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ASSESSING NUTRITIONAL INTERVENTIONS FOR PEOPLE WITH AUTISM SPECTRUM DISORDER: A REVIEW

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Abstract

The aim of this study is to identify and evaluate existing research on nutritional interventions for individuals with Autism Spectrum Disorder (ASD). The study followed the research approach for conducting an integrative review. Two researchers independently searched the PubMed, Scopus and Google Scholar databases for relevant literature. Using carefully developed search terms, 102 articles were selected from these databases. After reading the full text of 67 articles, the reviewers selected 33 studies that were eligible for inclusion. Based on the findings of this review, individuals with ASD have been treated with various nutritional interventions, including gluten-free, casein-free diets, ketogenic diets, specific carbohydrate diets, prebiotics and probiotic supplements, as well as vitamins and minerals. These interventions have resulted in improvements in cognition, sociability, and behavioral symptoms associated with ASD. Furthermore, these interventions also resulted in improvements in gastrointestinal symptoms, adaptive functioning, sensory profiles, quality of life, nutritional status, emotional, and intellectual aspects of life for individuals with ASD. Whereas the existing literature suggests potential benefits, further research is needed to clearly understand the effectiveness and potential risks associated with these nutritional interventions among individuals with ASD. The authors highlighted the research and clinical implications of nutritional interventions when working with individuals with ASD.

Keywords: Autism Spectrum Disorder, Diet, Nutrition, Nutritional Intervention, Nutrition Therapy

INTRODUCTION

An individual with Autism Spectrum Disorder (ASD) experiences persistent challenges in communication and forming social connections, as well as a profound impact on their cognitive functioning. Autism manifests in individuals in diverse ways, presenting with a range of symptoms, levels of cognitive ability, and difficulties. ASD is categorized as a neurodevelopmental disorder that primarily affects communication and behavior in individuals (Regier et al., 2013). In addition, individuals with ASD may have a limited range of food preferences due to heightened sensitivity to visual, tactile, auditory, and gustatory stimuli (Elsabbagh et al., 2012). Individuals on the autism spectrum exhibit a wide range of personalities and capabilities. They may have heightened sensitivity to smell, taste, appearance, and texture, particularly in relation to food (Schmidt et al., 2011). They often face challenges related to eating and tend to prioritize meal selection based on texture, showing a preference for high-energy density foods rather than low-energy density foods (Sánchez et al., 2015). Food can impact specific behaviors commonly observed in individuals with ASD, including a focus on details, resistance to change, sensory sensitivities, social withdrawal, and difficulties in demanding situations. This can result in a highly restricted diet and daily struggles with nutrition and eating. The main approach to treating ASD is a combination of psychological therapies and medications, with the goal of improving

social functioning and reducing behavioral symptoms. Nutritional interventions have become increasingly prominent as an additional treatment option for ASD. Nutritional intervention involves working with a dietitian or nutritionist who specializes in assisting individuals with ASD. These experts develop personalized therapy strategies based on the unique preferences and dislikes of the individuals they are assisting. Marti (2014) suggests that interventions for certain conditions may involve various dietary approaches, such as the gluten-free and casein-free diet (GFCF), ketogenic diet, prebiotic and probiotic supplements, specific carbohydrate diet, yeast-free diet, polyunsaturated fatty acids, and dietary supplements (including vitamins A, C, B6, folic acid, B12, minerals like magnesium, and omega-3 fatty acids), among others.

Research has indicated that children with ASD exhibit greater selectivity in their food choices compared to typically developing children. This leads to restricted dietary patterns and a notable vulnerability to nutritional deficiencies (Reynolds et al., 2012). Additionally, these children have distinct preferences for food attributes such as moisture level, color, shape, packaging style, and brand. Children diagnosed with ASD face significant difficulties when it comes to trying new foods and expanding their food choices (Bjørklund et al., 2019). Moreover, Guo et al. (2020) conducted a study that revealed children diagnosed with ASD are more likely to experience deficiencies in essential vitamins and minerals compared to typically developing children. Furthermore, these deficiencies have been found to be associated with the symptomatic manifestation of ASD. However, there is a lack of consensus on the optimal nutritional approach for individuals with ASD. Therefore, it is crucial to understand the nutritional approaches that have been used and shown to be effective in managing individuals with ASD. This will enable nutritionists and other clinicians involved in their care to make more informed clinical treatment decisions. Thus, the main objective of this study is to identify and evaluate existing literature on nutritional interventions for people with ASD.

Research Question

What types of nutritional interventions are used in the management of persons with ASD?

METHODOLOGY

The study examined nutritional interventions used in the treatment of individuals with ASD through an integrative literature review methodology. The study did not have ethical approval because it relied on empirical literature analysis. By using the integrative literature review approach, the authors successfully identified and explained the chosen literature and its implications for both research and practice. The bibliographic search was independently conducted by the two researchers using the PubMed, Scopus and Google Scholar databases.

A total of 102 articles were selected using carefully crafted search phrases from these databases. After a thorough evaluation, two reviewers selected a final set of 33 studies by reading the entire text and excluding 69 others. The search terms considered included "Autism Spectrum Disorder," "nutrition," "nutrition therapy," "diet," "diet therapy," and "nutritional interventions." The search algorithms were further created using Boolean operators as follows: 1) Nutrients OR Diet AND Autism Spectrum Disorder; 2) Diet AND Autism Spectrum Disorder; 3) Nutrients AND Autism Spectrum Disorder; 4) Nutritional intervention OR Diet Intervention AND Autism Spectrum

Disorder; 5) Nutritional intervention AND Autism Spectrum Disorder; 6) Diet Intervention AND Autism Spectrum Disorder; 7) Nutrition Therapy OR Diet Therapy AND Autism Spectrum Disorder; 8) Nutrition Therapy AND Autism Spectrum Disorder; 9) Diet Therapy AND Autism Spectrum Disorder.

The search was limited to research conducted between 2010 and 2023, with a focus on papers published in English. Specifically, the study examined the effects of nutritional or diet interventions on these individuals and assessed certain behaviors before and after the intervention. Therefore, reviews, articles written in languages other than English, animal research, and studies without an outcome variable were excluded. Based on these selection criteria, a total of 33 articles met the inclusion criteria. The study consisted of three stages, starting with an extensive database search that resulted in the identification of full-text papers. The second phase involved reviewing abstracts and full-text papers. In the third phase, the publications were carefully read, synthesized and classified into five distinct groups based on the specific nutritional intervention they focused on. The literature retrieval process adopted in this study can be seen in Figure 1.

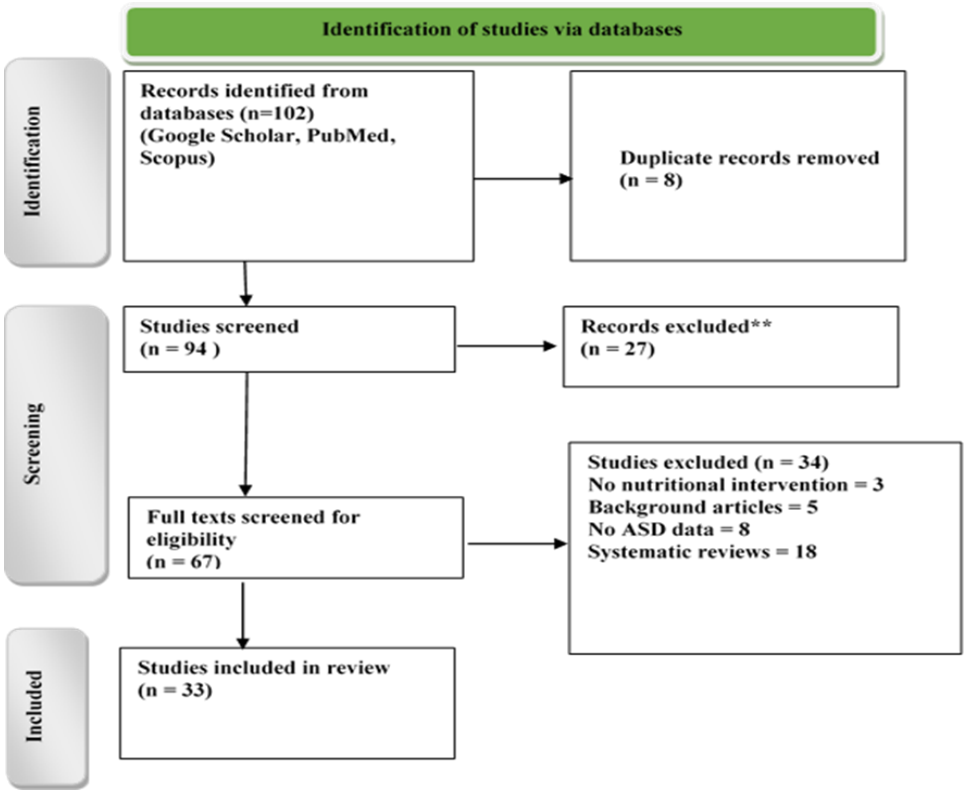

Figure 1: Flow chart illustrating the literature retrieval process in this research

RESULTS

From Tables 1 to 5, findings from this research reveals that the 33 articles selected for data extraction were published between 2011 and 2021. Out of the 33 studies reviewed, 15 were conducted in the US, 4 were conducted in China and Spain respectively, 3 were conducted in Egypt, and one study each was conducted in Poland, Iran, Morocco, Denmark, Italy, Singapore, and New Zealand respectively.

Table 1: Literature on Nutritional Interventions using Gluten and Casein-Free Diet (GFCF) for People with ASD

S/N	Studies/ year	Intervention goal	Duration/ Location/ Population	Method/ sample	Description of Intervention	Results
1	Piwowarczyk et al. (2020)	To determine whether a gluten-free diet (GFD) compared with a gluten-containing diet (GD) influences functioning of children with autism spectrum disorders (ASD).	8-weeks / Warsaw, Poland / children (36–69 months) with ASD, within the normal IQ (>70) range.	Randomized, controlled, single-blinded trial /Sixty-six children (GD n=33; GFD n=33), males= 56, females=10; mean age: 48±11 months (36–69 months).	After an 8-week run-in period on a GFD, the GFD group continued this diet and the GD group consumed at least one normal meal containing gluten per day for 6 months.	There were no differences between groups in autistic symptoms, maladaptive behaviors, or intellectual abilities after the intervention. A GFD compared with a GD did not affect functioning of children with ASD.
2	Ghalichi et al. (2016)	To examine the effect of gluten-free diet on gastrointestinal and behavioral indices for children with autism spectrum disorders	6 weeks /Iranian schoolchildren	n = 80; A randomized clinical trial Case-control study	n=40 Gluten-free diet n=40 normal diet	Significant decrease in stereotyped behavior ($p < 0.001$). i.e., there is a significant reduction in the gastrointestinal symptoms in the treatment group but increased in the control group significant reduction in behavioral symptoms in the treatment the group compared to the control group
3	Hyman et al. (2016)	To obtain information on the safety and efficacy of the gluten-free/casein-free (GFCF) diet	30 weeks/ US preschoolers	n = 14; 3-5 years; A randomized double-blind, placebo-controlled trial	GFCFD	Dietary challenges did not have statistically significant effects on measures of physiologic functioning, behavior problems, or autism symptoms.
4	Hafid and Ahami (2018)	To verify the efficiency of gluten-free casein-free diet for children with autism spectrum disorder	48 weeks /Moroccan schoolchildren	n = 30; A randomized clinical trial	GFCFD	No significant findings
5	González-Domenech et al. (2020)	To determine the influence of a GFCF diet on behavior disorders in children and adolescents diagnosed with ASD and the potential association with urinary beta-casomorphin concentrations	48 weeks/ Spanish schoolchildren	n = 29; A randomized controlled clinical trial	GFCFD	No significant findings
6	González-Domenech et al. (2019)	To investigate the influence of a Gluten-free, Casein-free Diet on Behavioral Disturbances in Children and Adolescents Diagnosed with Autism Spectrum Disorder	3 months/Spanish children and adolescents	n=28; Crossover trial	normal diet +GFCF diet GFCF diet alone	No significant change in behavior symptoms were noticed after the GFCF diet

7	Grimaldi et al. (2018)	To examine the impact of exclusion diets and a 6-week Bimuno® galactooligosaccharide (B-GOS®) prebiotic intervention in 30 autistic children.	10 weeks/ US schoolchildren and adolescents	n = 26; The design was not specified	GOS + GFCFD	Significantly lower scores of abdominal pain andbowel movement, as well as lower abundance of Bifidobacterium spp. and Veillonellaceae family, but higher presence of Faecalibacterium prausnitzii and Bacteroides spp..
8	Stewart et al. (2015)	To investigate the Dietary Supplementation in Children with Autism Spectrum Disorders	3 days/ US/children	Cross-sectional study; 2 to 11 years (N=288).	gluten/casein-free diet (GFCF)	Children receiving GFCF diets had similar micronutrient intake but were more likely to use supplements (78% vs 56%; P¼0.01). Supplementation led to excess vitamin A, folate, and zinc intake across the sample, vitamin C, and copper among children aged 2 to 3 years, and manganese and copper for children aged 4 to 8 years.
9	Whiteley et al. (2016)	To examine the impact of a gluten- and casein-free dietary intervention for children with autism spectrum disorders.	24-months/ Danish children	N= 72; (aged 4 years to 10 years 11 months); A randomised, controlled, single-blind study	gluten/casein-free diet (GFCF)	Dietary intervention positively affected developmental outcome for some children diagnosed with ASD
10	Marí-Bauset et al. (2016)	To compare anthropometric, nutrient intake, the Healthy Eating Index and food variety in children with autism spectrum disorder (ASD)	3 months/ Valencia (Spain)/ children	A case–control study; 6–9 years old; n= 85	GFCF diet	Autistic children on a GFCF diet showed less tendency to be overweight or obese than those on a regular diet: underweight.
11	Navarro et al. (2015)	To explore the effects of gluten and milk on IP and behavior in children with ASDs	4 weeks/ Texas/ children	Randomized double-blind, placebo-controlled study;	gluten-free, casein-free (GCF) diet	The changes observed were noted to be small and not clinically significant. That is, there was no association between dietary gluten/milk, IP, and behavioral changes in subjects with ASD.

Table 2: Literature on Nutritional Interventions using Ketogenic Diet for People with ASD

S/N	Studies/ Year	Intervention goal	Duration/ Location/ Population	Method/ Sample	Description of Intervention	Results
1	El-Rashidy et al. (2017)	To investigate the effects of Ketogenic diet versus gluten-free casein-free diet in autistic children	Duration was not specified/ Egyptian children	n=45 3-8years; Randomized controlled trial	15- ketogenic diet + modified Atkins diet 15- gluten free casein free diet 15- control (balanced nutrition)	Both groups showed improvements in childhood autism rating scale and autism treatment evaluation test ketogenic diet scored better results in cognition and sociability compared to the GFCF diet group.
2	Lee et al. (2018)	To examine the effects of a modified ketogenic gluten-free diet with MCT improves behavior in children with autism spectrum disorder.	3 months/Hawaii USA/children	n= 15 2-17years; Open-label clinical trial	Modified ketogenic GFCF with Mid chain triglycerides	no improvements in restrictive and repetitive behavior there were improvements in imitation, body use, nervousness
3	Barnhill et al. (2016)	To document combined medical, behavioral, and nutritional intervention for a toddler with ASD and comorbid feeding disorder.	4days/ US female child	n=1; 28-month-old; A case study involving a female child	Feeding therapy involving shaping, differential reinforcement, prompting, and escape extinction.	The participant in this study rapidly increased her food acceptance and consumption. There was also an increases in appropriate feeding behaviors such as self-feeding, sitting appropriately for the meal, and eating new foods. The study also found a decreases in challenging behavior as a result of intervention. Crying, screaming, throwing the plate/food, and tantrums all decreased to zero rates.

Table 3: Literature on Nutritional Interventions using Prebiotics and Probiotics for People with ASD

S/N	Studies/ Year	Intervention goal	Duration/ Location/ Population	Method/ Sample	Description of Intervention	Results
1	Sanctuary et al. (2019)	To examine the influence of probiotic/colostrum supplementation on gut function in children with autism and gastrointestinal (GI) symptoms.	12 weeks/ US preschoolers and schoolchildren	n = 8; Randomized double-blind controlled trial	combined treatment probiotic/prebiotic Bifidobacterium infantis) and Bovine colostrum product	Combined treatment well tolerated in both groups, reduction in the frequency of GI symptoms, as well as a reduction in particular aberrant behavior.
2	Liu et al. (2019)	To examine the effects of Lactobacillus Plantarum PS128 on Children with Autism Spectrum Disorder in Taiwan	4 weeks/ Taiwanese, China schoolchildren and adolescents	n = 71; A Randomized, Double-Blind, Placebo-Controlled Trial.	probiotic/prebiotic supplementation (Lactobacillus plantarum PS 128)	Improvement in opposition/defiance autism-associated behavior in the ASD group compared to the control group
3	Santocchi et al. (2020)	To investigate the effects of Probiotic Supplementation on Gastrointestinal, Sensory and Core Symptoms in Autism Spectrum Disorders.	6 months/ Italian preschoolers	RCT-double blind randomized Placebo-controlled trial; n=85	probiotics [de-simone formulation n=42, and placebo n=43	Autism diagnostic observation schedule-for calibrated severity score improved in the treatment group compared to the control group improved in GI symptoms, Adaptive functioning, and sensory profiles
4	Kong et al. (2021)	**To examine the effects of Probiotic and Oxytocin combination therapy on individuals with ASD**	28 weeks/USA/children & adult	Randomized, double-blinded, placebo-controlled, 2-stage pilot trial; n=35; age 3-20	Probiotic and Oxytocin	Improvements in ABC and SRS scores and significant improvements in CGI-improvement between those receiving probiotics and oxytocin combination therapy compared to those receiving placebo (***p* < 0.05).**
5	Shaaban et al. (2018)	To examine the role of probiotics in children with ASD	3 months/Egypt/Children	n=60, 5-9 years; Prospective open-label non-controlled Trial	n=30 ASD Lactobacteria acidophilus, L.rhamosus and bifidobacteria longum	Improved GI symptoms in treatment than controls

Table 4: Literature on Nutritional Interventions using Specific Carbohydrate Diet for People with ASD

S/N	Studies/ Year	Intervention goal	Duration/ Location/ Population	Method/ sample	Description of Intervention	Results
1	Barnhill et al. (2020)	To investigate the effect of Implementation of a Specific Carbohydrate Diet for a Child with Autism Spectrum Disorder and Fragile X Syndrome.	4 months/USA/child	n=1, 4 years; RCT	specific carbohydrate diet	Improvements in nutrition status, gastrointestinal problems, and behavioral symptom improvements.

Table 5: Literature on Nutritional Interventions using Other Supplements for People with ASD

S/N	Studies/ year	Intervention goal	Duration/ Location/ Population	Method/ sample	Description of Intervention	Results
1	Guo et al. (2020)	To investigate the vitamin A (VA) and vitamin D (VD) levels in children with autism spectrum disorders (ASD) and to determine whether co-deficiency of VA and VD exacerbates clinical symptoms in autistic children.	24 weeks/ Chinese schoolchildren	n = 65; RCT	vitamins/minerals supplementation (200.000 IU of vitamin A in a single dose)	Improvements in relation to people ($p = 0.0255$), emotional response ($p = 0.0270$), body use ($p = 0.0374$), adaptation to change ($p = 0.0345$), taste, smell and tact ($p = 0.0426$), anxiety ($p = 0.0446$), verbal and nonverbal communication ($p = 0.0450$), general impression ($p = 0.0169$), and total score ($p = 0.0141$) on CARS scale.
2	Saad et al. (2016)	To examine the relationship between vitamin D deficiency and the severity of autism	12 weeks/ Egyptian preschoolers and schoolchildren	n = 83; A case-controlled cross-sectional clinical trial	vitamins/minerals supplementation (300 IU/kg up to 5000 IU/ day of calciferol)	Improvement in irritability ($p = 0.021$), lethargy/social withdrawal ($p = 0.028$), hyperactivity ($p = 0.01$), and stereotypic behavior ($p = 0.04$) on the ABC scale. Improvement in social, emotional and imitation response ($p<0.001$), body and object use ($p = 0.01$), visual response ($p = 0.003$), general impression and total score ($p<0.001$) on the CARS scale
3	Adams et al. (2018)	To examine the Comprehensive Nutritional and Dietary Intervention for Autism Spectrum Disorder	12 months/US children/adults	Single-blind-randomized case-controlled trial; n=67, 3-58 years ASD n=50 Controls 3-18 years	vitamin /mineral supplement essential fatty acids, Epsom salts, carnitine, digestive enzyme, GFCF diet	Improved nutritional status, autism symptoms and non-verbal intellectual ability or IQ in ASD treatment group than in controls. Parents reported that the vitamin/mineral supplements, essential fatty acids, and HGCSF diet were the most beneficial.
4	Keim et al. (2018)	To examine the effects of ω-3 and ω-6 Fatty Acid Supplementation May	90 days/USA/toddler	n=31 18-36 months born at <29 weeks; randomized fully	n= 15 omega 3-6-9 n=16 canola oil placebo	significant reduction of autism-related symptoms in the treatment the group compared to controls

		Reduce Autism Symptoms Based on Parent Report in Preterm Toddlers.		blinded placebo controlled trial		
5	Liu et al. (2017)	To examine the effect of vitamin A supplementation on gut microbiota in children with autism spectrum disorders	6 months/China/ children	n=64, 1-8 years; RCT	vitamin A supplementation n=20 controls n=44 treatment group	Improvements in ASD-associated symptoms
6	Xia (2011)	To examine the effectiveness of nutritional supplements for reducing symptoms in autism spectrum disorder	5 months/USA/C hild	n=1, 9 years; RCT	vitamin B6 supplements	Improvements in ASD-related symptoms
7	Hendren et al. (2016)	To examine the efficacy of Methyl B12 for Children with Autism.	8 weeks/ USA/ Children	n=57; Randomized controlled placebo Trial	Methyl B12	Improved clinical rated ASD symptoms
8	Frye et al. (2019)	To investigate if Folinic acid improves verbal communication in children with autism and language impairment	12 weeks/USA/C hildren	n=48 7 years; Double-blind controlled placebo	folic acid n=23 high dose folic acid n=25 placebo	Improvement in verbal communication in treatment compared to control improvements in autism-related symptoms
9	Sun et al. (2016)	To examine the efficacy of Folic Acid Supplementation in Autistic Children Participating in Structured Teaching	3 months/ China/ Children	n=66; A randomized controlled clinical trial	n=44 folic acid n22 placebo	folic acid improved ASD symptoms toward sociability, cognitive verbal receptive language improved folic acid concentrations
10	Voigt et al. (2014)	To determine whether docosahexaenoic acid (DHA) supplementation improves the behavior of children with autism.	6 months/ Boston/childre n	A double-blind randomized placebo-controlled trial; N=48; 3- to 10-year-old	docosahexaenoic acid (DHA) supplementation	Dietary DHA supplementation of 200 mg/day for 6 months does not improve the core symptoms of autism.
11	Ooi et al. (2015)	To examine the efficacy and safety of a 12-week omega-3 fatty acids supplementation among children suffering with Autism Spectrum Disorders (ASD)	12 weeks 1 g/day/ Singaporean schoolchildren and adolescents	n = 41; 7-18 years; An open-label trial	polyunsaturated fatty acid supplementation (EPA + DHA + Vit E in two doses)	Significant improvements in social awareness ($p = 0.01$), social communication ($p = 0.001$), social cognition ($p = 0.001$), social motivation ($p = 0.01$), stereotyped and repetitive behaviors ($p = 0.001$), and score total on SRS scale ($p = 0.001$)
12	Parellada et al. (2017)	To investigate if omega-3 supplementation improves erythrocyte membrane ω6/ω3, plasma antioxidant status (TAS) and autistic behaviors.	8 weeks/ Spanish children and adolescents,	A randomized, crossover, placebo-controlled study; n=68	omega-3 supplementation	All groups benefitted from PUFA supplementation, but patients with lower baseline ω3/ω6 show a larger effect. Also, social motivation of children and adults with autism improved during the trial, with no significant treatment-order effect.
13	Mazaher y et al. (2019)	To investigate the use of vitamin D and omega-3 long-chain polyunsaturated fatty acids in the treatment of irritability and hyperactivity among children with autism spectrum disorder.	12 months/ children/ New Zealand	n=73; 2 × 2 factorial-double blind controlled trial	Vitamin D 2000 IU, n-3 LCPFA's 722 mg Both 2000 IU and 722mg, or placebo (4 randomized treatments)	Irritability and hyperactivity scores showed a significant effect of time ($p<0.001$). There was a reduced inflammation in the group given both vitamin D and n-3 LCPFA's

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Additionally, 22 out of the 33 papers reviewed were randomized controlled trials. Three were open-label clinical trials, and two studies each used a cross-over trial and case-controlled study designs respectively. Three of the studies used cross-sectional, single case, and factorial double-labelled designs respectively. However, one of the 33 studies reviewed did not report the type of design used. Furthermore, 26 of the studies reviewed assessed school children, including toddlers and preschoolers. Five studies assessed both children and adolescents, while two of the studies assessed both children and adults.

The review also found that 13 out of the 33 studies employed other dietary supplementation such as vitamins and minerals. Eleven studies employed gluten-free and casein-free diets, five employed prebiotics and probiotics supplements, three employed ketogenic diets, and one study employed a specific carbohydrate diet as nutritional interventions in the management of people with autism spectrum disorders. The duration of the administration of reviewed nutritional interventions ranged from 3 days to 24 months, excluding weeks of follow-ups and monitoring of patients for results. A summary of the nutritional interventions found in the literature for assisting individuals with ASD can be seen in Figure 2.

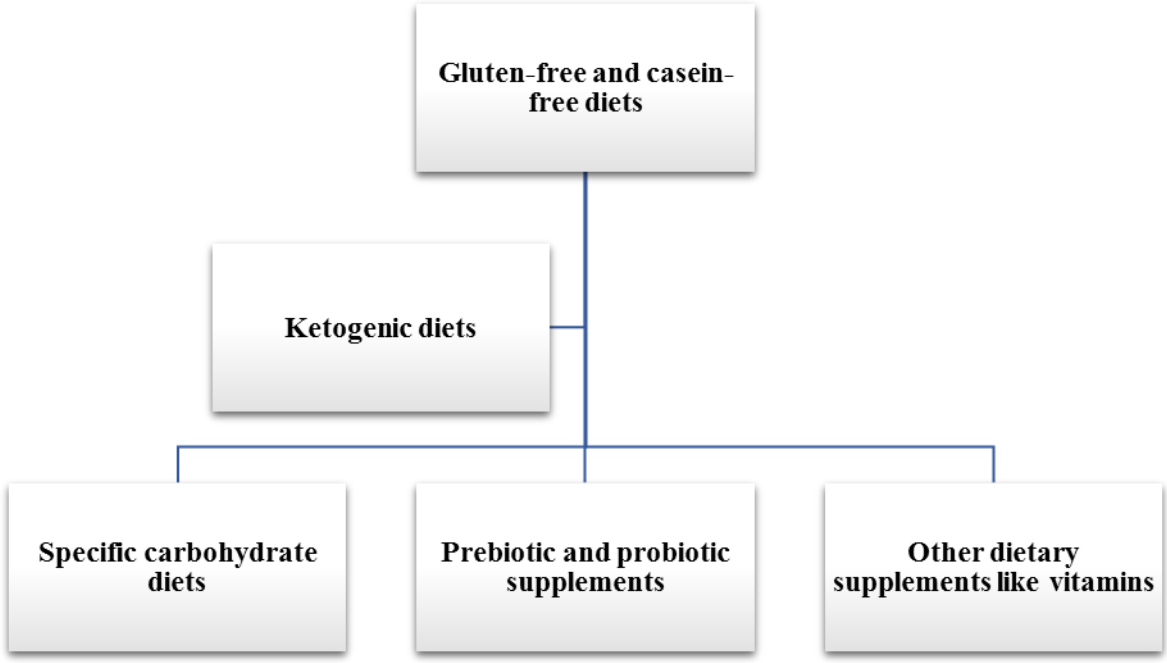

Figure 2: Illustration of nutritional intervention strategies for individuals with ASD

DISCUSSION

The objective of this study was to identify and evaluate existing research on nutritional interventions for individuals diagnosed with ASD. After examining previous articles, the review found that gluten-free and casein-free diets, ketogenic diets, specific carbohydrate diets, prebiotic and probiotic supplements, as well as other dietary supplements such as vitamins and minerals, have been used as nutritional interventions for individuals with ASD. The discussion of this current review will be based on the different forms of nutritional interventions found in the literature.

The Gluten and Casein-Free Diet (GFCF) diet eliminates gluten (found in wheat, barley, and rye) and casein (found in milk and dairy products) from the child's daily diet. In some cases, parents of persons with ASD use this diet to alleviate autism symptoms as a result of food allergies. In this diet, peptides and proteins found in gluten and casein are said to contain opiate-like chemicals, which can alter behavior and reactions. Individuals with ASD may experience exacerbated symptoms as a result of this chemical reaction. As shown in the studies reviewed, GFCF diets, are gaining popularity in the autism community. Eleven of the reviewed articles used GFCF diets as part of their intervention. The nutritional intervention with GFCF diets did not show a significant result in seven of eleven studies (González-Domenech et al., 2019, 2020; Hafid & Ahami, 2018; Hyman et al., 2016; Navarro et al., 2015; Piwowarczyk et al., 2020; Stewart et al., 2015), but four studies found that children with ASD benefit from GFCF diets. In some cases, GFCF diets appear beneficial, but indifferent in others. This assertion can be substantiated by studies conducted by Ghalichi et al. (2016) and Grimaldi et al. (2018), who conducted randomized clinical trials and found that the GFCF diet significantly decreased stereotyped behavior in people with ASD. Whiteley et al. (2016) and Marí-Bauset et al. (2016) also conducted randomized studies on children with ASD. The GFCF diets improved developmental outcomes for the children by reducing their tendency to become overweight or obese compared with a regular diet. The conflicting results indicate that GFCF diets are not supported enough to be recommended as nutritional strategies in the treatment of ASD. While they are safe, they may pose nutritional risks if not followed by a nutritionist on a long-term basis. In other words, a GFCF diet for ASD is not conclusively proven effective despite its increasing popularity among patients and clinicians.

Diets involving a reduction in carbohydrates and their replacement with fat are known as ketogenic diets. This results in a faster metabolic state called ketosis, in which fat becomes the body's main source of energy. Keto diets require that one avoid carbohydrates. In this diet, meats, dairy products, low-carb vegetables, nuts, seeds, avocados, and artificial sweeteners dominate. Among the reviewed studies, three assessed the effectiveness of ketogenic diets for improving cognition and sociability in people with ASD, as well as modifying behavior symptoms related to the disorder. The claims can be supported by Lee et al. (2018) and Barnhill et al. (2016), who conducted open-label clinical trials and case studies, respectively, on children and toddlers. According to Lee et al. (2018), there was an improvement in imitation, body use, and nervousness, while in Barnhill's study, there was an increase in appropriate feeding behaviors such as self-feeding, sitting appropriately for meals, and eating new foods after the intervention. As a result of the intervention, challenging behavior decreased as well. The number of tantrums, crying, screaming, and throwing of the plate/food decreased. Using a randomized controlled trial on 45 3-8-year-old children, El-Rashidy et al. (2017) found that the ketogenic diet improved cognitive and sociability scores compared to the GFCF diet group when using the Childhood Autism Rating Scale and Autism Treatment Evaluation Test.

The Specific Carbohydrate Diet (SCD) diet is one of many diets that can support good digestive health. In the SCD, complex carbohydrates (e.g., starch and disaccharides, including lactose, maltose, and sucrose) are restricted to reduce symptoms of carbohydrate malabsorption and pathogenic intestinal microbiota growth. Fruits, vegetables, honey, nuts, meats, and eggs, all of which contain monosaccharides (such as glucose, fructose, galactose), are recommended instead. There are a number of

restricted foods, including grains, potatoes, most dairy products, sugar, and processed foods. By avoiding most grains that are high in carbohydrates, the SCD diet aims to aid digestion and prevent gastrointestinal problems. There are very few studies on the effects of SCDs on individuals with ASD. Only one study used SCD, and it was found to be effective in improving behavioral symptoms for people with autism spectrum disorder. A randomized controlled study conducted by Barnhill et al. (2020) on a 4-year-old child who had ASD adopted an SCD as a nutritional intervention and found that there was an improvement in nutritional status, gastrointestinal problems, and behavioral symptoms.

Regarding prebiotic and probiotic supplements, probiotics interact with gut microbiota and may reduce inflammation and intestinal permeability. It is becoming increasingly common to use prebiotic and probiotic diets to treat individuals with ASD. However, there is limited knowledge about the adverse effects, therapeutic actions, appropriate dosages, and strains of prebiotic and probiotic supplements for people with ASD. This review identified five nutritional intervention studies that used prebiotic and probiotic supplements. Prebiotic and probiotic supplements were found to be beneficial for individuals with ASD in terms of improving gastrointestinal (GI) symptoms, adaptive functioning, and sensory profiles. These findings align with studies (Sanctuary et al., 2019; Santocchi et al., 2020; Shaaban et al., 2018) that observed a reduction in GI symptoms and specific aberrant behavior. Santocchi et al. (2020) also reported improvements in adaptation and sensory profiles. Additionally, Liu et al. (2019) and Kong et al. (2021) conducted randomized, double-blinded, placebo-controlled trials on children and adolescents using probiotics in nutritional interventions. Liu et al. (2019) found that defiance autism-associated behavior improved in the ASD group, while Kong et al. observed a significant improvement in CGI for participants who received probiotics and oxytocin combination therapy compared to those who received a placebo.

Several dietary supplements, including vitamins A, C, B6, B12, D; folate; polyunsaturated fatty acid supplements; omega-3 supplements; and ferritin, have been identified to be useful in nutritional interventions for individuals with ASD. Various clinical trials have studied the use of these dietary supplements for treating ASD symptoms. A total of 13 different nutritional intervention studies were identified in the literature, all of which found these dietary supplements to be beneficial and effective in improving the quality of life for individuals with ASD. For instance, Mazahery et al. (2019) conducted a study evaluating 73 children with ASD over 12 months and found that the group given both vitamin D supplements experienced a significant reduction in inflammation, while hyperactivity and irritability scores were significantly affected by time. Dietary supplements have also been found to effectively improve the nutritional, emotional, intellectual, and social well-being of individuals with ASD. Adams et al. (2018) conducted a single-blind, randomized case-controlled trial on 67 US children and adults using vitamin/mineral supplements and found that the ASD treatment groups experienced improvements in nutritional status, autism symptoms, and non-verbal intelligence. Guo et al. (2020) conducted a 24-week randomized controlled trial on 65 Chinese children using vitamin and mineral supplements and observed improvements in relationships with people, emotional responses, body use, and adaptation to change, among other factors, in the emotional and intellectual domains. Clinical controlled trials (Ooi et al., 2015; Parellada et al., 2017; Saad et al., 2016; Sun et al., 2016) also indicate that dietary supplements improve the social lives of

individuals with autism. Studies (Frye et al., 2019; Hendren et al., 2016; Keim et al., 2018; Liu et al., 2017; Voigt et al., 2014; Xia, 2011) have demonstrated the reduction of autism-related symptoms through the use of different dietary supplements in nutritional interventions when compared to control groups.

LIMITATIONS, IMPLICATIONS AND RECOMMENDATIONS

It is possible that evidence pertaining to nutritional interventions for individuals with autism was overlooked due to the exclusive inclusion of English-language articles. The findings of this study, nevertheless, bear significance for future investigations concerning the efficacy of nutritional interventions among individuals with ASD. Furthermore, the majority of the existing empirical literature pertaining to nutritional interventions for people with ASD was produced in the following countries: Poland, Denmark, Morocco, China, New Zealand, Spain, Egypt, Italy, and Singapore. As a result, additional research should be undertaken to substantiate the potential efficacy of nutritional interventions in sub-Saharan Africa and other regions where ASD is prevalent.

In an effort to improve the lives of individuals with ASD, there is a growing interest in investigating novel interventions as the prevalence of the disorder continues to increase. ASD is widely acknowledged as a complex disorder in which both genetic and environmental factors play a role in its development. Consequently, scholars have been investigating a range of interventions, including nutritional interventions, in an effort to alleviate the symptoms and enhance the general welfare of individuals with ASD. Through an integrative analysis of the existing literature on this topic, we identified and evaluated various nutritional interventions used in the management of people with ASD. This study offers insights into the potential benefits and considerations for implementing nutritional interventions among individuals with AD, thereby guiding future research and clinical practice in the field of ASD. In other words, this study contributes to an understanding of the role nutritional interventions play in assisting individuals with ASD.

The findings of this study emphasize the need for additional research that will focus on evaluating the efficacy and safety of some nutritional interventions for individuals with ASD. Future research should focus on well-designed randomized controlled trials to assess the impact of various nutritional interventions on symptoms, behavior, and overall quality of life in individuals with ASD. Systematic reviews and meta-analyses are necessary to gain a comprehensive understanding of the potential usefulness of these interventions. According to this study findings, nutritional interventions show promise as a potential treatment option for individuals with ASD. However, it is important to note that there is currently insufficient robust evidence to support certain nutritional intervention strategies, such as the use of GFCF, in this population. Thus, nutritionists should consider the potential benefits and risks of nutritional interventions while taking into account individual patient characteristics and preferences. In order to implement any of the nutritional intervention strategies that have been identified, it is crucial for nutritionists to take into account the overall treatment goals and address any concerns through collaborative decision-making with patients and their families.

CONCLUSION

This research has shown nutritional interventions that are being applied to assist individuals with ASD. These interventions involved the use of gluten-free casein-free diets, ketogenic diets, specific carbohydrate diets, prebiotic and probiotic supplements, as well as other dietary supplements such as vitamins. These nutritional interventions are beneficial for children with ASD. For GFCF diets, there is conflicting evidence regarding their effectiveness. More studies are needed to specifically substantiate the existing literature on the use of SCD and ketogenic diets for nutritional interventions. Further studies should be conducted to more clearly determine whether and how the GFCF diets can be effective in meeting the nutritional needs of individuals with ASD. Collaboration between researchers and practitioners is essential to ensuring the integration of evidence-based nutritional practices into clinical settings, ultimately benefiting individuals with ASD.

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Authors Contributions

CE and ERS initiated the research, conducted the literature search, analyzed and interpreted the data, and wrote the manuscript. CE and ERS approved the submitted version of this paper.

Conflict Of Interest

The authors have no conflict of interest to disclose.

Data Availability

The data related to this research are included in the manuscript in tabular formats.

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