reason to hope in the coming time to know the exact cause of autism, which in turn will lead to more effective treatments, appropriate services & improvements in the lives of those affected by autism.Autism spectrum disorder impacts the nervous system and affects the overall social, cognitive, emotional, and physical health of the affected individual. The range and severity of symptoms can vary widely among individuals. Common symptoms include difficulty with communication & social interactions, obsessive interests and repetitive stereotyped behaviors along with various co-occurring physical and nutritional related conditions (Siegel; 1997).

Typical characteristics of an autistic child

Autism being a complex neurodevelopmental disorder is manifested with impaired behaviors along a wide spectrum & usually commences as early as 3 years of age. The 3 core symptoms include social interaction difficulties, communication challenges & repetitive actions. The other features include accelerated brain overgrowth which coincides with the onset of signs & symptoms of the disorder. Brain scans show differences in the shape and structure of the brain in children with autism compared to neuro-typical children. Further, five behaviors among children of less than 2 years of age warrants early evaluation asdescribed by The National Institute of Child Health and Human Development (NICHD) are listed below;

- Does not babble or coo by 12 months
- Does not gesture (point, wave, grasp) by 12 months
- Does not say single words by 16 months
- Does not say two-word phrases on his or her own by 24 months
- Has any loss of any language or social skill at any age.

In addition to the above mentioned features, autistic individuals also exhibits serious behavioral disturbances such as aggression, self-injurious, temper tantrums, hyperactivity, in response to usual environmental demands as they grow older (Kar & Khanna *et al*; 1997).

Dietary problems in autism

Physical conditions observed in individuals with autism include diarrhea, constipation, bloating, GI discomfort, leaky gut, recurrent infections, sleeping pattern alterations, and generalized inflammation/pain. Along with these, autistic children are also affected by micronutrient deficiencies, feeding problems, food neo-phobia, increased sensory problems, persistence to food presentations, selective or picky eating habits and decreased food varieties (Feingold & Song *et al*; 2002). All these dietary risk factors affect the normal development of the children which make them vulnerable to serious nutritional deficiencies. The sequence of nutritional related complications is as shown in the figure 2. Therefore, categorizing autism as a whole body disorder comprehends what happens inside the body and cells & how it affects the brain and how the food fed to a child affects the body and its biochemistry is the need of the hour for proposing the nutritional intervention studies.

Objectives

With this background the aim of this review is to focus on the dietary risk factors & importance of diet in reducing the symptoms of autism. For understanding the role of diet in a better perspective, the current study paper has been arranged in a systematic review format, under the following subtopics: General nutritional status of children with autism, feeding problems, dietary risk factors and dietary approaches in managing autism - Role of food supplements, elimination diets.

General Nutritional Status

Numerous research papers discussing the dietary status of children affected with autism have contradictory results on the nutritional status and have reported that though the adequacy/deficiency of macronutrients does not vary much among the typically developing and autistic children; but in terms of micronutrients, there are significant differences. A classical longitudinal study by (Massaroa and Raiten;1986) reported higher intake of carbohydrates, proteins and total energy requirements and lower levels of fats. However, the nutritional status of autistic children and typically developing children had similar overall nutrient adequacies. Another study by (Morales *et al*; 2014) compared the nutrient intakes and body mass index (BMI) of Autism Spectrum Disorder (ASD) children and typically developing (TD) children. This was a case control study which was studied among (n=40) ASD children and (n=113) TD children in the age group of 6-10 years.The study evaluated the nutrient intakes of the two groups and found that there were significant differences between the vital nutrients. The results of the study projected lower intakes of fluoride and vitamin E levels. The study also assessed the overall quality of diet and its impact on dietary restriction. Many other studies have also reported similar conclusions about the nutritional profile of the children with autism (Zimmer *et al*., 2012; Levy *et al* 2007; Emond *et al*., 2010 & Schmitt *et al*., 2008). All the findings of these studies suggest that despite food selectivity and repetitive behavior which is a characteristic feature of autistic children, the energy and macronutrient requirements are well fulfilled. However, other authors have reported the extent of inadequate intake of micronutrients-Folic acid, Niacin, Iron, B6, Riboflavin (Herndon *et al*., 2009; Wei *et al*., 2010; Shearer *et al*., 1982& Cornish *et al*., 1998) among these children. (Bandini *et al* 2010; Ho *et al* 1997; Johnson *et al*, 2008; Lindsay *et al* 2006)have reported lower intake of Calcium, Vitamin A, C and D levels.

Feeding problems

Children with autism have problems of food selectivity, food refusal, behavioral meal problems and restricted dietary intake implying risk of nutritional deficiencies disorders. (Sarah Hurwitz; 1998) describes feeding problems in children with autism from milder to severe forms which can have negative impact on their nutritional status. The common issues of feeding as experienced by parents includes swallowing difficulties, vomiting, food neo-phobia, emotional under-eating or over-eating which makes them difficult to manage their children (Soumyanath; 2014).

Dietary risk factors

The dietary offending risk factors which aggravate the physical conditions in autistic patients include microbial overgrowth, opiates, food additives, phenolic foods, salicylates, oxalates, amines & glutamines. In addition to these, there are certain food substances (most notably gluten and casein) which are known to trigger the problems in autism, and should therefore be eliminated in the diets. Studies also indicate pica, food allergies & sensitivities observed in autism patients.These factors are described below;

Microbial overgrowth includes bacteria, fungi & yeast which can cause gut inflammation & is also associated with decreased gut function. Many studies have indicated that overgrowth of yeast is common in autistic children as it is triggered due to overuse of antibiotics. Toxins of yeast can cross the blood brain barrier & can cause symptoms ranging from drunken behaviors to affecting energy levels & critical thinking. The GI complications associated with them are mal absorption, mal digestion and leaky gut syndrome. The events of symptoms include diarrhea, constipation, bloating, gastric irritability, feeding problems, esophageal reflux (Adam & Powell *et al*; 2011).

There are certain protein component when ingested can bring about various digestive problems, such as gluten, casein. The main sources of these are wheat, rye, barley, commercial oats & dairy products. In people who are compromised for the indigestion of these proteins including the autistic ones, consumption of these proteins can cause inflammation of the gastrointestinal lining & other associated complications of the gut like pain, diarrhea, bloating, etc. These problems are emerged due to the formation of opiates which are the results of protein indigestion. Opiates or morphine like compounds can initiate irritability, foggy thinking & inattentiveness in autistic children.

Role of food in alleviating the symptoms

Though there are no effective medications or treatments to cure or relieve the core symptoms of autism, other alternative treatments like occupational therapies, sensory integration therapies, pragmatic skill therapies to facilitate language & increase social interactions, dietary intervention through supplementation or elimination of certain diets can be used to improve the conditions of ASD. It has been noted, 'where there is no cure, there are hundred treatments' (Cohen & Volkmar *et al*., 2002). Many studies have been postulated with theories & hypothesized on the dietary aspects& its relationship on overcoming the episodes of autism symptoms.
The road to recovery begins with proper diet not only in medical related diseased conditions but also controlswell in autism cases too. In this present context, autistic individuals are subjected to various alternative therapies with a prime focus on dietary approaches. The physical conditions can be aggravated among individuals with autism with digestive problems, imbalanced biochemistry within the body and nutritional deficiencies. Therefore, altering food choices & possible food interventions could help in improving the symptoms both physical and as well as behavioral.

A healthy diet is essential for optimal health & to accomplish this proper digestion is critical. The physiological and behavioral symptoms of autism in many cases may start from impaired digestion and GI ill health. Food has direct contact & immediately affects the gut, which is an essential component to understand and address in autism. The gut breaks down thefood so that the nutrients are made available to the body which is needed to support biochemical processes and allow

the brain to function properly. The largest part of the immune system is found in the gut-a system often imbalanced in autism causing an inability to fight against viruses, yeast, and other pathogens properly while contributing an overactive inflammatory and allergic response. Foods which are not properly digested in the body can create inflammation & the contaminants in the gut from bad bacteria and yeast can produceoff toxins that affect the brain. About 90% of serotonin (calming brain chemical/hormone) is found in the gut, which is essential in maintaining normal activity of the brain & is lacking in autistic patients. Poor digestion can lead to various manifestations such as leaky gut, malabsorption of nutrients, lack/low levels of beneficial bacteria, inflammatory responses to foods that are not broken down, and a burden to the detoxification system.

Dietary treatments

As autistic patients are currently subjected to numerous 'alternative interventions' by caregivers and researchers, many are specifically aim at diet & are intended in improving the gut health. According to a study by (Wheeler *et al*; 2006) treating the digestive system abnormalities has tremendously decreased the core symptoms of autism & other spectrum disorders. In this present context, the described interventions include gluten-free and casein-free diets, dietary supplementation with essential fatty acids, pre and probiotics, vitamins & minerals.

Elimination diets

While nutritional therapies & dietary restrictions may not completely cure the symptoms, they can definitely be beneficial as complementary to other treatments. Elimination diets are based primarily on reducing or completely removing the foods from the diet that triggers the symptoms, mostly those ones causing food intolerance or allergies. GFCF (gluten free & casein free) foods are planned for the autistic cases as the basic elimination diets. A study by (Hediger *et al*; 2008) have indicated that the physical conditions are drastically reduced while on GFCF diets in autism. This diet is considered as the golden diet for the autism.

In addition, there are several other elimination diets which are based on reducing or completely removing those foods from the diet that adversely affect the autistic people. They include Feingold diets whose principle is based on the removal of dyes or food colors, intentional additives, chemical preservatives from the daily diets (Feingold B.F., 1975). Another study by (Schwartz *et al*., 2009) indicated a high-fat, low-protein & low-carbohydrate diet called Ketogenic diet used to treat refractory epilepsy which provides 90% of the energy from fats & remaining from proteins & carbohydrates. However, this classical diet should be used under expertized medical & dietician supervision on the patients whose serum ketone bodies level is in controlled limits if not, they can be subjected to risk their lives with a number of metabolic disorders.

(Gottschall., 2004) first introduced specific carbohydrate diet to treat autistic individuals aimed at relieving the symptoms of mal absorption & preventing the growth of intestinal micro flora. This diet is recommended to restore back the normal functioning of the gut by including only monosaccharide such as fruits, honey, certain vegetables & avoiding complex carbohydrates as they take longer time to get digested. Thus the residual growth may account for microbial overgrowth resulting in excessive production of intestinal mucus secretion thereby causing intestinal dysbiosis& leaky gut formation (Song Y *et al*; 2002).

Though autism is a genetic disorder, certain metabolic disorders aggravates the clinical symptoms & may pose one of the reasons for pathogenesis of autism such as high concentration of oxalates in the blood serum levels. Oxalates are known to hamper the neurological development & therefore must be limited in autism (Levy *et al*; 2007). Low oxalate diets ranging from 40-50mg/day is generally recommended to autistic patients against 250mg/day which is the acceptable daily intake (Barr & Murphy *et al*; 2002).

Dietary supplementations

Mental disorders can begin from various commotions in the body ranging from biochemical reactions, genetic issues to dietary issues-micronutrient deficiencies or nutritional complications (Pauling; 1968). Appropriate supplements therefore, can be recommended to the ASD individuals to ameliorate the symptoms & correct the deficiencies. A study by (Murray *et al*; 2010) indicates that autistic children consumes lesser foods than compare to control counterparts. Due to their selective eating habits & stereotyped behavior problems they are more prone to nutritional deficiency disorders. Hence, there is escalating evidence based research carried out in various foods that can be supplemented to this kind of individuals to prevent nutritional related deficiencies.(Geis *et al*; 2011) conducted a randomized, double blind, placebo-controlled 3 month study on vitamin & mineral supplements to assess the pre & post symptoms of autism. According to this study, supplementation can be effectively used as an adjunct therapy for reducing the complications as these supplements are well tolerated by the autistic children.

Essential fatty acids

Studies have reported that insufficient intake of essential fatty acids particularly omega 3 fatty acids has detrimental effects on the nervous system of autistic people, resulting in loss of concentration, hyperactivity, dyslexia, dyspraxia (Tsalamanio; 2006). Low levels of essential fatty acids in autism is due to the enzyme defects which removes the essential fat from the brain cell membranes compared with the normal typically growing control groups (Bell *et al*; 2004). Supplementation of EPA & DHA & vitamin E (1.5g/day dosage) significantly improved speech & pronunciation among autistic children who were on investigation for 6 weeks along with the control groups in a pilot study by (Schafer M.R. *et al*; 2007).

Probiotics

Probiotics increases the body's utilization of food components & essential vitamin synthesis along with impeding the development of harmful pathogens. Reports also indicate their various immuno-modulatory effects (Weichselbaum E; 2010). Due to the recurrent occurrence of the gastrointestinal dysfunction evident in autism cases, use of probiotics has proven to exert a beneficial effect on restoring the normal gut flora & maintaining the associated complications (Crocen & Selvin *et al*;2002).

Minerals

A comprehensive study by (Adams JB *et al*; 2011) found out that autistic children have lower levels of essential minerals (especially calcium, magnesium) and vitamins (B-complex)

which was evident from their inadequate dietary intakes. (Latif *et al*; 2002) stated that iron deficiency is commonly linked with autistic children with low levels of serum ferritin, which could be due to insufficient intake of dietary iron. Iron deficiency during the developmental stage is associated with poor cognitive, motor, social functioning of the individual during his/her later years of life. A study by (Dosman *et al*; 2007) indicated that iron deficiency can cause sleep & nervous system disorders. Need for the screening of iron deficiency anemia was indicated in this study. Iron deficiency could be due to mal absorption syndrome resulting from gastrointestinal symptoms. Therefore, supplementation with ferrous sulfate in iron deficient individuals has shown to significantly improve verbal learning and memory issues in autism (Rossignol D.A; 2009) & also sleep disturbances.

Zinc deficiency is also implicated in autism. Low levels of zinc in typically developing children are allied with learning problems, mental retardation & hyperactivity (Rossignol D.A; 2009). Another study by (Lei & Wang, *et al*; 2014) has indicated clinical depression with zinc deficiency. Lowered levels of zinc in RBC's by 40% constitute for the development of oxidative stress in autism persons. On the contrary excess of zinc can aggravate the digestive function (McGinnis*et al*; 2004).

Vitamins

Autistic individuals generally have poor nutritional status, resulting in impaired digestion &intestinal inflammatory conditions that limit nutrient absorption. Due to these complications vital bacteria from the intestines gets depleted & therefore the production, absorption and availability of some vitamins are reduced. Many studies have been indicating promising results in restoring back the functioning of gut considerably in autistic cases with vitamin supplementations. Vitamin status biomarkers are employed to examine the possible association of them with the severity of ASD symptoms. Vitamin A is essential for the normal cell growth & differentiation particularly the epithelial cells lining the gut, brain etc. Supplementation of vitamin A (cod liver oil- rich source) has been effective in treating the symptoms of autism where marked improvements were seen in language skills & maintaining eye contact (Megson;2006). However, comprehensive clinical studies are required to confirm these findings.

(Kalueff *et al*; 2006) reported that Vitamin D has neuro-protective effect & also hinders the neurotransmitters interaction in the brain & hormones which can influence the patient behaviors. Another study by (Grant & Soles 2009) examined the association of vitamin D deficiency posing a risk factor for the development of autism in newborns in pregnant mothers. According to the findings mentioned above it is suggested that sufficient intake of vitamin D may reduce the risk of developing autism by supporting proper development of the brain & immune system.

Vitamin C is important for normal functioning of metabolic, antioxidant pathways & other co- enzymes for the synthesis of neurotransmitters. Deficiency of this vitamin is associated with dysregulation of brain signaling glutamatergic system, associated with ASD's (Blaylock & Strunecka; 2009). It has been shown that vitamin C supplementation may be positively affecting the pathological behavior of autistic people (Adams & Holloway; 2004). From the above mentioned findings, it can be postulated that food/diet has a significant role in managing the symptoms of autism and the possible benefits of it are as follows;

Potential benefits of nutritional interventions

- Improved alertness or 'being present'
- Improved speech & or usageof language & increase in effort to speak, number of words spoken, complexity of sentences & conversational speech.
- Improved social interactions including increased interest in peers & siblings, initiation of play, appropriate use of toys & improved tolerance in larger groups.
- Reducedself-stimulating&self-injurious behavior.
- Increased ability to focus & enhancement of cognitive function.
- Improved digestion, sleep & immune function.

CONCLUSIONS

Autism is a multi-factorial disorder having a wide range of genetic and environmental causes. A sharp increase in the prevalence of autismand increased difficulties in managing both physical & behavioral conditions has stimulated intense research around its potential factors and consequences so that curative & appropriate measures can be taken on time. Studies have provided extensive data on the dietary related factors (nutritional deficiencies, gastrointestinal complications, food allergies) which could aggravate the symptoms. Although numerous studies on the dietary problems have been studied globally, there is lack of literature among the Indian scenario. Nutrients are essential to regulate the biochemical processes in autistic people. Therefore, adequate nutritional status requires the consumption of nutrient dense food and proper digestion to breakdown and absorbs these foods. Dietary interventions should be substantiated with biochemical data which will benefit the autistic populations from timely and intensive interventions and in adulthood expand their options for living independently. Evidence has clearly shown that early intervention programs particularly nutritional approaches may yield a novel hope for efficiently managing the problems& treating autism. Along with the intervention, parental involvement & support groups is very important. Therefore, this area of research warrants focused attention and effort.

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