International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

A Systematic Review on Recent Advantages in Autism: Causes, Risk Factors, Diagnosis, and Management

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Abstract: ***A neurological disease called autism is marked by difficulties with social interaction, as well as by narrow interests and repetitive activities. This page explains variables that may affect prevalence rates, such as recent modifications to the diagnostic criteria, in light of current worries about rising prevalence. We now understand that autism is one of the most genetically predisposed conditions, with very little environmental influence. Recent research has also revealed that both common gene variations with minor effects and unusual variants with substantial effects all increase the risk of autism. These findings expose the enormous variation in autism and push the bounds of conventional diagnostic categories. In this paper, the authors review the various causes which lead to autism, the signs, and symptoms of the disorder, and various ways to manage and diagnose the disease.***

Keywords: Autism, Neurological disorder, Genetics, Disease

1. Introduction

In 1943, an Austrian-American psychiatrist Kanner described 11 boys with an emotional contact problem associated with autism in a major clinical study that helped establish autism as a cohesive condition. Along with the growing understanding that diseases of cognition and behaviour have an intrinsic, brain-based origin, psychiatric views of this condition have undergone substantial modification. Autism was fundamentally seen in the 1960s and 1970s as a type of psychotic comparable to childhood schizophrenia, and the common view was that it could have been substantially attributed to upbringing methods [1]. Early identification of certain uncommon genetic or medical diseases, such as phenylketonuria [2]. The discovery that autism was heritable and connected to a number of genetic disorders was a major factor in the present conception of the condition as a biological problem [1]. The main characteristic of autism is a rigidity and constriction that affects thinking, remembering, empathy, concentration, and behaviour, especially in social realm[3]. Infantile autism (IA) is a behaviourally defined condition that manifests in infants and young children from an early age and is characterized by extensive abnormalities in reciprocal social interaction, impairment in verbal and nonverbal communication, and the prevalence of stereotypes. There are a number of theories as to what is wrong in a child's growing brain when they exhibit the signs of autism. The co-morbidity of phenylketonuria (PKU), a metabolic disorder, with the autism spectrum in certain kids raises the possibility that this condition is perhaps one of the dual abnormalities [2]. It has been observed that there are various reasons leading to autism and advancement in studies in relation to mitigating autism and related manifestations.

2. Background

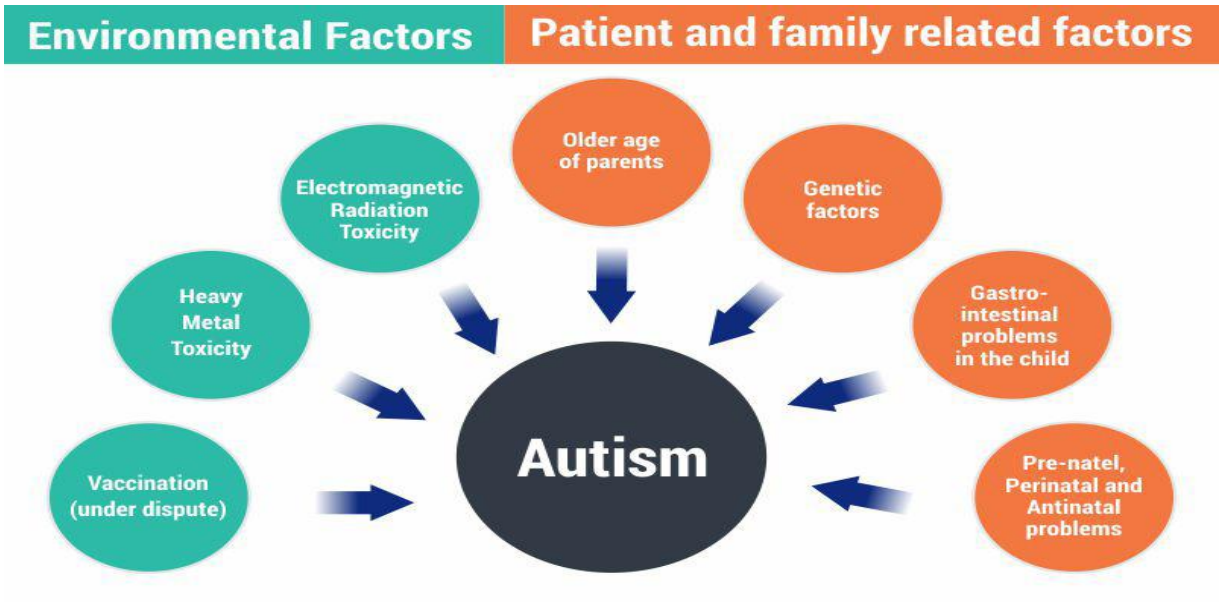
Autism is a neuro-developmental illness included in the category of widespread developmental disorders. Three basic deficiencies that define these diseases are poor human involvement, confined, repetitious, and stereotypical patterns of behaviour, and restricted communications [4]. The extent and severity of how these deficits exhibit themselves vary, and they frequently alter as new developmental abilities are learned. When this illness is at its worst, a person may become totally unable and need lifelong supported care, frequently in a long-term care facility. Possessing mastered adaptive mechanisms, autistic people can live typical, fulfilling lives that are profitable. Regardless of race and nationality, culture, or economic status, autism affects individuals everywhere. According to socioeconomic psychology studies, autism is a neurobiological disease marked by the inability of the impaired individual to socially interact and communicate with one another. Patients with autism frequently exhibit constrained, monotonous, and stereotypical patterns of behaviour. For instance, autistic people may continue to approach and play with items like toy cars in a repetitious manner as toddlers, instead of communicating with people. Stimming is the term for these repeated activities, which typically involve repeating noises or gestures [5]. Since then, milder forms of autism have been incorporated into the description and diagnosis of these illnesses. Early as the age of three, a child is considered to have autism if there are difficulties with language and reciprocating social engagement, as well as the existence of constrained repetitious and stereotypical patterns of behaviour or preferences [6]. The behaviours of autism children from infancy have been studied in both retrospective and prospective research, using information from parents' accounts, early home films, screening instruments, and sibling studies. Various information is available on the age at which the early indicators appear. For

instance, the initial drop in social interactions may happen between 2 and 6 months [7]. The number of published molecular genetic studies on autism has greatly increased during the past ten years. Genome-wide research in the fields of medicine, psychology, and the social sciences has examined genetic variation to look for associations between certain polymorphisms and disorders or characteristics. Genomic variation can be classified according to the population it occurs in and whether it affects DNA structure or sequencing. People with clinical disorders are at one end of the susceptibility curve for autism, which may be thought of as a spectrum of risks in the community. The majority of population risk appears to come from common gene variations; but environmental and stochastic factors also play a role, and as we shall describe, rare variants operate in opposition to these other factors to move individual susceptibility along the risk spectrum towards abnormality[8]. Signs of autism are a challenge to diagnose because they lack gold-standard autopsy pathophysiology, necessitating the monitoring of behaviour and intellectual traits even without the assistance of scientific testing, neuroimaging data, or molecular parameters. Another significant challenge in placing sufferers into prognostic groups based on the analysis of behaviour and cognition is that impairment in these areas is not ultimate, but ongoing and quantifiable, necessitating a degree of haphazard classification.

Approaches in Structural Genetics to Understand Autism

The number of scientific molecular genetic studies on autism has greatly increased during the past ten years. Genome-wide research in the medical fields, psychology, and related fields have examined genetic variation to look for associations between certain polymorphisms and disorders or characteristics. Population frequencies or if a variation affects Genetic code or sequence are two ways to describe genomic diversity. Society might be thought of as having a danger gradient for autism, with someone who has a clinical diagnosis at one end. As we shall explore, uncommon variations function in contrast to these other factors to move individual liability along the danger gradient towards disorder. Prevalent gene mutations seem to account for the majority of public risk; environmental and probabilistic effects will also assist [8].

The causes behind Autism



Source: autismconnect.com

Autism is a neurological disease that is impacted by ecological and biological variables that have an effect on the maturing brain. Although no one, overarching explanation for Autism has yet been identified, ongoing research is expanding our understanding of multiple etiologic processes that may contribute to the disorder. Despite the paucity of these researches, cerebellar architecture and connection discrepancies, limbic system abnormalities, frontal and temporal lobe cortical changes, as well as other modest anomalies, have all been identified [9]. In a modest exploratory investigation of younger people's neocortex structure, most patients had localized cortical laminar architecture disruption, pointing to issues with cortex layer creation and neural division [10]. Children having Autism have indeed been documented to possess enlarged brains in terms of cortex size as well as an elevation in extra-axial fluid; these findings are the subject of continuing research to help us explore the genesis of the disorder as well as to identify a possible biomarker[11]. If contrasted to normative data, siblings of Autism individuals have a greater likelihood of being diagnosed, and genetically identical twins have a substantially higher, but not 100%, concurrence of autism identified. Genetic variables play a role in Autism [12]. Good evaluation of these genes can provide insight into probable biological pathways. Genome-wide association analyses and whole-exome sequencing techniques have improved our knowledge of the genes associated with Autism vulnerability. The majority of the chromosomal anomalies linked to Autism contain signalling molecules like transcription factors, which are important at the neural synapses or engaged in interactions & alterations in the neuron. In the current research, 16 recently discovered genes

linked to Autism were described. These genes suggest novel possible processes, such as intracellular actomyosin organisation and ion transport. Compared to the national average, couples with one autistic kid had a higher likelihood of having a second autistic child. According to estimates, there is a 1 out of 6 chance of having further afflicted children. There is mounting evidence that parents who are older (over 45 years old) have a higher chance of having an autistic kid. Generally speaking, children with developmental and other abnormalities are more likely to be born to older parents. Older moms are more prone to experience pregnancy and delivery problems even though the hereditary component is most likely the explanation. Early infancy and pregnancy, though to a lesser extent, appear to be critical times when brain development may be impacted. Although this is a modest effect, it has been discovered that bacterial or viral illnesses in the mother during pregnancy may slightly raise the chance of autism. A micronutrient shortage, diabetes mellitus, and the usage of some antidepressants in pregnancy are other variables in the mother that may be linked to autism in the kids, although there is no solid evidence for any of these associations. The past ten years have seen an upsurge in studies on environmental factors that may possibly be linked to autism. Despite extensive investigation, however, no single environmental element has ever been identified as a certain cause of autism. Although genetics undoubtedly contributes to the etiology of Autism, the morphological manifestation of genetic predisposition within Autism is nonetheless incredibly heterogeneous. An elevated probability of having a kid with Autism has indeed been demonstrated for both older mothers and fathers [13]. A new thematic identified multiple prenatal, perinatal, and postpartum health risks that increased the hazard ratio of Autism in children, but this also found high inconsistency, making it impossible to determine the underlying significance of these variables. In the end, studies will seek to define variables that are associated with an increased risk of Autism, but no causative links have been shown. This gives a lot of potential for discovery as researchers work to identify novel genetic susceptibility alleles or novel ecological factors that need additional investigation [14]. Hundred autism children's hair specimens were analysed for levels of aluminium, lead, and mercury and were contrasted with age- and gender-normal subjects. The researchers chose hair sample because it is regarded as the best non-invasive method for determining the body's amount of a certain mineral. The results showed greater levels of all tested heavy metals in the examined autistics relative to patients, with a good association to occupational exposure for heavy metal toxicity, such as extensive prenatal fish eating by mothers who smoke, cooking with aluminium pots, and ingestion of levo-D [15].

Signs and Symptoms to Identify Autism

Source: momjunction.com

The various signs and symptoms by which autism can be identified are enlisted below;

Delayed Speech and Development: Genuine social connections are hampered for kids with autism due to social communication difficulties. Despite the fact that youngsters with high-functioning autism may be significantly more socially adept than those with more severe forms of the disorder, the same problems exist across the autistic spectrum[16].

For example: - They don't answer when you call their names or make any vocal efforts to get their attention, failure or are sluggish in learning gestures, especially indicating and expressing to others. Speak exclusively in single words or rehash specific phrases, appearing unable to put words together to form complete sentences.

Preferred to play alone: Children that are usually maturing notice how others play with gadgets and copy them. For instance, a youngster with typically developing could

arrange the pieces in a pattern when they first play with it. But as quick as they witness others using the pieces to construct anything, that youngster will copy them. An autistic youngster might not even be aware that some people are using pieces to play. They are quite reluctant to copy the actions of others after observing them [17].

Hyperactivity: According to some theories, children's minds don't secrete enough dopamine, which leads to hyperactivity. Functioning issues in the frontal lobe of the brain are primarily inherited. It could be important to delay diagnosis until the start of the school year. If kindergarteners have trouble adhering to group activities, hyperactivity may be detected. The majority of autistic youngsters also have difficulty focusing. Around age two, the excessive movement might also be seen. It is possible for this to endure a very long period in people with autism. This presents a big challenge to handle the situation. It can get lessened after some time. In truth, excessive movement can be seen occasionally, but only in specific circumstances and locations.

Sleep Problem: Autism sufferers typically experience sleeplessness; it takes them an extra Eleven mins to drift off to sleep, and most of them rise up repeatedly even during the night. Many times, throughout the course of the night-time, some persons with the illness have sleep problems, which causes them to cease breathing. Additionally, sleeping would be less therapeutic for autistic individuals than it does for the overall public. The rapid eye movement (REM) phases of sleep, which is essential for learning and memory retention, occupy around 15 percent of the overall of their total sleep duration. By comparison, roughly 23 percent of the total of REM sleep occurs for the majority of typically developing persons each night.

Risk Factors

Source: healthsoul.com

There are various risk factors in autism those are enlisted below;

- **Prevalence in the future:** Typically, autism runs in families. Kids are more likely to develop autism if they have a sibling or brother who seems to have Autism. Couples who already have one kid with Autism are still more likely to get another one. Families of autistic children are also more likely to experience minor language or interpersonal skills issues.
- **Premature Child Delivery:** Autism can appear prior to, throughout, or immediately following childbirth. Premature births can occur as a result of pregnancy issues. According to studies, these issues might be related to Autism. Even more at risk for having one of these illnesses are infants delivered extremely early, before twenty-six weeks of gestation.
- **Genes:** Why certain individuals get Autism while another do not may be influenced by genetics? According to research on identical twins, the likelihood that the second twin will have Autism ranges from 36 to 95 percent when one sibling is afflicted. Additionally, there is a relationship between autism and several hereditary disorders. One or more genetic or chromosomal disorders are present in 10% of children with ASD,which include Tuberous sclerosis, Tourette syndrome, Fragile X syndrome, and Down syndrome. Mutations, or Random gene alterations, can potentially raise the chance of autism.
- **Chemicals:** A child's susceptibility to Autism may rise if they are exposed to particular compounds before delivery. Certain drugs may increase the risk of having a kid with a few of those illnesses in pregnant women. These include medications to regulate mood (Thalidomide), control seizures (Valproic acid), or prevent preterm labour (Terbutaline). Agrochemicals and compounds commonly present in polymers (Phthalates) may enhance the incidence of autism in innocent foetuses.
- **Pollution:** The likelihood of having a kid with autism is higher than average for pregnant women who are subjected to high pollutant emissions. As environmental exposure increases, the chance of autism tends to increase. When consumption takes place in the later several weeks of gestation, this connection is highest. The genetic composition of a child may increase this risk. Kids who have been exposed to environmental pollution before birth and which also possess a certain variant of the MET gene are more likely to develop autism.

Diagnosis and Management

Since there is not a specific diagnostic test forautism, such as a genetic test, it might be challenging to make the diagnosis. In order to determine diagnoses, doctors consider the patient's condition and chronological stages. Autism can occasionally be identified in children as early as Eighteen years of age. By the age of two, a qualified specialist's assessment can be trusted.

Developmental monitoring seems to be an intensive, continuing method that entails observing a kid improve and promoting discussions about one kid's skillsets among parents and providers. Developmental monitoring entails keeping track of your baby’s progress and determining if they have attained the regular developmental stages, or

abilities, in areas like exploring, studying, communicating, acting, and performing that most kids do by a given age. Developmental monitoring can involve parents, grandparents, early childhood educators, and other caregivers. Learn the Signs from the CDC. The Act Early, initiative has created free resources, like the CDC Milestone Tracker app, to assist parents and caregivers in keeping track of their child's development and identifying any potential red flags or the need for additional screening. To gauge your child's development, follow a quick milestones checklist. If you see that your kid is not developing at the expected rate, discuss your worries with your doctor or nurse and inquire about developmental screening. Learn more about milestone checklists, the CDC Milestone Tracker app, and other parent resources.

A developmental screening examines your child's development more closely.

Compared to developmental monitoring, developmental screening is more formal. Even if there is no known issue, it is a standard component of certain well-child check-ups.

During routine well-child visits at these ages, the American Academy of Paediatrics (AAP) advises developmental and behavioural screening for all kids:
1) 90 days
2) One year
3) Three years

A quick examination with a screening instrument does not offer a diagnosis, but it can show if a kid is progressing normally or whether further examination by an expert is necessary. It could be necessary to do a formal developmental review if the diagnostic test reveals a problem area. A qualified professional, such as a developmental paediatrician, child psychologist, speech-language pathologist, occupational therapist, or other specialist, often conducts this formal evaluation, which is a more thorough examination of a child's development. The specialist may observe the kid, provide a formal test to the youngster, interview the parents or other caregivers, or request that they complete questionnaires. The outcomes of this formal assessment show your child's abilities and areas for improvement, and they may help determine if they satisfy the requirements for a developmental diagnosis.

Autistic disorder, pervasive developmental disorder not otherwise, and Asperger syndrome are now all included in an Autism diagnosis in addition to numerous additional disorders that were formerly diagnosed individually. You can comprehend and navigate the diagnostic procedure with the aid of your doctor or another healthcare professional [18], [19].

There are no drugs that are sold expressly for treating autism. However, there is a substantial body of research outlining both open-label and controlled drug studies for the treatment of both autistic children and adults. Although some of the more well-researched drugs, such as Haloperidol and Risperidone, are frequently effective in treating autism-related symptoms, they can also have unfavourable side effects. Although preliminary research on serotonin reuptake inhibitors is encouraging, not all age groups may benefit from their use. Methylphenidate and clonidine may be used to treat hyperactivity in autism, according to small, controlled research on these drugs. The fundamental social or communicative deficits are seen in autism have not yet been effectively treated by drugs [20].

3. Conclusion

Autism is a neurobiological disease that is impacted by environmental and genetic variables that have an impact on the developing brain. There are still many variables that are associated with an increased risk of autism, and these findings may help direct future etiologic research, but no definitive causative chain has been established. Clinical examination begins with developmental screening of the general paediatric population to identify children who are at risk, then is followed by a specialist referral for a precise diagnosis and thorough neuropsychological evaluation. Additionally, prevalent co-morbid disorders should be checked for in children with autism. The first medical examination should include clinical genetic testing even if there are no obvious biomarkers or diagnostic techniques. Here, parents, guardians play a great role to manage the disorder. Based on certain patient features, additional medical testing or subspecialist referrals may be requested.

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