REVIEW ARTICLE

AUTISM SPECTRUM DISORDER - AN OVERVIEW

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ABSTRACT

Autism spectrum disorder is one of the childhood psychiatric disorders. As the awareness of parents regarding the mental health of their children is increasing day by day, many cases of autism spectrum disorder come into focus. This article is a sincere effort to give an overview of Autism Spectrum Disorder.

INTRODUCTION :

The autism spectrum disorders (ASD) are characterized by disturbancesin social interactions, language, and communication[1]. Two-thirds of cases have evidence of atypical development before 12 months, and one-third of cases have a regression in speech and language before 18 months[2].

HISTORY AND NOSOLOGY :

In last 60yrs,autism has been puzzling, fascinating and massively researched[3].It was Kraepelin's description of dementia praecox which was rapidly extended to children, and the terms childhood schizophrenia and childhood psychosis became synonymous[4]. The first concept of ASD began with Leo Kanner's (1943) description of 11 children with "fascinating peculiarities" which he labeled as early infantile autism. Kanner noted that there was lack of social relatedness in these children, which included their seeming not to acknowledge the presence of others and their difficulties in recognizing the feelings of others[1]. They had also the problem in language (when it developed at all) - echolalia, pronoun reversal, and concreteness. Behaviorally, these children engaged in repetitive, apparently purposeless activities (stereotypy), and were intolerant of change[5].

In 1944 Asperger described a similar syndrome, but in this group, children had more language and communication skills than the patients reported by Kanner and this collection of symptoms were calledautisticpsychopathy[1]. In 1966, Andreas Rett described an unusual syndrome in girls with initial normal development, subsequent head growth deceleration, and the development of characteristic clinical findings such as breathing difficulties, movement problems, in addition, some features suggestive of autism were present[6]. Later his findings were replicated and extended by Hagberg et al[7].

Lornaintroducedtheconceptofanautism"spectrum" in the 1980s. She was among the first to realize that autism could be considered dimensionally and affected people of all ages and abilities. Her 1981 paper on Asperger's work introduced the term Asperger's syndrome[8].

It is seen that in the first and second editions of DSM (DSM-I and DSM-II), autism was not officially recognized; rather, it was viewed as being on some continuum with schizophrenia. In DSM-III-R, more attention was given to developmental concerns and a set of 16 very detailed criteria were provided, which were grouped in the traditional three

categories of social disturbance, communicative disturbance, and restricted and repetitive behaviors. There was also multiaxial placement of autism and other pervasive developmental disorders[4]. In DSM IV Pervasive developmental disorder was included where five disorders - autistic disorder, Rett's disorder, childhood disintegrative disorder, Asperger's disorder, and pervasive developmental disorder not otherwise specified were described[5]. Recently, in DSM5, new name ofAutism Spectrum Disorder was given which includes DSM IV's Autistic Disorder (autism), Asperger's Disorder, Childhood Disintegrative Disorder, & PDD-NOS; Rett's disorder is excluded from DSM5[9].

EPIDEMIOLOGY :

Autistic disorder is believed to occur at a rate of about 8 cases per 10,000 children (0.08 percent)[10]. Recent surveys suggest that the rate of all PDDs is about 60 per 10,000. The prevalence of autism today is estimated at 13 per 10,000, Asperger's disorder is approximately 3 per 10,000, and childhood disintegrative disorder is very rare at about 0.2 per 10,000[11]. Male : Female ASD ranges from 2:1 – 6.5:1. Autistic disorder is four to five times more frequent in boys than in girls. Rett's disorder is exclusively a female disorder[10].

ETIOLOGY :

Currently, the precise etiology and pathogenesis of ASDs are not known. Efforts are made to understand the etiology of ASD[12].

GENETIC FACTORS :

Genetic studies in ASD found that there is involvement of chromosomes 2q21–33, 3q25–27, 3p25, 4q32, 6q14–21, 7q22, 7q31–36, 11p12–13, 17q11–21[13]. Due to Deletions of chromosome 16p11 not only ASD but also mental retardation and other developmental disabilities are seen[14]. Mode of inheritance of autism is not Mendelian but rather must reflect a polygenic, multifactorial etiology with multiple gene-gene and/or gene-environment interactions[15].

Chromosomal abnormalities associated with ASD-Fragile X syndrome (trinucleotide expansion at Xq27.3), Down's syndrome (trisomy 21), Prader-Willi syndrome (deletion or maternal isodisomy of chromosome 15)[12].

Twin studies show that concordance rate is more in monozygotic twins than dizygotic twins in ASD[16,17].

IMMUNOLOGICAL FACTORS :

It is seen that immune system dysregulation is one of the causes of ASD which is likely to precede the inflammatory and autoimmune manifestations in the brain. Abnormal levels of blood lymphocytes, incomplete or partial activation of T-cells following stimulation, as well as lower levels and decreased activity of circulating natural killer (NK) cells are seen in ASD. Exposure to pediatric vaccine like MMR vaccine are one of the causes of ASD[18]. Autoantibodies against fetal brain proteins have also been detected in mothers of ASD children, suggesting a disruption of BBB in utero[19].

PERINATAL FACTORS :

Many studies have shown increased rates of pre-, peri-, and neonatal complications in children with autism[5].

NEUROANATOMICAL FACTORS :

Many neuroimaging studies have found that abnormality of some brain areas is one of the causes of ASD. In 1998, Muller and colleagues showed that a small group of high functioning ASD adults had the reversal of the usual left hemisphere dominance when listening to sentence[1]. MRI studies show that autistic children have larger brain volume, although autistic children with severe mental retardation generally have smaller heads. There is increase in size in the occipital lobe, parietal lobe, and temporal lobe[5].

The temporal lobe is believed to be one of the critical areas of brain abnormality in autistic disorder and it is based on reports of autistic-like syndromes in some persons with temporal lobe damage. It is seen that decrease in cerebellar Purkinje's cells is one of the causes of ASD, which is believed to account potentially for abnormalities of attention, arousal, and sensory processes. Lesions in orbital & medial pre-frontal cortex andhypoactivity in amygdala-cortical loopassociated with loss of social cognitive process are one of the causes of ASD[10].

NEUROCHEMICAL FACTORS :

In the last few decades, it is seen that one-third of patients with autistic disorder have high plasma serotonin concentrations. High concentration of homovanillic acid (the major dopamine metabolite) in cerebrospinal fluid (CSF) is associated with increased withdrawal and stereotypes in ASD. Symptom severity decreases as the ratio of 5-hydroxyindoleacetic acid (5-HIAA, metabolite of serotonin) to homovanillic acid in CSF increases[5].

PSYCHOSOCIAL AND FAMILY FACTORS :

It is seen that autistic children have exacerbated symptoms due to psychosocial stressors. Disorders may be extremely sensitive to even small changes in their families and immediate environment.

According to Leo Kanner, emotional factors might be involved in the pathogenesis of autism which led others to conclude that the condition was always caused by the experience of a "refrigerator" mother who was not responsive to the child's emotional needs[12].

CLINICAL FEATURES :

AGE OF ONSET :

It typically occurs in young children before the age of 3 years[5].

SOCIAL DISTURBANCES :

It is seen that autistic children do not exhibit the expected level of subtle reciprocal social skills that demonstrate relatedness to parents and peers[10]. Lack of eye contact, fewer socially directed behaviors such as facial expressions, vocalizations, or pointing, and a lack of interest in other children are typical[4].

Autistic children often do not acknowledge or differentiate the most important persons in their lives-parents, siblings, and teachers and may show extreme anxiety when their usual routine is disrupted, but they may not react overtly to being left with a stranger. When autistic children have reached school age, their withdrawal may have diminished and been less obvious, particularly in higher-functioning children. These children also haveproblem with making friends and inability to play with them Cognitively, children with autistic disorder are more skilled in visual-spatial tasks than in tasks requiring skill in verbal reasoning[10].

DISTURBANCES IN COMMUNICATION AND LANGUAGE :

Autistic children also have the problem with communication. Deficits in language development and difficulty using language to communicate ideas are among the principal criteria for diagnosing autistic disorder[4]. When individuals with autism do speak, their language is remarkable in various ways like echolalia,speech tends to be less flexible,some may have nonreciprocal speech in nature,lack of meaning /empathy in speech,intonation is monotonic and robot-like[10]. There are also deficits in nonverbal communication, including the use of gestures such as pointing, showing and nodding. Ther is also failure to develop the usual pattern of symbolic imaginative play[12].

RESTRICTED, REPETITIVE AND STEREOTYPIC PATTERNS OF BEHAVIORS, INTERESTS, AND ACTIVITIES :

Autistic Children often have difficulty in tolerating change and variation in routine. In this children repetitive behaviors are commonly observed which include motor mannerisms such as hand-flapping, rocking, flipping objects or lining up toys in a fixed fashion[12]. These children also have the obsessive desire for sameness, interested in repetitive activities e.g. collecting things, memorizing numbers, compulsive behavior (arranging objects in certain ways), ritualistic behavior and attachment to particular inanimate object[10].

INTELLECTUAL FUNCTION :

Some chlidren with Autism havepoor intellectual function (70-75%). About 30 percent of children function in the mild to moderate range, and about 45 to 50 percent are severe to profoundly mentally retarded[10].

OTHER ASSOCIATED FEATURES :

These children also present with self-injury and aggression, inappropriate affect, sudden mood change, laughing, crying, giggling to self without apparent reason, hypoactive/hyperactive response to sounds, pain, erratic sleep patterns, difficulty in falling asleep, frequent nocturnal awakening, liking/disliking particular food, refusal to try new food, pica; neurological problem like hypo or hypertonicity, choreiform movements, abnormal posture and gait, tremor, myoclonic jerking, epilepsy-10-35% by young hood[10].

ASSOCIATED PHYSICAL ILLNESS :

The higher-than-expected incidence of upper respiratory infections and other minor infections, gastrointestinal symptoms, excessive burping, constipation, and loose bowel movements, increased incidence of febrile seizures[12].

DIFFERENTIAL DIAGNOSIS :

Differential diagnosis of ASD are childhood onset schizophrenia, structural language disorder, intellectual disability, acquired epileptic aphasia, selective mutism, psychosocial deprivation, hearing impairment, and visual impairment[20]

COURSE AND NATURAL HISTORY :

With age child with autism has undergone many changes. During preschool years, autistic child has poor social interaction, no speech or echolalia in speech, sterotyped behavior. When they enter school some children develope improved interaction, less echolalia but stereotypic, ritualistic behavior persists. During the age of puberity, some child may understand about menstruation, sexual drive; but some have public masturbating behavior[1].

Though autism is generally a lifelong disability with earlier intervention, long-term outcome improves for many individuals, with perhaps 15 to 20 percent able to achieve independence and self-sufficiency in adulthood and perhaps another 20 to 30 percent of individuals able to function with occasional support[10].

CHARACTERISTICS OF AUTISTIC SPECTRUM DISORDER :

DISORDER	CLINICAL FEATURE
AUTISM	Severe impairment of social interaction and communication Restricted, repetitive, and stereotypic patterns of behavior, interest, and activities Onset before age 3 Mental retardation common
Asperger disorder	Impairment in social interactions Preoccupation with one or more restricted patterns of interest No delay in language or cognitive development Nonverbal learning disability cognitive profile common Motor clumsiness
Childhood disintegrative disorder	Normal development for at least 2 years Severe loss of developmental skills before 10 years of age
Rett disorder	Normal at birth, but onset by 2 years Deceleration of head growth Loss of motor skills with hand-wringing movements; gait disturbance Loss of language Loss of social engagement
PDD, NOS	Does not meet criteria for autism because of late age of onset, atypical symptoms, or subthreshold symptoms

ASSESSMENT :

There are no diagnostic laboratory tests for ASD. The diagnosis of ASD based on complete psychiatric examination, full developmental history, including all information regarding pregnancy and delivery[1].

ASSESSMENT TOOL :

- Autism Diagnostic Observation Schedule-Generic (ADOS-G)
- Checklist for Autism in Toddlers (CHAT)
- Modified Checklist for Autism in Toddlers (M-CHAT) - a 23-item parent questionnaire modified from the CHAT.
- Pervasive Developmental Disorders Screening Test (PDDST)
- Childhood Autism Rating Scale (CARS)[12]

TREATMENT :

The main aims of the treatment of ASD are :

1. To facilitate and stimulate the normal development of cognition, language, and socialization;
2. To decrease autism-bound maladaptive behaviors such as rigidity, stereotypy, and inflexibility;
3. To reduce or even eliminate non-specific maladaptive behaviors such as hyperactivity, irritability, and impulsivity; and
4. To alleviate stress and burden for the family[12].

NONPHARMACOLOGICAL AND BEHAVIORAL TREATMENTS

Autistic disorder is a chronic disorder with a

changing course and therefore it requires the long-term course of treatment that includes the necessity of an intervention with various treatments at different times[1].

PSYCHOSOCIAL TREATMENT :

- Educational
- Curricula that target communication
- Behavioral techniques
- Structured milieu
- Vocational interventions such as speech training and placement : other specialized and language therapy,
- Physical therapy and occupational therapy
- Social skills training
- Individual psychotherapy for high-functioning individuals[1].

PHARMACOTHERAPY :

Before starting pharmacotherapy clinician should explain about the treatment :

Medications are only to reduce the target symptoms, it doesnot alter the etiology of the disease; they should be also warned about the side effect of the given drugs[1].

Drugs mainly used for symptomatic management. For restricted repetitive behaviorsmost widely prescribed medications SSRIs (fluoxetine, fluvoxamine, sertraline, citalopram, and escitalopram)[21]. In cases where there are increased activation and agitation second-generation antipsychotics, anticonvulsants and the neuropeptide, oxytocin is useful[21].

In patients with ADHD features, methylphenidate and atomoxetine areuseful. For increased aggression, irritability second generation antipsychotics, anticonvulsants andlithium are useful[21].

CONCLUSION :

In last few years there are many types of researches regarding its neurobiology,early identification, and intervention. But till now there is no specific treatment for ASD[22]. Nevertheless, there is still a need to identify more accurately those abnormalities that are potentially specific as well as to understand the possible interactions among different processes early in development[12].

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