

Study of Effectiveness of Gluten- Free Casein- Free Diet in an Egyptian Sample of Autistic Children

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَقَدْ أَعْمَلُوا فَسَيَرَى اللَّهُ
عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ

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List of Abbreviations

AAN	: American Academy of Neurology
AAP	: American Academy of Pediatrics
ABC	: Autism Behavior Checklist
ADHD	: Attention deficit hyperactivity disorder
ADI-R	: Autism Diagnostic Interview-Revised
ADOS-G	: Autism Diagnostic Observation Schedule- Generic
ADOS-T	: Autism Diagnostic Observation Schedule- Toddler Module
ASD	: Autism spectrum disorder
ATEC	: Autism treatment evaluation checklist
AUC	: Analytical ultracentrifugation
CARS	: Childhood Autism Rating Scale
CS	: Cesarean section
DCD	: Developmental coordination disorder
DHA	: Docosaheptaenoic
DPPIV	: Dipeptidyl peptidase IV
DSM-5	: Diagnostic and Statistical Manual of Mental Disorders, fifth edition
EEG	: Electroencephalography
EPA	: Epicosapentaenoic
FDA	: Food and Drug Administration
GABA	: Gamma-aminobutyric acid
GARS	: Gilliam Autism Rating Scale
GDD	: Global developmental delay
GFCF	: Gluten free Casein free
GI	: Gastrointestinal
GSRS	: Gastrointestinal symptoms rating scale
HBDI	: Human biological data interchange
HS	: Highly significant
ICD-10	: International Classification of Diseases, 10 th revision
ID	: Intellectual disability

List of Abbreviations (Cont.)

IQR	: Interquartile ratio
IVIG	: Intravenous immunoglobulin
LBW	: Low birth weight
NICE	: National Institute for Health and Clinical Excellence
NREM	: Non rapid eye movement
NVD	: Normal vaginal delivery
OCD	: Obsessive compulsive disorder
ODD	: Oppositional defiant disorder
PDD-NOS	: Pervasive developmental disorders not otherwise specified
RDA	: Recommended Dietary Allowances
RDA	: Recommended Daily Allowance
RR	: Relative risk
RTT	: Rett syndrome
SGA	: Small gestational age
SIGN	: Scottish Intercollegiate Guidelines Network
SPSS	: Statistical Package for the Social Sciences
SSRI	: Selective serotonin reuptake inhibitors

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Introduction

Autism spectrum disorders (ASDs) represent a group of neurodevelopmental disorders typified by impairments in verbal and non-verbal communication, social withdrawal and stereotypical behaviors, which may or may not be associated with cognitive deficits, self-injurious behaviors and other neurological comorbidities. (*Majewska et al., 2010*)

Autism spectrum disorders (ASD) affect more than 1% of children and is usually evident in behaviour before the age of three years. (*Oono IP et al., 2013*). Genetics has a key role in the aetiology of autism, in conjunction with developmentally early environmental factors. (*Lai et al., 2013*)

Epidemiologic studies indicate that environmental factors such as toxic exposures, teratogens, perinatal insults, and prenatal infections such as rubella and cytomegalovirus account for few cases. (*Muhle et al., 2004*)

The incidence and prevalence of autism have dramatically increased over the last 20 years. (*Katherine et al., 2011*)

It is more prevalent in males, with a male : female sex ratio in the range 2:1 to 3:1. (*Lai et al., 2013*)

There is growing interest in possible dietary involvement in the aetiology and treatment of Autistic Spectrum Disorders (ASD). (*Cornish, 2002*). The most popular dietary intervention is the Gluten free -Casein free (GFCF) diet. (*McColl et al., 2013*)

It has been suggested that peptides from gluten and casein may have a role in the origins of autism and that the physiology and psychology of autism might be explained by excessive opioid activity linked to these peptides. Researches have reported abnormal levels of peptides in the urine and cerebrospinal fluid of people with autism. **(Millward et al., 2009)**

This gluten-free casein-free ketogenic diet used medium-chain triglycerides rather than butter and cream as its primary source of fat. Medium-chain triglycerides are known to be highly ketogenic, and this allowed the use of a lower ratio (1.5:1) leaving more calories available for consumption of vegetables with their associated health benefits. Secondary benefits included resolution of morbid obesity and improvement of cognitive and behavioral features. **(Herbert et al., 2013)**

Analyses indicated several factors to be potentially pertinent to a positive response to dietary intervention in terms of symptom presentation. Chronological age was found to be the strongest predictor of response, where those participants aged between 7 and 9 years seemed to derive most benefit from dietary intervention. **(Pedersen et al., 2013)**

Most parental and teacher reports of ASD children who, after being placed on the restricted diet, have been cured of their autism, having aquired language and showing marked improvement in social relatedness. **(Elder et al., 2006)**

Diet efficacy among children included greater improvement in ASD behaviors, physiological symptoms, and social behaviors. **(Christine et al., 2012)**

Aim of the Study

The Aim of this study is to evaluate and assess severity of autism before and after 6 months-Gluten free, Casein free diet in an Egyptian sample of autistic children.

Chapter 1

Autism

Definition :

Autism spectrum disorder (ASD) is a biologically based neurodevelopmental disorder characterized by impairments in two major domains: 1) deficits in social communication and social interaction and 2) restricted repetitive patterns of behavior, interests, and activities. (*American Psychiatric Association, 2013*).

ASD encompasses disorders previously known as autistic disorder (classic autism, sometimes called early infantile autism, childhood autism, or Kanner's autism), childhood disintegrative disorder, pervasive developmental disorder-not otherwise specified, and Asperger disorder (also known as Asperger syndrome) if the current diagnostic criteria are met. (*Augustyn, 2014*)

Historical review :

Autism was first reported by Kanner (1943) with a clinical description of 11 children showing “extreme aloneness from the very beginning of life, not responding to anything that comes to them from the outside world.” He proposed the behavioral combination of autism, obsessiveness, stereotypy, and echolalia as childhood schizophrenia. (*Won et al., 2013*)

However, until the 1980s, ASD was not accepted as an individual developmental disorder with a biological origin. In the early 1980s, studies demonstrated the high heritability of ASD and its association with other genetic syndromes, providing compelling evidence for a genetic etiology of ASD and fueling the conceptualization of

autism as a distinct neurodevelopmental disorder. From the definition of “childhood or early-onset schizophrenia” put forward by Kanner, autism was renamed “infantile autism” in 1980, “autism disorder” in 1987 and, more recently, “autism” or the umbrella term “ASD”. (*Won et al., 2013*)

The primacy of the social deficit is widely recognized, and lack of social reciprocity is a central part of the diagnosis. Beyond that, there have been great changes in the past decade in the conceptualization of autism and related disorders, eventually reflected in the draft of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). (*Chaste and Leboyer, 2012*). Figure (1) shows classification of pervasive developmental disorders

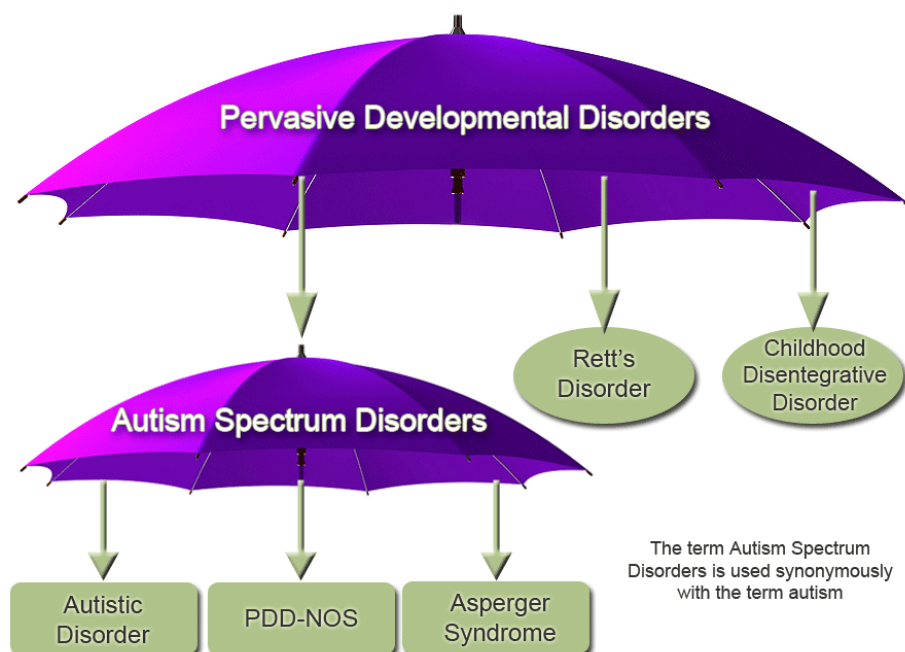


Figure 1 : Pervasive developmental disorders (*Crandell ,2010*)

Epidemiology:

Prevalence :

The reported incidence of autism spectrum disorders has increased dramatically over the past two decades. *(Schaefer, 2013)*

It is more prevalent in males, with a male : female sex ratio in the range 2:1 to 3:1. Most biological studies of autism have predominantly focused on males. *(Lia et al., 2013)*

Although there are increasing numbers of children diagnosed with ASD, it is not clear whether the increase is related to changes in diagnostic criteria, study methodology, a true increase in the incidence of autism, or a combination of these factors. *(Fombonne , 2009)*. Factors associated with an increased prevalence of Autism summarized in Table-1.

Table (1): Factors Associated with an increased prevalence of Autism :

- A sibling with autism
- Birth defects associated with central nervous system malformation and/or dysfunction, including cerebral palsy
- Gestational age less than 35 weeks
- Parental schizophrenia-like psychosis or affective disorder
- Maternal use of sodium valproate in pregnancy
- Intellectual disability
- Neonatal encephalopathy or epileptic encephalopathy, including infantile spasms
- Chromosomal disorders such as Down's syndrome
- Genetic disorders such as fragile X
- Muscular dystrophy
- Neurofibromatosis
- Tuberous sclerosis

(National Institute for Health and Clinical Excellence (NICE) 2011)