INTRODUCTION

The definition of Autism Spectrum Disorders (ASDs) indicates a diverse group of complex heterogeneous neuro-developmental conditions influencing the ability to relate to and communicate, as they are characterized by a wide range of cognitive, emotional and neurobehavioural abnormalities. The main core symptoms include impairments in social skills and communication, restricted interests, repetitive and stereotypic verbal and non-verbal behaviours ***(Siniscalco et al., 2012).***

They are enigmatic conditions having their origins in the interaction of several genes and environmental factors. More in depth, ASD are multifactorial and polygenic disorders, as they result from a complex combination of genetic and environmental (i.e. air pollution, organophosphates, heavy metals), and immunological factors ***(Herbert, 2010).***

Nowadays, ASDs are being recognized as a real public health problem ***(Sequeira et al., 2012).*** Their frequency is dramatically increasing in the last years ***(Siniscalco, 2012).*** Unfortunately, too often ASDs are underestimated and affected children are poorly addressed. The autism diagnosis is suffering by the lack of a specific biomarker for autism, making these pathologies very difficult to be diagnosed. Indeed, despite many research efforts, currently there are no biomarkers for an exact ASD diagnosis. A correct and an early diagnosis is required for future ASD management ***(Siniscalco et al., 2013).***

Anthropometric assessment might be an additional research helpful to early diagnosis. There has been attempts to correlate anthropometric variables with different specific psychiatric disorders. As a consequence of their behavioral differences or associated comorbid conditions, some children with autism or other autism spectrum disorders might have anthropometric development that deviated from normal children ***(Bauset et al., 2013). Berry et al., (2012) and Marcus Autism Centre-Atlanta (2012)*** have focused on aberrations in conduct during meals, selectivity of food as well as problems in timing of meals.

Early identification allows early intervention. children with autism spectrum disorders may be at risk of suboptimal development due to poor nutrition (eg, low dietary calcium and vitamin D intake) associated with repetitive or restrictive eating behaviors ***(Schreck et al., 2004),*** the adoption of gluten- and/or casein-free diets ***(Knivsber et al., 2001)*** the use of medications that suppress appetite or interfere with metabolism, and/or decreased or limited physical activity and exposure to sunlight (ie, low endogenous vitamin D) associated with activity restriction, movement disorders, and requirements for supervision ***(Knivsber et al., 2002).***

On the other hand, there is a growing rate of obesity in autistic children and adolescents ***(Memari et al., 2012)*** especially in girls rather than boys with ASD. Different dietary patterns and lifestyles that the children with ASD have can be associated with the development of under or overweight ***(Bicer et al., 2013).***

Children with autism can be normocephalic, macrocephalic and microcephalic ***(Miles et al., 2000).*** The prevalence of macrocephaly among autism cohorts is greater than that seen in children with learning delays, where the prevalence of macrocephaly can be up to 15% of children ***(Williams et al., 2008).***

The microcephalic autistic children appeared to have a unique genetic profile. This different genetic profile for the microcephalic individuals suggests that the pathogenesis of their autism is also different, perhaps involving different genes. Another possible explanation is that genetic and environmental insults on brain growth resulted in microcephaly ***(Miles et al., 2000).***

The abnormal growth is not specific to the head, but is more generalized and also present in height and/or weight. Thus, growth rates of head circumference in relation to height appear abnormal in the first years of life in ASD and together may give the most accurate picture of the nature of early growth abnormalities in ASD ***(Schrieken, 2013).***

AIM OF THE WORK

The purpose of our study is to examine body height, body weight, body mass index, circumferences of (mid upper arm, hip,head and waist) and skin fold thickness in Egyptian children diagnosed with autism spectrum disorders.

Also to compare diagnostic reliability and validity for the Childhood Autism Rating Scale and Gilliam Autism Rating Scale.

Autism Spectrum Disorders

Definition:

The definition of Autism Spectrum Disorders (ASDs) indicates a diverse group of complex heterogeneous neuro-developmental conditions influencing the ability to relate to and communicate, as they are characterized by a wide range of cognitive, emotional and neurobehavioral abnormalities. The main core symptoms include impairments in social skills and communication, restricted interests, repetitive and stereotypic verbal and non-verbal behaviors ***(Siniscalco et al., 2012).***

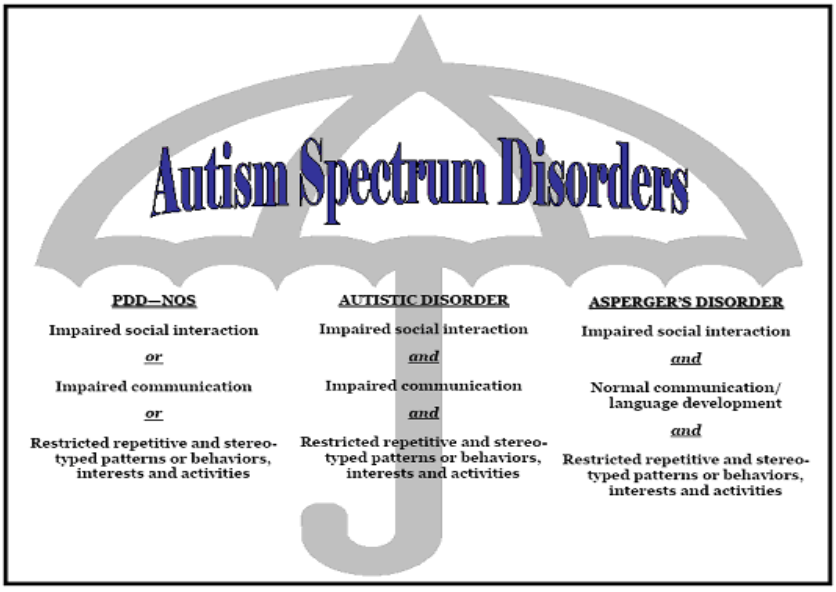

Figure (1): Autism Spectrum Disorders. In May 2014, the American Psychiatric Association published sweeping new guidelines for the diagnosis of autism spectrum disorders in its Diagnostic and Statistical Manual of Mental Disorders, or DSM-5. Changes in DSM-V this spectrum has included separate diagnoses: Autistic Disorder, Rett's Disorder, Childhood Disintegrative Disorder, Asperger's Syndrome, and Pervasive Developmental Disorders PDD Not Otherwise Specified.

The ASDs aetiology, pathophysiology and defined molecular and cellular mechanisms of pathogenesis remain still unclear. There is no effective pharmacotherapy for treatment of core symptoms of ASDs and current drug options target specific symptoms, without addressing the basic underlying etiologies ***(Stanković et al., 2012).***

Etiology:

The etiology of autism is unclear and autistic symptoms had been attributed to an abnormal functional imbalance in neurotransmitter amines such as dopamine, noradrenaline and serotonin. Autistic children had lower levels of some plasma amino acids except for glycine and glutamic acids and phosphoserine were increased with normal serum levels of urea, ammonia, total proteins, albumin and globulins (alpha 1, alpha 2, beta and gamma) ***(El-Baz et al., 2014).***

These enigmatic conditions have their origins in the interaction of multiple genes and environmental factors. Dysfunctions in social interactions and communication skills, restricted interests, repetitive and stereotypic verbal and non-verbal behaviors are the main core symptoms. Several biochemical processes are associated with ASDs: oxidative stress, endoplasmic reticulum stress, decreased methylation capacity, limited production of glutathione, mitochondrial dysfunction, intestinal impaired permeability and dysbiosis increased toxic metal burden and immune dysregulation.

Current available treatments for ASDs can be divided into behavioral, nutritional and medical approaches, although no defined standard approach exists ***(Siniscalco et al., 2013).***

The autism diagnosis is suffering by the lack of a specific biomarker for autism, making these pathologies very difficult to be diagnosed. Indeed, despite many research efforts, currently there are no biomarkers for an exact ASD diagnosis. A correct and an early diagnosis is required for future ASD management. Novel findings in genetics and neuroscience are achieved in order to better elucidate the molecular, biochemical and cellular basis of ASDs, focalizing the real needs of every patient. Novel treatments are strictly related to these findings in order to design new strategies in the pharmacotherapy of ASDs ***(Canitano, 2012).***

Newest research projects are being performed: the involvement of stem cells as possible therapeutic option in ASDs ***(Sequeira et al., 2012)***; gluten and casein antibodies production related to gluten and casein sensitivity in ASDs; involvement of glutamatergic and GABAergic neurotransmission signals; changes in vitamins levels and their link with the cellular oxidative state; gene expression changes in ASDs; interleukins and cytokines expressions; role of immune system in ASDs are only some examples of new research ways in exploring ASDs ***(Siniscalco et al., 2013).***

Epidemiology:

Prevalence:

The prevalence of autism has been steadily increasing since the first epidemiological study, which showed that 6,1 of every 10 000 individuals in the UK had autism in 2007. The increase is probably partly a result of changes in diagnostic concepts and criteria ***(Fisch et al., 2012).***

However, the prevalence has continued to rise in the past two decades, particularly in individuals without intellectual disability, despite consistent use of DSM-IV criteria ***(Keyes et al., 2012).*** However, the rise is probably also due to improved awareness and recognition, changes in diagnosis, and younger age of diagnosis ***(Elsabbagh et al., 2012).***

Overall ASD prevalence for the Autism and Developmental Disabilities Monitoring Network 2010 surveillance was 14.7 per 1,000(one in 68) children aged 8 years, ASD prevalence was 23.7 per 1,000 (one in 42) boys and 5.3 per 1,000 (one in 189) girls (prevalence ratio:4.5 for all sites combined). the prevalence of ASD with co-occurring intellectual disability was 4.7 per 1,000 children aged 8 years, whereas prevalence of ASD without co-occurring intellectual disability was 10.2 per 1,000 in 2010 ***(CDC, 2014).***

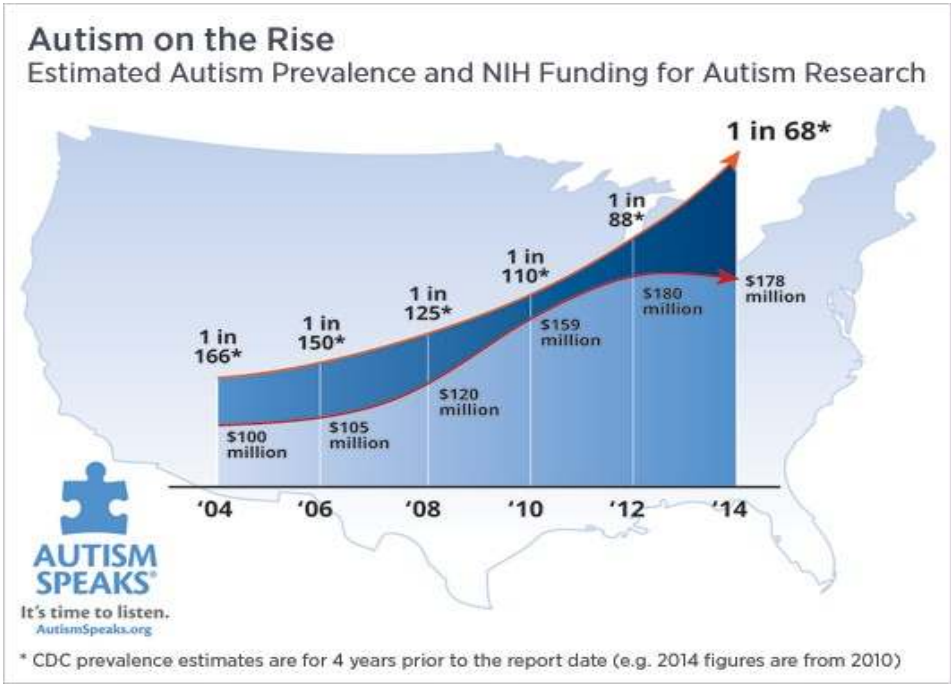

Figure (2): Autism on the rise. Data & Statistics: 10 Things to Know About New Autism Data ***(CDC, 2014).***

Seif Eldin et al., (2008), focused on Arab countries, but included two African countries (Egypt and Tunisia) in North Africa. The prevalence of ASD among children with developmental disorders in Egypt and Tunisia was documented as 33.6% and11.5% respectively. Prevalence of autistic spectrum disorders in Saudi Arabia is 6:1000 ***(Al-Salehi et al., 2009).*** A study conducted in UAE found a weighted prevalence of 29 per 10,000 for PDD in the 3-year-old UAE national population ***(Eapen et al., 2007).***

Autism affects 4–5 times more males than females ***(Fombonne et al., 2011)***. However, large-scale population-based studies ***(Idring et al., 2012; Saemundsen et al., 2013)*** have shown that 2–3 times more males are affected. Females with autism might have been under-recognised ***(Baron-Cohen et al., 2011).***

Risk and protective factors:

Epidemiological studies have identified various risk factors, but none has proven to be necessary or sufficient alone for autism to develop ***(Rodier et al., 2011).*** Understanding of gene–environment interplay in autism is still at an early stage ***(Corrales et al., 2011).***

Advanced paternal or maternal reproductive age, or both, is a consistent risk; the underlying biology is unclear, but could be related to germ line mutation, particularly when paternal in origin ***(Lampi et al., 2013).*** Meta-analyses of epidemiologic studies have shown that autism risk in offspring increases with advancing age of either parent. ***Sandin et al., (2012)*** reported that, after controlling for paternal age, the adjusted relative risk for autism was 1.52 in the offspring of mothers aged 35 years or older compared with mothers aged 25-29 years. ***Hultman et al., (2011)*** found that, after controlling for maternal age, offspring of men aged 50 years or older were 2.2 times more likely to have autism than offspring of men aged 29 years or younger.

Gestational factors that could affect neurodevelopment, such as complications during pregnancy ***(Brown et al., 2012)*** and exposure to chemicals ***(Volk et al., 2013)*** have been suggested to increase risk of autism.

A broad, non-specific class of conditions reflecting general compromises to perinatal and neonatal health is also associated with increased risk ***(Gardener et al., 2011).*** ASD was 4 imes more prevalent in infants <27 weeks compared with term infants. Each week of shorter gestation was associated with an increased risk of ASD. High frequency ventilation and intracranial hemorrhage were associated with ASD among infants <34 weeks ***(Kuzniewicz et al., 2014).*** Exposure of the mother to selective serotonin reuptake inhibitors, particularly during the first trimester, may increase the risk that her offspring will develop an ASD ***(Croen et al., 2011).***

Severe, early-gestation maternal hypothyroxinemia is associated with an increased risk of having a child with autism by almost 4-folds ***(Román et al., 2013; Brooks, 2013).***

Conversely, folic acid supplements before conception and during early pregnancy seem to be protective ***(Suren et al., 2013).***

Familial factors influence the risk for autism spectrum disorders. The rate of autism spectrum disorder in children born into families that already have a child with an autism spectrum

disorder is as high as18.7 %, and the risk is twice as high in children born to families with 2 or more children with an autism spectrum disorder. Girls born to a family that has a child with an autism spectrum disorder have 2.8 times the risk of having such a disorder ***(Ozonoff et al., 2011).***

Fragile X syndrome, a condition associated with autism, can be identified through genetic testing ***(Garber et al., 2008).*** Autism has also been associated with tuberous sclerosis, a disorder with specific genetic mutations ***(Curatolo et al., 2008).***

Air pollutant exposure may interact to increase the risk of autism spectrum disorder ***(Volk et al., 2014).*** Studies have reported an association between exposure to the organochlorine pesticides dicofol and endosulfan during the first trimester of pregnancy and the subsequent development of autism spectrum disorder in children. Potential mothers can wisely be advised to avoid exposure to organochlorine pesticides ***(Roberts et al., 2007; Samson et al., 2007).***

The rates of autism spectrum disorder diagnosis did not differ between immunized and non-immunized ***(Abu Kuwaik et al., 2014).*** A study by **Wakefield in 1998** claimed to link autism to vaccines in children and Media spread this correlation like wildfire resulted in:

- Millions of parents have refused to vaccinate their children.

- Measles and Rubella cases increased dramatically
- Many parents still refuse to vaccinate their children because they are afraid it will cause autism.

However, ***Fombonne*** refused the claim that vaccines are the culprit ***(Fombonne et al., 2001).***

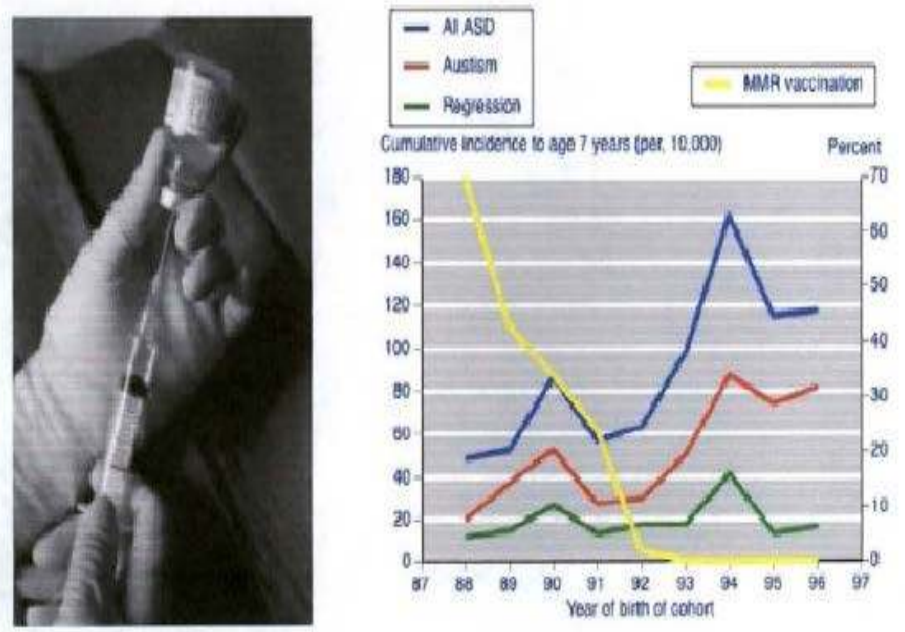

Figure (3): The graph above illustrates the increase in cases of autism and other autism spectrum disorders even after the cessation of the MMR vaccination. Evidence shows that MMR vaccinations are helpful, rather than harmful to the children who receive them ***(Fombonne and Chakrabarti, 2001).***

Co-occurring conditions:

More than 70% of individuals with autism have concurrent medical, developmental, or psychiatric conditions ***(Lai et al., 2013).*** Some co-occurring conditions, such as epilepsy and depression can first develop in adolescence or adulthood ***(Simonoff et al., 2013).***

Developmental Co-occurring conditions as Intellectual disability affects about 45% of individuals with autism ***(Lai et al., 2013).*** Its Prevalence estimate is affected by the diagnostic boundary and the definition of intelligence (e.g., whether verbal ability is used as a criterion). General medical co-occurring conditions as epilepsy that affects 8– 30% increased frequency in individuals with intellectual disability or genetic syndromes, gastrointestinal problems that affects 9–70% common symptoms include chronic constipation, abdominal pain, chronic diarrhea, and gastro-esophageal reflux. Genetic syndromes affects about 5% ***(Lai et al., 2013).*** Collectively called Syndromic Autism examples include: fragile X syndrome, Rett syndrome, tuberous sclerosis complex, Down's syndrome, phenylketonuria, CHARGE syndrome, Angelman syndrome. Psychiatric co-occurring conditions as: anxiety 42–56%, depression 12–70%, obsessive-compulsive disorder7–24%, oppositional defiant disorder 16–28%, eating –5%. Behavioural co- occurring conditions as aggressive behaviours ≤68% ***(Lai et al., 2013).***

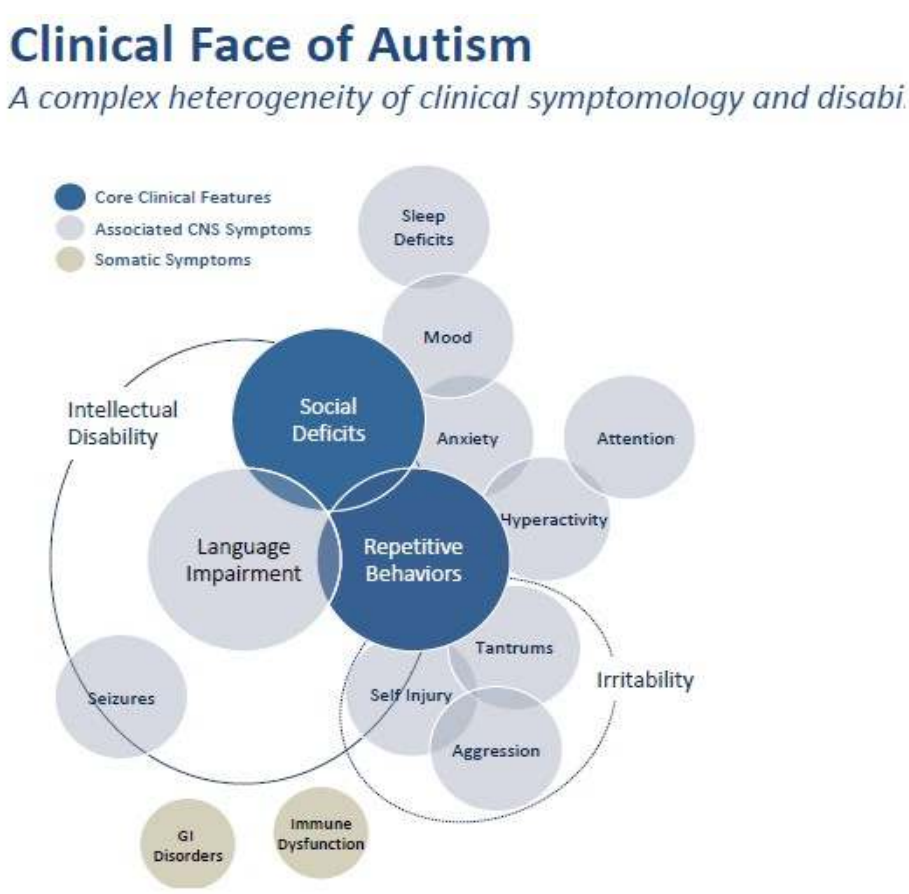

Figure (4): Clinical face of autism ***(Ring, 2013).***

Prognosis and outcome:

A meta-analysis showed that individuals with autism have a mortality risk that is 2•8 times higher than that of unaffected people of the same age and sex. This difference is mostly related to co-occurring medical conditions ***(Bilder et al., 2013).***