Journal of Agricultural Engineering and Food Technology
p-ISSN: 2350-0085; e-ISSN: 2350-0263; Volume 6, Issue 1; January-March, 2019, pp. 64-70

http://www.krishisanskriti.org/Publication.html

The Symptoms of Neuro-Behavioral Conditions of ASD are Helped by Diet Free of Gluten and Casein when Followed Intensively for a Time Span of 24 Weeks Along with Intermittent one on one Skill Building Session- A Case Study

Heena Sahi[*1] and Himanshu Joshi[2]

[1]Pediatric Physiotherapist Consultant Head, Yellow Door World Pediatric Therapy Centre, Gurgaon
[2]Pediatric Physiotherapist Consultant Head, Vrridhi Pediatric Therapy Centre, Gurgaon
E-mail: [1]heenasahi97@gmail.com, [2]himanshupt20@gmail.com

Abstract—*Introduction-Effective treatments for core symptoms of autism spectrum disorders (ASD) are lacking. The gluten free, casein free (GFCF) diet is heralded by strong anecdotal parental reports to greatly improve and even "cure" symptoms of Autism Spectrum Disorders (ASD). The opioid-excess hypothesis of autism suggests that autism is the consequence of the incomplete breakdown and excessive absorption of peptides with opioid activity (derived from foods which contain gluten and casein), causing disruption to biochemical and neuro-regulatory processes. Biochemical evidence has indicated the presence of increased levels of peptides in the urine of people with autism, and previous behavioral studies have demonstrated a connection between the long term exclusion of gluten and casein from the diet and improvements in the behavior of some children with autism.*

Objective-*The purpose of this paper is to provide an overview of the efficacy of gluten and casein free diets as an intervention to improve behavior, cognitive and social functioning in individuals with autism. Research Design and Level of evidence: Descriptive Case Study, Level VI*

Procedure and Intervention- *A 4 year old child with concern of ASD was undergoing occupational therapy and special education interventions, but his behaviors and social interactions concerns were getting very difficult to manage and also interrupted his ability to focus for the task in hand. He was then advised a regular GF-CF diet by pediatric dietician for a duration of 24 weeks.*

Result and Discussion*: The subject was re-assessed on CARS, Social skill Checklist and Adhd rating scale that demonstrated improvement in domains of social interactions and decrease in impulsivity and inattention*

Conclusion*: Overall, there is little evidence that a GFCF diet is beneficial for the symptoms of ASD in children. Studies point to the need for identifying subsets of individuals who may be the best responders to the GFCF diet. Identifying these subsets is critically needed to enhance rigor in this research area.*

Keywords*: GFCF diet, Autism Spectrum Disorders, review, gluten-free, casein-free, dietary intervention.*

1. INTRODUCTION

1.1 Autism Spectrum Disorder and associated eating habits and choices

Autism Spectrum Disorder, or ASD, is a complex developmental and neurological condition that typically appears during the first three years of life. It affects brain function, particularly in the areas of social interaction and communication skills. Classic symptoms include delayed talking, lack of interest in playing with other children, not wanting to be held or cuddled and poor eye contact. There is no known cause for ASD, but both genetics and environment are believed to play a role. People with ASD often repeat behaviors and have narrow, obsessive interests. These types of behavior can affect eating habits and food choices, which can lead to the following health concerns. Someone with autism may be sensitive to the taste, smell, color and texture of foods. They may limit or totally avoid some foods and even whole food groups. Common dislikes include fruits, vegetables and slippery, soft foods. Kids with autism may have difficulty focusing on one task for an extended period of time. It may be hard for a child to sit down and eat a meal from start to finish. This problem usually is caused by a child's limited food choices. It typically can be remedied through a high-fiber diet, plenty of fluids and regular physical activity. Some stimulant medications used with autism, such as Ritalin, lower appetite. This can reduce the amount of food a child eats, which can affect growth. Other medications may increase appetite or affect the absorption of certain vitamins and minerals. If your child takes medication, ask your healthcare provider about possible side effects. For children with ASD, a nutritious,

balanced diet can make a world of difference in their ability to learn, how they manage their emotions and how they process information. Because children with ASD often have restricted diets as well as difficulty sitting through meal times, they may not be getting all the nutrients they need, particularly calcium and protein[1].

1.2 Gluten Free and Casein Free Diet and Its Features

There is increasing interest in the use of gluten- and casein-free diets for children with autism spectrum disorders (ASDs). Effective treatments for core symptoms of autism spectrum disorders (ASD) are lacking. The gluten free, casein free (GFCF) diet is heralded by strong anecdotal parental reports to greatly improve and even "cure" symptoms of Autism Spectrum Disorders (ASD). The opioid-excess hypothesis of autism suggests that autism is the consequence of the incomplete breakdown and excessive absorption of peptides with opioid activity (derived from foods which contain gluten and casein), causing disruption to biochemical and neuro-regulatory processes. Biochemical evidence has indicated the presence of increased levels of peptides in the urine of people with autism, and previous behavioral studies have demonstrated a connection between the long term exclusion of gluten and casein from the diet and improvements in the behavior of some children with autism. A gluten-free/casein - free diet is also known as the GFCF diet. It is one of several alternative treatments for children with autism. When following this strict elimination diet, all foods containing gluten (found in wheat, barley and rye) and casein (found in milk and dairy products) are removed from the child's daily food intake.Some parents of children with autism believe their children are allergic or sensitive to the components found in these foods. Some seek allergy testing for confirmation. Yet, even when no allergy is confirmed, many parents of autistic children still choose to offer the GFCF diet. Among the benefits they report are changes in speech and behavior or high sensitivity to foods containing gluten or casein. Children with autism, according to the theory, process peptides and proteins in foods containing gluten and casein differently than other people do. Hypothetically, this difference in processing may exacerbate autistic symptoms. Some believe that the brain treats these proteins like false opiate-like chemicals. The reaction to these chemicals, they say, leads a child to act in a certain way. The idea behind the use of the diet is to reduce symptoms and improve social and cognitive behaviors and speech. When someone is on a gluten-free diet, most bread and grain products are forbidden. Therefore, it is important to make sure that the child (or other person) receives ample fiber, vitamins, and minerals. Supplementation can help make up for the lack of these nutrients when foods containing gluten are eliminated.[2]

1.3 The gut and brain axis in Autism

Gastrointestinal symptoms are a common comorbidity in patients with autism spectrum disorders (ASD), even though the underlying mechanisms are largely unknown. In addition, alteration in the composition and metabolic products of the gut microbiome has long been implicated as a possible causative mechanism contributing to ASD pathophysiology, and this hypothesis has been supported by several recently published evidence from rodent models of autism induced by prenatal insults to the mother. Recent evidence in one such model involving maternal infection, that is characterized by alterations in behavior, gut physiology, microbial composition, and related metabolite profile, suggests a possible benefit of probiotic treatment on several of the observed abnormal behaviors. Mechanisms as to how the microbiota are affecting gut–brain signalling are only now being unravelled. These mechanisms may include alterations in microbial composition, immune activation, vagus nerve signalling, alterations in tryptophan metabolism, production of specific microbial neuroactive metabolites and bacterial cell wall sugars.[3]

1.4 Celiac Disease and Gluten

An extensive literature search was carried out to identify any randomised control trials of gluten and/or casein free diet as an intervention to improve behaviour, cognitive and social functioning in individuals with autism. Only three papers reporting on two randomised control trial were identified, two small scale trials the first with ten participants in each arm of the trial and the second with fifteen participants recruited into the trial. The results for the first study indicated that a combined gluten and casein free diet reduced autistic traits and the second study showed no significant difference in outcome measures between the diet group and the control group. This is an important area of investigation and large scale, good quality randomised control trials are needed. None of the studies reported on adverse outcomes or potential disbenefits. Gluten-restricted diets have become increasingly popular among parents seeking treatment for children diagnosed with autism. Some of the reported response to celiac diets in children with autism may be related to amelioration of nutritional deficiency resulting from undiagnosed gluten sensitivity and consequent malabsorption. A case is presented of a 5-year-old boy diagnosed with severe autism at a specialty clinic for autistic spectrum disorders. After initial investigation suggested underlying celiac disease and varied nutrient deficiencies, a gluten-free diet was instituted along with dietary and supplemental measures to secure nutritional sufficiency. The patient's gastrointestinal symptoms rapidly resolved, and signs and symptoms suggestive of autism progressively abated. This case is an example of a common malabsorption syndrome associated with central nervous system dysfunction and suggests that in some contexts, nutritional deficiency may be a determinant of developmental delay. It is recommended that all children with neuro developmental problems be assessed for nutritional deficiency and malabsorption syndromes.[4]

2. REVIEW OF LITERATURE

1. Mari- Bauset S et al (2014) conducted a literature review titles as "Evidence of the gluten-free and casein-free diet in autism spectrum disorders: a systematic review. They concluded future research should be based on this type of design, but with larger sample sizes.[5]

2. Milward C et al (2008) conducted a review study titled as Gluten and casein-free diets for autism spectrum disorder. They bought light to the subject by concluding that there is evidence of widespread use by parents of complementary and alternative therapies (CAM) including exclusion diets for their children with autism. Despite the problems of maintaining the integrity of such diets in the community it is possible to carry out randomised control trials to address these questions and more and adequately powered trials are needed in this area.[6]

3. Jennifer Harrison Elder et al (2015) conducted a metastasis study design titled as "A review of gluten- and casein-free diets for treatment of autism: 2005–2015.Evaluation of search results yielded eleven reviews, seven group experimental studies including five randomized controlled trials, five case reports, and four group observational studies published during the last 10 years. These studies represent a marked increase in the number of reported studies as well as increased scientific rigor in investigation of GFCF diets in ASD.[7]

4. Bui T et al(2013) conducted a research to decipher the " the relationship of autism and gluten. A literature review was performed, identifying previously published studies in which a gluten-free diet was instituted as an autism treatment. These studies were not limited to randomized controlled trials because only 1 article was available that used a double-blind crossover design. Most publish reports were unblinded, observational studies. In the only double-blind, crossover study, no benefit of a gluten-free diet was identified. Several other studies did report benefit from gluten-free diet. [8]

5. Piwowarczyk et al (2018) conducted a study titled as "Gluten- and casein-free diet and autism spectrum disorders in children: a systematic review." Six RCTs (214 participants) were included. With few exceptions, there were no statistically significant differences in autism spectrum disorder core symptoms between groups, as measured by standardized scales. One trial found that compared with the control group, in the GFCF diet group there were significant improvements in the scores for the 'communication' subdomain of the Autism Diagnostic Observation Schedule and for the 'social interaction' subdomain of the Gilliam Autism Rating Scale.[9]

6. Sausmikat J et al (2016) conducted a study on "Nutritional Therapy for Children and Adolescents with Autism Spectrum Disorders: What is the Evidence?" Applying defined inclusion and exclusion criteria, a systematic literature research in Pub Med, Cinahl and The Cochrane Library was conducted. Studies published earlier than 1999 were excluded. Study quality was assessed by using the CONSORT, STROBE or PRISMA checklist, respectively. Based on available data, no evidence based recommendations regarding nutritional interventions for children and adolescents with autism spectrum disorders can be made. Future studies need to clarify whether particular patients may yet benefit from certain diets.[10]

7. Marcason W et al (2009) conducted a research work on a study design titled as "What is the current status of research concerning use of a gluten-free, casein-free diet for children diagnosed with autism?"They concluded at that time two studies were underway concerning the use of such diets in the field of autism. A single blind trial in Norway and a double blind study in United States of America. Also stated that it is mandatory to evaluate the pros and cons of the dietary approaches to the treatment.[11]

8. Catassi C et al (2013) proposed a research study on "Non Celiac Gluten sensitivity: the new frontier of gluten related disorders." Non Celiac Gluten sensitivity (NCGS) was originally described in the 1980s and recently a "re-discovered" disorder characterized by intestinal and extra-intestinal symptoms related to the ingestion of gluten-containing food, in subjects that are not affected with either celiac disease (CD) or wheat allergy (WA). Recent studies raised the possibility that, beside gluten, wheat amylase-trypsin inhibitors and low-fermentable, poorly-absorbed, short-chain carbohydrates can contribute to symptoms (at least those related to IBS) experienced by NCGS patients. In this paper they reported the major advances and current trends on NCGS. [12]

9. A M Knivzberg et al (2013) conducted a "A Randomised, Controlled Study of Dietary Intervention in Autistic Syndromes." A randomly selected diet and control group with 10 children in each group participated. Observations and tests were done before and after a period of 1 year. The development for the group of children on diet was significantly better than for the controls.[13]

10. Sara Hurwitz et al (2013) conducted study titled as " The Gluten Free**,** Casein Free Diet and Autism." A review of the literature from 1999 to 2012 identified five studies meeting inclusion criteria. Research rigor was examined using an evaluative rubric and ranged from Adequate to Strong. In three of the studies, no positive effects of the diet were reported on behavior or development, even after double-blind gluten and casein trials. Two studies found positive effects after 1 year but had research quality concerns. Reasons why families continue to expend effort on GFCF diets despite limited empirical evidence are discussed[14]

3. CASE HISTORY

1. Miss X is a 4 years old girl with diagnosis of Autism Spectrum Disorder. The parents of the child first noted that the child was not able to develop any speech and communication even when she was 2 years like other kids in their family. She could not visually track and maintain the eye – contact. They also noticed that she did not mingle at all with little kids of her age during the same time and always started to cry in front of strangers and did not liked to be cuddled and cared for.

2. So the parents got a red flag and consulted a pediatrician in Max Hospital, Saket, New Delhi. The doctor referred it as developmental delay and further guided them to meet a developmental psychologist. The psychologist performed the standardized tests and confirmed to the parents that the subject was under spectrum. So the child and her parents were given the confirmed diagnosis of ASD by the age 2 .3 years. Thereafter she received rigorous speech and occupational therapy session at a pediatric therapy center located in Greater Kailash in New Delhi.

3. The speech was better after few years and she could indicate her needs, like and dislikes. Also, post the occupational therapy sessions, she showed improvement in play skills with motor planning and ideation abilities.

4. She had lot of inflexible and rigid patterns and behaviors. She would do lot humming and flapping of hands. She would scream and could not manage her tolerance. Because of her challenging behaviors, her social skills and emotional regulation became compromised.

5. She could perform brilliantly in academic tasks like english, numeracy, general awareness as per the special educator.

6. On account of her rigidity and extremes of behavior, she could not participate well in school and engage in group activities at school as well as group therapy sessions. All these concerns had a foundation of various sensory concerns and lack of repertoire of interests.

7. The parents re-consulted the developmental psychologist, by this time she was 3.5 years.

The psychologist suggested the parents to meet an ABA therapist and start the behavior modification therapy. The child responded to the behavior modification techniques for short span of time only. The child developed new behaviors as the time passed like playing with saliva, throwing objects in hand and pushing other, her impulsivity and aggression grew more with her passing age.

8. The parents were then suggested by the play therapist of the child to get the nutritional profile to be evaluated. Post the assessment it was noted dysregulated amino acid metabolism, increased homocysteine, and decreased folate, vitamins B-6 and B-12, and vitamin D.

9. The parents on recommendation of the pediatrician and nutritionist and play therapist went ahead and started GFCF diet for their child intensively. Along with this,the child took other therapies like special ed and play therapy sessions but only intermittently for total of 24 weeks starting from May 2018 to November 2018 during the course of GFCF diet.

4. METHODOLOGY, OUTCOME MEASURES AND INTERVENTION PROTOCOL

(i) Method

1. Subject: A four year old Girl with confirmed diagnosis of ASD

2. Criteria: Subject has only ASD with few features of Adhd like impulsivity and hyperactivity, celiac disease, leaky gut, IBS and food allergy and sensitivity is absent

3. Research Design: Descriptive Case Study

4. Level of Evidence: Level IV

(ii) Outcome Measures:

i) CARS (Childhood Autism Rating Scale is a 15 item behavioral rating scale)

ii) Conners ADHD Rating Scale is used to understand better social, behavior and academic issues in children

iii) Social Skills Checklist is used to monitor social reciprocation and emotional regulation of a child

The subject was pre and post assessed on three outcome measures mentioned above respectively to know the prognosis of GFCF diet intervention.

(iii) Intervention Program

A GFCF diet is an elimination diet in which a person does not eat anything that contains gluten or casein. On this regimen, all foods with gluten, which is a protein found in wheat, barley, and rye, and all foods containing casein, a protein found in dairy products such as milk, yogurt, and cheese, are removed from the diet, leaving other edibles like meat, eggs.

A GFCF diet is an elimination diet in which the person/subject concerned does not eat anything that contains gluten or casein. On this regime, the food item containing protein gluten which is found in wheat, barley, rye and all foods containing casein, a protein in dairy products like yogurt, milk, and cheese in removed from diet, leaving other edibles eggs, meat, chicken, nuts, fruits and vegetables are permissible.

The diet plan was adapted from “the Beginners Autism Diet Cook Book for children with Autism and their families” by Allison Lovering Iwata and also from “Getting your kid on a gluten free and casein free diet” by Susan lord. Susan lord is a doctor and head of an organization called “The Center of

Mind- Body Medicine" in Washington U S A. While the former, Allison Lovering Iwata is a therapist and diet consultant at the Idaho University, Pocatello, Idaho, USA. The parents frequently contacted the concerned dieticians for advise on frequency and quantity of food items according to age and weight of their child through mail and video calls.

The child won' t immediately comply to the changes in the diet, to which the play therapists and psychologist helped and applied their therapeutic strategies to build up the adaptability in the transition in the food eating pattern of child.

5. RESULTS

Post the 24 weeks of GFCF diet regime, there was a better and somewhat unexpected positive change in the maladaptive behaviors and negative developmental outcomes from baseline period. There was gradual improvement in various cognitive – behaviors.

Table 1: Baseline and Post – Intervention readings of CARS

CARS	BASELINE	POST
Score	38(moderate autism)	36(mild autism)

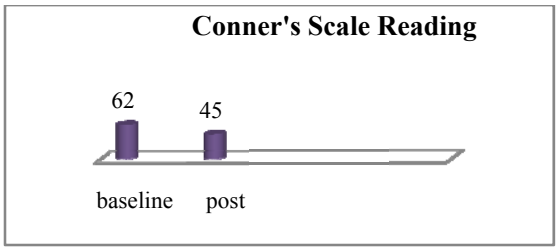

Figure 1: Cylinder bar chart depicting baseline and post – intervention readings of Conners ADHD rating scale

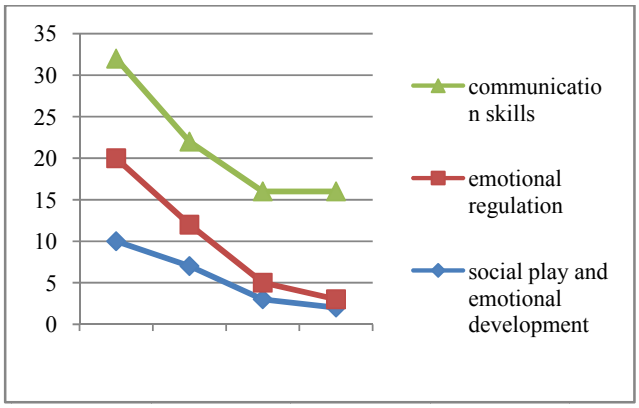

Figure 2: Line Diagram depicting baseline readings of Social Skill Checklist

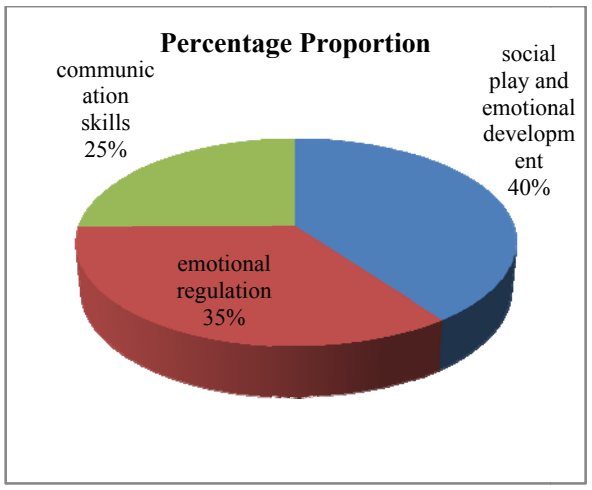

Figure 3: Pie chart depicting post-intervention readings of Social Skill Checklist

6. DISCUSSION

The diet is popular among families who have children with autism. Some propose that gluten (a protein found in wheat and some other grains) and casein (a protein found in dairy products) can worsen autism symptoms by causing inflammation in the gut that spreads to the brain.[15]

In relation to this, the elimination of gluten implies the exclusion of all food items containing wheat, oats, barley or rye, that is, all flours, bread, rusks, pasta, pastries, and other bakery products made with these cereals, while the elimination of casein means no intake of dairy products: milk, including breast milk, yogurt, cheese, butter, cream or ice cream, among others.[16]

Many surveys have shown that anywhere from 20% to 70% of respondents have tried a GFCF diet. Parents often report symptom improvement when placing their children on this diet.[15]

As the results of this case study suggests that there is change over in the social initiating, social responding and the child experiences fewer social behavioral symptoms. Thus it brings forward that GFCF intensive diet for mandatorily of 24 weeks span of time can be a boon for depleting ASD symptoms. Many studies in literature, case studies, metasynthesis or randomized control trials have emphasized on 6 to 12 weeks of diet program, thus questioning the duration of diet that is actually gainful for the person concerned. This research paper tries to brush away this perplexed assumption.

In relation to this, the elimination of gluten implies the

exclusion of all food items containing wheat, oats, barley or

On the other hand, in relation to children with autism spectrum disorders, these diets involve significant changes to their routine and such changes can, in themselves, may be affecting

their eating behaviors. Additionally, raising the ideology of elimination diets works against efforts to improve the social integration of such children, in that a personal diet is an isolating factor. But it is to be taken into note that the therapists and care givers engaged have provided lot of motivational strategies to promote the child to eat gfcf diet in group therapy sessions, birthday parties and other social surrounding. They have fabricated "the eating time" for the kid in a innovative way so that removes the perception that she is eating something different from her non gfcf peers.

A question might also arise as the child is also undergoing play therapy and other skill building classes which might actually be the true catalyst to accelerate the positive pool of changes in the behavior of the child. This can be clarified that the other therapies are playing role of an adjunct and are administered less regularly and infrequently. While the GFCF diet is main treatment intervention for those specific 24 weeks. This is to check the exact efficacy of this diet plan and prove the validity.

The connection between autism and gfcf diet is mainly linked to the abnormal activation of the opioid system due to excess receptor antagonists in the brain. It was found that gluten and casein are the source of compounds characterized with the activity of opioid peptides. This hypothesis, however, is being disputed. Some studies did report greater gut permeability in people with ASD, but others saw no difference. Moreover, highly sensitive measurement techniques consistently failed to find detectable concentrations of opioid peptides in the urine samples of patients with ASD. If significant amounts of opioid peptides were making it past the gut and into the bloodstream, urine tests should reveal their high levels as the body worked to eliminate them.[17]

This makes the data in literature limited both in quality and quantity. In the literature, figures are highly variable, For instance, Harrington et al reported rates of 66%; Wong et al,21 30%; Herndon et al,31.1%; Bandini et al,23 20.7%; and Hall et al24 and Sharp et al,25 30%groups, and Whiteley et al33 reported the appearance of a possible diet-related autism phenotype that seems to be emerging supportive of a positive dietary effect with slight improvement in certain groups with autism spectrum disorders. On the other hand, Sponheim did not observe any improvement after introduction of the elimination diet, but rather behavioral regression due to stigmatization. The first author to establish an association between the frequency and severity of schizophrenia and the intake of foods containing gluten and dairy products was Dohan. . It has been considered that gluten from cereal and casein from dairy products could be responsible, as they are a source of ''exorphins,'' peptides with opioid activity.

The trials conducted were of short duration, smaller sample sizes, were single blinded or not blinded at all and lastly there was no power calculation. This thereby fewer publications citing out safety of gluten free and casein free diet for ASD.

As a final recommendation, we underline that, when used, elimination diets must be at least as closely monitored as other types of intervention, to allow doctors, parents, and other caregivers to optimize treatments and hence health outcomes for these children. On the other hand, a diet-related specific end phenotype can be a target for future research and even a marker for the gluten-free, casein-free dietary intervention

The future research should include larger samples with longer duration of 24 weeks just like this case study.To assess the effectiveness in greater depths there should be consideration of both behavioral (verbal and non verbal communications, stereotypy and disruptive behaviors) as well as biomedical variables (urinary peptides, gliadins and nutrient intake.)As many questions are raised gluten and casein free diet may promote nutrient deficiencies in the children with ASD, thus many dietary supplements as potential treatments, including omega-3 fatty acids, melatonin vitamin D and a combination of vitamin B_6 and magnesium should also be investigated.

7. CONCLUSION

The adoption of gluten-free, casein-free diet, as an alternative treatment for ASD, is a poorly studied phenomenon. But the *gluten-free and casein-free* (GFCF) diet has become one of the more popular interventions among parents with ASD children. Also to make it a substantial treatment option both the domains of cognitive – behaviors through questionnaire as well as biomedical markers by laboratory tests of urinary peptides need to be considered.

8. ACKNOWLEDGEMENT

This research work has been supported by two well reputed pediatric therapy centers in Gurgaon, Haryana.

REFERENCES

[1] Marí-Bauset ,S, Zazpe I, Mari-Sanchis A, Llopis-González A, Morales-Suárez-Varela M, Evidence of the gluten-free and casein-free diet in autism spectrum disorders: a systematic review., **J Child Neurol.** 2014 Dec;29(12):1718-27

[2] Milward C Ferriter, M Calver,Gluten and Casein free diets in Autism.Cochrane Database of Systematic Reviews,2008. Issue 2

[3] ElderJ Kreider,A review of gluten and casein free diet for Autism, 2005-2015,Nutrition and DieterySupplements.1 December 2015, Volume 7, Pages 87-101

[4] Buie T, The relationship of autism and gluten. Clin Ther.2013 May;35(5):578-83.

[5] Piwowarczyk A, Horvath A, Łukasik J, Pisula E, Szajewska H, **Gluten**- and casein-**free diet** and autism spectrum disorders in children: a systematic review. Eur J Nutr. 2018 Mar;57(2):433-440

[6] Sausmikat J, Smollich M, Nutritional Therapy for Children and Adolescents with Autism Spectrum Disorders: What is the Evidence? Klin Padiatr. 2016 Mar;228(2):62-8.

[7] Wendy Marcason, RD, What Is the Current Status of Research Concerning Use of a Gluten-Free, Casein-Free Diet for Children

Diagnosed with Autism? Journal of the American Dietetic Association, 2009109 (3), pp. 572.
[8] Catassi C, Bai JC, Bonaz B, Bouma G, Calabrò A, Carroccio A, Non-Celiac **Gluten** sensitivity: the new frontier of **gluten** related disorders. **Nutrients.** 2013 Sep 26;5(10):3839-53
[9] Sarah Hurwitz, The Gluten-Free, Casein-Free Diet and Autism, **Journal of Early Intervention** 35(1):3-19 · October 2013
[10] Sekirov, I., Russell, S. L., Antunes, L. C. & Finlay, B. B. *Gut microbiota in health and disease*. Physiol. Rev. 90, 859–904 (2010)
[11] Clemente, J. C., Ursell, L. K., Parfrey, L. W. & Knight, R. *The impact of the gut microbiota on human health: an integrative view*. Cell148, 1258–1270 (2012).
[12] Banks, W. A. *The blood–brain barrier: connecting the gut and the brain*. Regul. Pept. 149, 11–14 (2008).
[13] James S, Montgomery P, Williams K. Omega-3 fatty acids supplementation for autism spectrum disorders (ASD) . Cochrane Database Syst Rev. (2011)
[14] Rossignol DA, Frye RE. Melatonin in autism spectrum disorders: a systematic review and meta-analysis . Dev Med Child Neurol. (2011)
[15] Mazahery H, et al. Vitamin D and Autism Spectrum Disorder: A Literature Review . Nutrients. (2016)
[16] Nye C, Brice A. Combined vitamin B6-magnesium treatment in autism spectrum disorder . Cochrane Database Syst Rev. (2005)
[17] Marí-Bauset S, et al. Evidence of the gluten-free and casein-free diet in autism spectrum disorders: a systematic review . J Child Neurol. (2014).