The Co-occurrence of ASD and ADHD in Pediatric Population and the Role of Clinicians and Parents in the Management of Neurodevelopmental Disorders

M.Phil Thesis

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This humble work is a small piece of gratitude to endless love by my mother.

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List of Abbreviations

Abbreviation	Description
ASD	Autism Spectrum Disorder
ABA	Applied behaviour analysis
ADHD	Attention-deficit/hyperactivity disorder
ADI-R	Autism Diagnostic Interview-Revised
CARS	Childhood Autism Rating Scale
CNS	Central Nervous System
DTT	Discrete trial training
EIBI	Intensive behavioural interventions
M-CHAT	Modified Checklist for Autism in Toddlers
NSCH	National Survey of Children's Health
PBS	Positive Behavior Support
PDD	Pervasive developmental disease
PECS	Picture Exchange Communication System
PFC	Prefrontal cortex
SCQ	Social Communication Questionnaire
SRS	Social Responsiveness Scale
VBA	Verbal behavioural intervention

Abstract

Autism is a pervasive developmental disease (PDD) that significantly impacts a child's development in three domains: language, social interaction, and repetitive and stereotyped behavior. Whereas ADHD is one of the most typical neurodevelopmental diseases and is defined as the existence of impairment symptoms of inattention, hyperactivity and impulsivity that begin before the age of twelve. In spite of the growing interest in co-occurring ADHD and ASD, very little study has been done on the subject. The current multi-center prospective observational study aims to investigate the occurrence of ADHD in ASD patients and assess the treatment diagnostic patterns of clinicians for ADHD and ASD in children as well as the role of parents in symptomatic management of their children. The first part has focused on the study subjects (children) for which screening tool of ADHD was employed. Second is the assessment of parents for their impact on improvement in the symptoms of the diseases on their children. This part is completed by using questions and the final part was the assessment of clinicians for evaluation of their diagnostic parameters. The result of this study shows the greater incidence of co-occurrence and that too related with the demographics of parents. It is anticipated that this study would point clinicians and parents in the direction of dimensional ways to identifying impairment that may be helpful in situations with co-occurring ADHD and ASD.

CHAPTER 1

INTRODUCTION

1. INTRODUCTION

1.1. Background

Co-occurrence of Autism Spectrum Disorder (ASD) and Attention Deficit Hyperactivity Disorder (ADHD) is a common phenomenon, with studies suggesting that up to 30-50% of individuals with ASD also have indications of ADHD (Leyfer *et al*., 2006). In addition, there is an increased prevalence of ADHD among first-degree relatives of individuals with ASD (Landa *et al*., 2007). Managing the co-occurrence of ADHD and ASD can be challenging for both parents and clinicians. Parents of children with co-occurring conditions may face additional stress and difficulty in identifying appropriate interventions and supports (Carroll *et al*., 2014). Clinicians may also face difficulties in accurately assessing and diagnosing the co-occurrence of these conditions, as well as developing effective treatment plans (Davis and Kollins, 2012). The use of parent training programs to manage the occurrence of ASD and ADHD is one of the good approaches. These programs have been shown to enhance parent-child interactions by using positive parenting strategies, which can lead to improvements in child behavior.

1.2. Literature Review

Autism is a pervasive developmental disease (PDD) that has a considerable impact on a child's development in three domains: language, social interaction, and repetitive and stereotyped behavior (Kolvin, 1971). In ASD, persistent and impaired social communication, and interaction difficulties in numerous contexts, as well as confined, repetitive behaviors, hobbies or activities, or sensory complaints exists. Persons who demonstrate a certain set of obsessive behaviors, severely circumscribed interests, and/or sensory routines from a very early age are referred to as having "autism spectrum disorder." This phrase is used to define people who have been detected with autism spectrum disorder (Bruchmüller *et al*., 2012). The condition can start as early as infancy, although it often shows symptoms in the first three years of life. Even though their child can memorize lines from films or pronounce the letters, parents usually become concerned when their youngster doesn't use language to communicate (Burns *et al*., 1999). Social deficits may not be obvious right away in the beginning, but as a child becomes more active and as other children get more socially skilled,

they gradually become more obvious (Klin, 2003). Those with ASD may have varying degrees of impairment, but both the affected people and their families must adapt to a new way of life. The prevalence of autism has been rising over time. This increase is being attributed to a number of environmental factors working in tandem with genetic susceptibilities. Rett syndrome and autism spectrum disorders have been related to mecp2 mutations and poor methylation (Goffin *et al*., 2012).

Cytochrome P450 gene polymorphisms, particularly CYP27B1, which is required for the correct metabolism of vitamin D, have also been linked to autism (Mbadiwe and Millis, 2013). Autism has been associated with vitamin D deficiency or metabolic problems, and vitamin D is essential for neural development and growth. Considerations have been made for epigenetics, maternally produced antibodies, heavy metal exposure, maternal sickness, folic acid supplements, MMR vaccinations, as well as electromagnetic radiation. Each time, the results—direct or indirect—have a detrimental impact on the neurological system, neurodevelopment, and genes that respond to the environment (Mattila *et al*., 2007). Midway through the 1940s, American and European medical literature began to identify the illness; nevertheless, references to both mythical and real-life people who appear to fit the ASD clinical profile date several centuries ago. Up until the 1980s, ASDs were thought to be extremely uncommon, with a frequency of no over than 5 per 10,000 people, and were viewed as an unusual clinical conundrum rather than a serious public health issue (APA, 2013).

Researchers have recently been able to precisely identify autism in children aged two to three years old. Initial diagnoses have been documented with delays of 20–60 months between parental concern and diagnosis, depending on the severity of the disease (Guthrie *et al*., 2013). Whereas ADHD is one of the most typical neurodevelopmental diseases and is defined as the existence of impairment symptoms of inattention, impulsivity and hyperactivity that begin before the age of twelve, are evident in two or more settings, and cannot be explained by another disorder (Mattila *et al*., 2007). Children who have ADHD could have trouble focusing andcontrolling their impulses (doing things without thinking about the possible outcomes) or be very energetic. Over the course of the previous twenty years, there has been a discernible rise in the incidence of ASD cases (Mattila *et al*., 2007; Hoseini *et al*., 2014). Autism prevalence is estimated to be little under 1% globally, but larger in developed nations.

A minor morphological and functional distinction has been found in post-mortem, neuroimaging, and electrophysiological studies, despite the fact that autism is not depicted by extensive brain damage (Hampson & Blatt, 2015). Along with this rise, the frequency of ASD among kids with ADHD has also increased. In reality, figures from the National Survey of Children's Health (NSCH) based on several years show that in 2003, 33% of children aged 4 to 17 years who ever get an ADHD diagnosis also received an ASD diagnosis, compared to 9.7% in 2007 and 10.2%t in 2011 (Fereshetyan *et al*., 2021). Additionally, these two illnesses have been connected by shared additive genetic and environmental risk factors, including as preterm delivery and the use of certain psychiatric medicines by the mother (Robinson and Bergen, 2021; Pettersson *et al*., 2019).

The coexistence of ASD and ADHD may aggravate social impairment above what is seen in ASD alone, resulting in a different manifestation of social deficits (Harkins *et al*., 2022). Previous research has shown that when behavioral signs of both disorders co-occur, they may be more severe. Both ASD and ADHD symptoms can considerably impede functioning, social interaction, and adaptive abilities, and individuals with both conditions appear to display specific and overlapping behaviors. Increased autistic symptoms and maladaptive activities are linked to the comorbidity ADHD symptoms are among the most prevalent mental health issues for people with ASD (Tick *et al*., 2016*b*; Rao and Landa, 2014).

Few population-based studies have been done on the diagnosis of ASD in kids with clinical ADHD diagnoses, despite the similarities between the two disorders. The evaluation scales have been psychometrically tested, have a high level of internal consistency, and can be given to a wide population quickly. Nevertheless, research that relies just on symptoms without a focus on diagnosis may lead to misclassifications given the substantial degree of symptom overlap between ADHD and other disorders (Zablotsky *et al*., 2020). The awareness and impression of a parent regarding their child's behavior may be too influential (Milberger *et al*., 1995). Our understanding of the ADHD phenotype may be improved by looking at ASD diagnoses in children with ADHD. This will help us better understand the treatment needs of this growing group and, in turn, provide insight into the best ways to treat co-occurring mental illnesses (Stevenson *et al*., 2005).

The occurrence of ASD has significantly risen over the past few years, leading to allegations that autism is "epidemic." In order to deliver sufficient funds and proper services for children and individuals with ASD and their families, accurate prevalence estimates of ASD are crucial. This is because it help in assessing the health and financial services of this condition (Rice *et al*., 2012). Systematic monitoring of ASD makes it possible to estimate prevalence and identify probable sources of variation over time and between locations. ASD incidence figures are currently available on a global basis. These estimations are derived from population-based studies or surveillance systems employing current health and education data (Presmanes Hill *et al*., 2015). A increasing number of people with ASD requires more services, such as formal training, as well as the discovery of potential new resources through the identification of instances in the community (Newschaffer *et al*., 2007). In addition, knowing the precise prevalence of ASD can assist identify which populations are more vulnerable to ASD due to climatic and geographic factors, as well as being subject to discrepancies in healthcare access for developmental examinations (Lyall *et al*., 2017).

The methodological discrepancies in case definition and ways to locate cases are key contributors to the disparities in prevalence estimates. Research is specifically conducted using preexisting administrative datasets, such as the ones relating to special learning, medical care, or social details gathered from national registers for case recognition, or registers for particular diseases (defined as "administrative data" when dependent on a single repository, or "multisource" when integrating information obtained from multiple databases). A two-stage or multistage technique is frequently used in research to uncover examples in the underlying populations (Fisk *et al.*, 2003).

1.2.1. Prevalence of ASD

Globally, the prevalence of ASD has been found to be higher in developed countries as compared to developing countries. A systematic review and meta-analysis of studies conducted in Europe, North America, and Asia found an overall pooled prevalence of 1.79% (95% CI: 1.55-2.03%) (Salari *et al*., 2022). Another systematic review conducted in Europe found a pooled prevalence of 1.84% (95% CI: 1.62-2.06%) (Elsabbagh *et al*., 2012).

In Pakistan, the prevalence of ASD is not well-studied, and there is a lack of comprehensive data on the subject. A study conducted in Lahore, Pakistan, found the prevalence of ASD to be 1.4% (95% CI: 0.9-1.9%) among children aged 5-18 years (Elsabbagh *et al*., 2012). However, this study had a small sample size, and the results may not be generalizable to the entire population.

Another study conducted in Karachi, Pakistan, found the prevalence of ASD to be 1.3% (95% CI: 0.8-1.8%) among children aged 3-10 years (Khalid *et al*., 2020). The results of this study specified that the prevalence of ASD in Pakistan is comparable to that which is seen in industrialized nations; nevertheless, further study is required to validate these findings and to determine the actual incidence of ASD in Pakistan.

Due to cultural and language obstacles, a lack of knowledge, and limited access to diagnostic services, it is crucial to remember that the prevalence of autism may be underreported or misdiagnosed in developing nations. This is something that has to be taken into consideration. As a result, there is a pressing need for more study to identify the accurate autism incidence rate in Pakistan and other developing nations.

In conclusion, the prevalence of ASD is estimated to be around 1-2% globally, but it can vary depending on the population and methods used to estimate it. Factors such as diagnostic criteria, methods of identification, age, and geographic location can all affect the estimated prevalence of ASD. Additionally, studies suggest that the prevalence of ASD may be higher than previously estimated, and more investigation is ought to establish a more accurate estimate of the prevalence of ASD clouding the diagnosis of ASD.

1.2.2. Genetic Components of ASD

The significant heritability of ASD is considered a sign of its complexity in the genetic code. ASD has a significant hereditary component, according to epidemiological twin studies (Tick *et al*., 2016a). Fraternal twin concordance rates range from 0–10%, while identical twin concordance rates are 70–90%. Familial clustering is visible in households where ASD patients already exist. Siblings who are younger and who have a family member with an ASD diagnosis are more likely to have the disorder; this is especially true of younger brothers. De novo mutations, frequent and uncommon genetic variants, and ASD-associated common

polymorphisms can all be used to pinpoint the genetic aetiology of ASD in 20–25% of children and adults (Rylaarsdam and Guemez-Gamboa, 2019).

1.2.3. Environmental Components of ASD

Parental age, maternal metabolism and nutrition, sickness during pregnancy, prenatal stress, and exposure to certain elements, drugs or heavy metals are examples of non-genetic features that might increase the likelihood of an individual developing autism spectrum disorder (ASD) (Karimi *et al*., 2017). Non-genetic variables that can raise the probability of a person acquiring autism spectrum disorder include the age of the parents, the diet and metabolism of the mother, illness during pregnancy, prenatal stress, and exposure to certain chemicals, heavy metals, or medicines (Ramaswami and Geschwind, 2018). The quality of the nutrition that the woman maintains during her pregnancy is a significant impact in the subsequent development of the child's brain. Certain micronutrients, including as zinc, folic acid, vitamin D, iron, and omega-3 fatty acids, may either be present in excessive amounts or insufficient amounts, both of which can be detrimental to neurodevelopment. The frequency of autism spectrum condition was found to be higher in children with lower folic acid levels, according to studies that compared the two groups (ASD) (Narzisi *et al*., 2021). Studies on epidemiology and animals have indicated that autism spectrum disorder is directly connected with the accumulation of toxic metals like and lead and mercury during pregnancy, in addition to a shortage of zinc, which is an essential element (Błażewicz and Grabrucker, 2022).

Maternal infection is another non-genetic element putting people at risk for ASD (Zerbo *et al*., 2015). The relevance of inflammatory responses and infections has been subject to ongoing scrutiny in light of the correlation between the onset of autism spectrum disorders and the presence of congenital rubella infections. The immune response that an infection may induce in the mother, which may include inflammation and cytokine activity, is now the primary focus of research. There are a variety of hypotheses that propose maternal cytokines may cross the placenta and cause the developing foetus to become inflamed, generate an abnormally high quantity of cytokines, and maybe lead to gene dysregulation (Yockey and Iwasaki, 2018). Multiple studies have indicated that people with ASD have impaired adaptive and innate immune function, suggesting that inflammatory problems are not limited to

gestation but continue after birth and into adulthood (Ji-Xu and Vincent, 2020). A neuroinflammatory phenotype in ASD that may be important in the development of ASD behavior is suggested by the activation of astroglia and microglia cells as well as elevated levels of proinflammatory cytokines over the course of life. ASD risk has been linked to maternal medication use during pregnancy, particularly those taken to treat and depression & epilepsy (Viktorin *et al*., 2017). However, there are signs that it may be dose-related. Studies have linked maternal valproate usage to a number of neurological changes in the offspring, including ASD. ASD development can be increased by antidepressant usage during pregnancy, including selective serotonin reuptake inhibitors (Croen *et al*., 2011). Co-morbidities are also more likely as a result of a variety of environmental variables, such as obesity, epilepsy, and gastrointestinal problems (Seidenberg *et al*., 2009).

1.2.4. Pathology of ASD

Since the beginning of ASD studies, scientists have been interested in studying how the brain forms and functions. Disorders of the central nervous system (CNS) have been identified through experimental and postmortem studies at the cellular and macroscopic morphological levels. These pathologies have been detected in both neuronal and glial cells (Silbereis *et al*., 2016). According to the findings of these investigations, neuropathologies can be observed in individuals with ASD. Recent research on gut-brain connection and immune responses, on the other hand, has indicated that problems in ASD might lie outside of the CNS (Taniya *et al*., 2022).

Numerous studies have documented anomalies in children with ASD who were later diagnosed, including enlarged head circumferences and intracranial volumes. A meta-analysis of volumetric studies found that young people with ASD have changed brain structures in the basal ganglia, the medial temporal lobe, and near to the right parietal operculum (Nickl-Jockschat *et al*., 2012). However, the anatomical abnormalities that have been identified in younger persons with ASD, like smaller cerebellar volumes, bigger intracranial volumes, modified cortical cortex sizes, and larger amygdala volumes, were not found in older adults with ASD (Donovan and Basson, 2017).

Theoretically, early brain expansion in ASD is preceded by a period of growth cessation or possibly degeneration during development.Additionally, there is no

obvious connection between the documented gross anatomical anomalies and the clinical phenotypes of people with ASD. According to reports, people with ASD have distinct brain connectivity (Courchesne *et al*., 2011). There is evidence that the connectivity between proximal and distal brain regions has diminished, while there is evidence that connectivity within proximal brain regions has risen. It was shown that individuals with ASD have less cerebellar Purkinje cells in their brains. Synaptic disruption, on the other hand, is the neuropathology of autism spectrum disorder that is most noticeable (Blatt, 2012). Many of the 207 SFARI genes are linked to a high risk (syndromic and category 1) of developing an autism spectrum disorder (ASD) encode for proteins that are essential for brain synapse activity. It is common knowledge that applicants at high risk for ASD vulnerability include members of the SHANK family of postsynaptic scaffolding proteins (SH3 and multiple ankyrin repeat domains), such as SHANK2/3, the cell adhesion family of neurexins, such as NRXN1, and neuroligins (i.e., NLGN2, NLGN4X)(Chen *et al*., 2014).

In in vitro and in vivo models that included genetic alterations, a large number of genes that have been linked to autism spectrum disorder have been shown to be involved in synaptic function, chromatin remodelling, as well as protein production and degradation pathways. These findings support the hypothesis that autism spectrum disorder is caused by a combination of factors. These pathways will, at some point, come together to play a role in synaptic homeostasis and synaptic plasticity. As a consequence of this, ASD is classified as a synaptopathy. It seems that two signaling pathways at synapses are crucial to the pathophysiology of autism spectrum disorder (ASD) (Guang *et al*., 2018). The NRXN-NLGN-SHANK pathway and the PI3K/mTOR pathway, which are both strongly linked to syndromic ASD. These pathways work as synaptogenesis' main regulators when combined. But since they are overwhelmingly restricted to excitatory synapses, there may eventually be an imbalance between excitatory and inhibitory transmission. Numerous genetic and non-genetic risk factors for ASD may mechanically combine at the synapse level, according to certain theories (Wang *et al*., 2023*b*).

1.2.5. Diagnosis of ASD

The three diagnostic characteristics that have historically been linked to ASD are diminished social connections, communication difficulties (verbal and nonverbal),

and restricted, repetitive behaviour patterns (Faras *et al*., 2010). No matter a person's colour, ethnicity, culture, or socioeconomic background, these fundamental characteristics are present. One characteristic may be more common than another, while ASD sufferers frequently differ from one another. Even with recent developments, there are still no trustworthy diagnostics markers for ASD (Shattuck, 2006). As a result, evaluating behaviours in light of the DSM-5 criteria established by the APA is the basis for making a clinical diagnosis of ASD today. ASD and other conditions may co-exist. These include mental health issues like ADHD, which has been reported to be the most common comorbidity in people with ASD (28%) as well as psychiatric diseases and conditions like anxiousness and fears, dissociative conditions, depression, bipolar disorder, along with intermittent emotional disorders (Bailey *et al*., 1995).

1.2.6. Diagnostic Tools for ASD

There are various diagnostic criteria available for ASD, and they vary greatly from one another. Two of the most crucial components of an ASD diagnosis are an extensive examination of the development of the child and assessments of the kid's interactions and connections among their parents and an outsider during either organised or unorganised assessment activities. (Robins *et al*., 2014). Even though a diagnosis of autism spectrum disorder (ASD) can be established at any age, it is most commonly done within the first few years of a person's life. The M-CHAT (Modified Checklist for Autism in Toddlers) and other screening tools are used in the public health systems of various European nations, notably Spain and Ireland, to detect young children with ASD (18-30 months)(Guo *et al*., 2019).

To identify ASD at a young age, numerous standardised screening techniques are available. These include the STATTM (20-minute observation of young children), a screening tool for autism in toddlers and young children that was developed in 2000 (Guo *et al*., 2019). A professional or clinician will do a 45-minute observation to diagnose ASD in patients aged 12 to adulthood using the more comprehensive and well-researched Autsm Diagnostic Observaton Schedul (ADOSTM) (Dallman *et al*., 2022).

Additionally, screening instruments that are appropriate for study exist. In the UK, examples include the Diagnostic Instrument for Social Communication Disorders (DISCO) and the Autism Diagnostic Interview-Revised (ADI-R) (Nygren *et al*., 2009). To evaluate a child's ASD symptoms, other screening measures can be utilised, including the Social Responsiveness Scale (SRS), the Social Communication Questionnaire (SCQ), and the Childhood Autism Rating Scale (CARS). Although there are other screening and diagnostic techniques for ASD, DSM-5 and M-CHAT (Modified Checklist for Autism in Toddlers) are now the two most popular autism diagnostic tools (Windiani et al., 2016, Yuen *et al*., 2018; Oner and Munir, 2020).

1.2.6.1. DSM-5

Since 2013, the DSM-5 has been used all around the world as a diagnostic guide for autism spectrum disorder (ASD) (Beighley et al., 2013). In order to get a diagnosis of autism spectrum disorder (ASD), a child must have consistent difficulties across all three of the following social communication and interaction domains, as outlined by the DSM-5:

- Reciprocity on the social and emotional level
- the process of establishing, comprehending, and sustaining connections.
- Communication that does not use words

In addition, at least two of the following four behaviors need to be demonstrated Rigidity toward changes in routine.

- Resistance to deviations from the established routine Hypo- or hyperactivity in reaction to sensory input
- Fixated or limiting interests that might be excessively intense or concentrated on a certain topic
- Involvement of hypoactivity or hyperactivity as a response to sensory input
- Words or deeds that are repeatedly repeated

Early-stage symptoms should produce clinically substantial function impairment (in some circumstances, early-stage symptoms may be concealed and become predominant later). Finally, if alternative explanations of intellectual impairment or developmental problems cannot adequately explain the symptoms, ASD may be suspected. The DSM-5 is distinctive in that it now includes Asperger's syndrome as part of the spectrum that encompasses ASD (Magaña and Vanegas, 2017). The DSM-

5 also allows for the co-diagnosis of ASD along with concomitant conditions like ADHD (28 percent of those with ASD have ADHD), mental disorders like anxiety, depression, and aggression, or genetic conditions like fragile X syndrome. DSM-5 is therefore among the most trustworthy diagnostic methods for ASD and is widely accepted. The UK's National Institute for Health and Care Excellence Guidelines, the Centers for Disease Control and Prevention in the United States, and the Autism Spectrum Disorder Guidelines in New Zealand all use the DSM-5 (Magaña and Vanegas, 2017; Pulsipher and Lieb, 2022).

1.2.6.2. M-CHAT

M-CHAT, which was created from the less reliable Checklist for Autism in Toddlers (CHAT) and the less well-liked Communication along with Symbolic Behaviour Scales (CSBS), has grown in prominence among carers and even professionals due to its simplicity and low price (Windiani *et al*., 2016). In primary care settings, M-CHAT has been independently evaluated and shown to be reliable. M-CHAT is accessible worldwide in a number of different languages. The M-CHAT is designed to screen infants between the ages of 16 and 30 months. In order to explain the parent questionnaires and reduce the possibility of false positives, it also includes a conversation with parents. The 23 "yes/no" questions cover a range of developmental domains. This checklist relies on the parent's consideration of the kid's behaviour and abilities rather than a professional's observations (Yuen *et al*., 2018; Oner and Munir, 2020).

1.2.7. Treatment of ASD

1.2.7.1. Behavioral treatment

Educational and behavioral interventions are very necessary if they are to be implemented in order to address interaction, interpersonal skills, play, everyday living abilities, academic capabilities, and inappropriate behavior. Because autistic persons display such a broad variety of symptoms and have such varied functional capacities, they require individualized treatment (Kasari and Lawton, 2010). There is a widespread consensus that it is extremely important to start psychotherapy as fast as is humanly feasible, whether that means immediately following a diagnosis or even in circumstances when a diagnosis is just suspected. It is also very important to think

about the ways in which friends, siblings, and parents might assist (Vismara and Rogers, 2010).

It is generally agreed upon that initiating psychotherapy as soon as is physically possible is of the utmost significance. This may imply beginning treatment immediately after receiving a diagnosis, or it could refer to situations in which a diagnosis is just suspected. It is of the utmost importance to consider the ways in which one's friends, siblings, and parents could be able to aid (Matson and LoVullo, 2008). It has shown significant progress in IQ, intellectual abilities, and language over the past few years. Distinctive trial training (also known as DTT), early intensive behavioral interventions (also known as EIBI), pivotal response training (often known as PRT), and verbal behavioral intervention are all examples of the various types of ABA therapies (VBI) (Smirnov and Kucher, 2019).

DTT is offered to children in preschool (ages 3-5) and is taught in a classroom setting. The term "Skill-based developmental training" refers to a variety of other developmental strategies (Park *et al*., 2015). Picture Exchange Communication System (PECS) and PBS are a few of these (Positive Behavior Support). A system of augmentative communication based on trading flashcards with pictures, PECS is used with non-verbal children (replacing or integrating speech) (Gonzales *et al*., 2012). The prompt, reinforce, reward success/correct, and error ABA concepts form the foundation of this system (Leroy and De, 2010).

1.2.7.2. Pharmacological and dietary treatment

Aripiprazole and risperidone are the medications that are most frequently recommended to people with ASD (Cohen *et al*., 2013). Although the FDA has given its blessing for the use of these drugs in ASD patients, the condition was not the original purpose for which they were developed as treatments. An example of an atypical antipsychotic medication is the drug aripiprazole (Ghanizadeh *et al*., 2014). Additionally, some kids with ASD additionally suffer from co-occurring disorders like problems with digestion (reflux, protracted constipation, or diarrhoea), which are common in ASD patients. Some people with ASD may experience seizures. Other conditions that have been identified as comorbidities include bipolar disorders, sinusitis, depressive disorders, abnormal psychological responses and behaviours, sleeplessness, and migraines. (Gruber *et al*., 2014). By enhancing the beginning of

sleep, melatonin may be used to treat insomnia and sleep disorders. Alpha-2 agonists, benzodiazepines, chloral hydrate, and antihistamines are other treatments for pediatric insomnia (Owens and Moturi, 2009). Magnesium, Omega-3 fatty acids, Vitamins B6, C, and B6 may all help children with ASD behave better. However, a great deal of advancement has been achieved, there are still few therapy choices available for patients with ASD (Adams *et al*., 2021).

1.2.8. Etiology of ADHD

Initial assumptions of altered brain function were based on a variety of findings of decreased grey and white matter volume or functioning in the brain. These observations were made by a number of researchers. This resulted in deficiencies in cognitive processing, attention, motor planning, speed of processing responses, and other behavioral difficulties that are typical of people diagnosed with ADHD. There is still a lot of mystery about what causes ADHD (Sciberras *et al*., 2017). More recently, the major regions exhibiting impairments in ADHD have been identified as the prefrontal cortex (PFC), caudate, and cerebellum (Brennan and Arnsten, 2008). A network of neurons that links these areas helps these regions work together to govern attention, thoughts, emotions, behavior, and actions via the activities of the connected neurons. In investigations of people who have ADHD, researchers have shown that their prefrontal cortex (PFC), caudate, and cerebellum all have lower volumes and less activity, and that their PFC11 regions take longer to mature (Prince, 2008). Dopamine and norepinephrine act in concert with one another via many receptors to maintain the network activity between these areas, which is "highly sensitive to the brain chemical environment." that could be either postsynaptic or presynaptic (Seidman *et al*., 2005).

Multiple studies have shown that people who suffer from ADHD have lower-than-normal concentrations of dopamine (DA) receptors in a variety of different regions of the brain (Oades, 2008). Dopamine D4 receptor gene polymorphisms (DRD4), dopamine D5 receptor gene polymorphisms (DRD5), and dopamine transporter gene polymorphisms (DAT-1) have all been linked to a diminished ability of the dopaminergic system to operate normally. The disruption of the function of 2A receptors causes worse attention, poorer impulse control, and hyperactivity; however, a decreased receptor density or genetic polymorphisms associated to the NE system in

ADHD have not been established. Despite the fact that a disturbance in the function of 2A receptors is what produces these symptoms, this is nonetheless the case (Swanson *et al*., 2007). When considered collectively, these investigations supported the idea that ADHD is characterized by impaired DA and/or NE function, which was completely consistent with the therapeutic drugs' mode of action (Volkow *et al*., 2009).

Nevertheless, a number of studies suggested that ADHD might be caused by an overactive DA and/or NE system (Pliszka, 2005). Further lately, it has been discovered that some ADHD patients have the DAT-1 mutations A559V and R615C, which either enhance the efflux of DA or decrease the presynaptic uptake of DA, respectively, indicating a hyperactive DA response in these people (Russell *et al*., 2000). Additionally, by preventing the elevated DA efflux, methylphenidate and amphetamine reduce the symptoms of ADHD in the A559V mutant cohort. Direct activation of the postsynaptic receptors is also claimed to lessen ADHD symptoms if there is only a little NT level shortfall (Dunn and Kronenberger, 2005).

The facts that DA and NE may have dose-response curves that are inverted U-shaped, similar to those seen with vitamins, where either extreme is a problem, as well as the existence of separate pools of DA14 and NE25 in the brain, have been used to integrate the hypoactive and hyperactive catecholamine propositions of ADHD (Chen *et al*., 2016). The PFC needs a suitable level of DA/NE to operate at its best, and disturbance causes ADHD (Li *et al*., 2007). To prevent inappropriately prescribing these medications to people who are not afflicted, an accurate diagnosis of ADHD must be made first.

1.2.9. Pathophysiology of ADHD

It is believed that between 2 and 18% of children in the United States between the ages of 6 and 17 suffer from ADHD, which is one of the most common neurobehavioral disorders (Albrecht *et al*., 2015). It is believed that ADHD, often known as hyperactivity, impulsivity, and inattention, is a hereditary, persistent neurobehavioral illness (Bijlenga *et al*., 2019). There are now three recognized subtypes of ADHD: one that is primarily inattentive, one that is primarily hyperactive-impulsive, and one that combines the first two.

Those with ADHD, whether in childhood or adolescence, have challenging developmental stages (Litner, 2003). As a consequence of their impulsive behavior and slower rates of cognitive processing, they have a tendency to do poorly on standardized exams, get worse grades, and have a higher propensity to drop out of school. Low self-esteem is associated with problems in interpersonal relationships, a tendency toward drug abuse, and conflicts with the law (Seidman *et al*., 1997). As a result of their impulsive conduct and slower rates of cognitive processing, they have a tendency to do badly on standardized tests, obtain inferior marks, and have a greater propensity to drop out of school. This is a consequence of their hyperactivity. Low self-esteem is linked to a variety of negative outcomes, including difficulties in interpersonal relationships, a propensity toward substance addiction, and run-ins with the police (Dahl and Lewin, 2002).

Between 60% and 80% of ADHD symptoms last throughout adulthood. Therefore, ADHD is not merely a childhood condition that goes away on its own after adolescence. In the US, between 4% and 4.5% of adults are thought to have ADHD (Reich, 2000). Adult manifestations include poor job performance, a reduced financial standing, and relationship and/or marital issues. Therefore, in order to prevent the numerous problems that those with ADHD confront as children, adolescents, and adults, and to improve their quality of life, they must receive treatment (Goodman *et al.*, 2000).

1.2.10. Diagnosis of ASD

Even though many imaging studies have been conducted with the goal of finding a diagnostic marker for ADHD, this promise has not yet been realized. This is most likely because the problem itself is so complicated. Therefore, in order to properly diagnose ADHD clinical professionals should follow to the guidelines outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) (Goodman *et al*., 2000). As a result of their impulsive behavior and slower rates of cognitive processing, they have a greater propensity to perform poorly on standardized tests, obtain lower marks, and have a greater tendency to drop out of school. This is because their impulsive behavior causes them to process information more slowly. Because of how hyperactive they are, this has happened as a result. A lack of self-esteem is associated with a range of unfavorable consequences, such as

difficulty in interpersonal relationships, a tendency toward drug addiction, and encounters with the law. In addition, given that there are three subtypes of ADHD, each of which has its (Cabral *et al*., 2020).

Because of their impulsive behavior and slower rates of cognitive processing, they have a greater tendency to perform poorly on standardized tests, obtain lower marks, and have a greater tendency to drop out of school. This is due to the fact that they have a greater propensity to perform poorly on standardized tests. This is because their impulsive conduct causes them to absorb information more slowly, which leads to the previously mentioned result. This occurred as a direct consequence of the hyperactivity level of the individuals in question. A low sense of self-worth is linked to a variety of undesirable outcomes, including difficulties in interpersonal relationships, an increased propensity toward substance addiction, and run-ins with the law (Wolraich *et al*., 2019*b*).

A variety of rating scales that are based on the DSM-IV-TR were created in order to provide objectivity and quantification to the subjective criteria that were outlined in that manual (Wang *et al*., 2023*a*). These rating scales can be generically categorised as either narrow band or broad band, based on whether they examine a single behaviour or set of behaviours, respectively. Although narrow band scales are more robust and require less time to administer, broad band scales do offer a better overall clinical picture. This is especially true when assessing therapy efficacy. These narrow-band scales can measure internalising behaviours like depression, anxiety, and eating disorders as well as externalising behaviours like hyperactivity, impulsivity, and inattention (Ogundele, 2018). They can be based on self-reports from teenagers or those completed by parents, teachers, or carers. Therefore, the adult-reported measures provide a more accurate way to gauge a treatment's effectiveness.

The Conners Rating Scales-Revised, the Inattention/Overactivity With Aggression (IOWA) Conners Teacher Rating Scale, the Swanson, Nolan, and Pelham-IV (SNAP-IV) Questionnaire, the Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) rating scale, the ADHD Rating Scale-IV, the Vanderbilt ADHD Rating Scale, and the ADHD Symptom Rating Scale are among the narrow band scales (Murray *et al.*, 2009). Whereas these ratings are built on DSM-IV-TR criteria for identifying ADHD, clinicians must understand that their limitations and dubious specificity and sensitivity

should preclude their use as the exclusive diagnostic criterion for ADHD (Bird *et al.*, 1993).

Recent research on the Conners Teacher and Parent Rating Scales for diagnosing ADHD found that despite their high sensitivity, they lack specificity, which frequently results in false-positive results. As a result, the use of the results from these scales should be restricted to documenting the subjective criteria stated in the DSM-IV-TR (and therefore serving as a part of the diagnosis) and assessing the effectiveness of the treatment (Bird *et al*., 1993; Sharma and Couture, 2014).

1.2.11. Treatment of ADHD

Treatment options for attention deficit hyperactivity disorder (ADHD) include medication, behavioral treatment, or a combination of the two. Therapy is recommended for all children diagnosed with ADHD, regardless of the approach that is used, because it has been demonstrated that beginning treatment at an early age can enhance results, lead to fewer challenges as adults, and allow some breathing room for both parents and teachers. Numerous behavioural approaches to treating ADHD were developed as a result of the initial belief held by many psychologists that ADHD might be caused by ineffective parenting (Rader *et al*., 2009). Furthermore, not all patients responded favourably to these treatments. When there was proof that ADHD had a neurochemical basis, medication therapy was thought to be superior to behavioural therapy.

FDA-approved medications for the treatment of ADHD include both stimulants (known as first-line medicines) and non-stimulants (known as alternative therapies), such as atomoxetine and extended-release -2 agonists (guanfacine and clonidine) (Pliszka and Issues, 2007). Bupropion, immediate-release -2 agonists, and tricyclic antidepressants (TCAs) have all been used off-label to treat ADHD; however, these are only utilised if the aforementioned medications are ineffective or cannot be taken (Pliszka and Issues, 2007).

Both amphetamines and methylphenidate are examples of stimulant-based medicines that have been granted permission for usage across all age groups in the United States by the Food and Drug Administration (FDA). Although the effective dose required for the majority of adults is greater than the daily maximum dose permitted by the FDA

and is therefore regarded as off-label. In addition, there is a paucity of knowledge on the efficacy and safety of these very higher dosages (Disorder, 1999).

In the United States, the Food and Drug Administration (FDA) has given its blessing to the use of stimulant-based drugs such as amphetamines and methylphenidate by patients of any age. This is the case even though both of these substances are classified as controlled substances (FDA) (Ruchala, 2017). Although both stimulants block monoamine oxidase, the enzyme that is responsible for breaking down catecholamines, amphetamine is far more potent than the other stimulant. Either stimulant will bring about a change in the number of neurotransmitters like dopamine and norepinephrine present in the synapses. Due methylphenidate and amphetamine have somewhat distinct modes of action, some patients who do not react well to one stimulant may react better to the other. This is because of the slightly different mechanisms of action between the two (Stiefel and Besag, 2010).

Amphetamines and methylphenidate are both regarded as equally effective for the long-term management of ADHD. Clinical investigations have shown equivalent efficacy for both immediate and extended-release versions, which are both accessible. Extended-release medications cost more than immediate-delivery medications, but they also have benefits like higher compliance, discretion at work or school, and convenience (Lydon and El-Mallakh, 2006). The long-acting medications are less likely to be misused or diverted in adolescents and may even enhance driving performance. Nonetheless, due to the potential for overdose with long-acting forms, only rapid release formulations that are accessible in quantities small enough can be utilised on young children (Hechtman and Greenfield, 2003).

Despite being first-line medications, stimulants may not be appropriate for roughly 30% of ADHD patients. Alternative medications classified as nonstimulants may be needed to treat ADHD if the patient is unresponsive to stimulants or only partially responsive to them, is tolerant of their side effects (such as insomnia), has a medical condition like a heart condition or tic disorder, or if the family is against using controlled substances. The extended-release -2 agonists clonidine and guanafacine, as well as atomoxetine (Strattera), have received FDA approval for the nonstimulant treatment of ADHD (Kratochvil *et al*., 2009).

It is beleived that stimulants have a more robust effect than nonstimulants. On the basis of many meta-analyses, stimulants (methylphenidate) have been shown to be more effective than nonstimulants (atomoxetine). However, there have been no well-controlled, head-to-head comparative studies conducted (Hanwella *et al*., 2011). Despite the fact that certain clinical tests and meta-analyses have shown that these two drugs had noninferiority or equivalent effectiveness, it is possible that this discrepancy might be largely explained by the research methodology and the varied outcome measures that were used in the meta-analyses (Faraone *et al*., 2006b). On the other hand, it has been said that while most trials are carried out over a very little period of time, the results favor stimulants due to the fact that it normally takes several weeks for nonstimulants to completely display their effects. These issues underscore the need for extensive comparative studies that are randomized, double-blind, controlled with a placebo, and lengthier than those comparing the two treatment groups (Kratochvil *et al*., 2008).

The FDA has given atomoxetine the approval to treat adults, adolescents, and children who suffer from ADHD (Kratochvil et al., 2003). Similar to stimulants, atomoxetine boosts NE and DA availability in PFC synapses to enhance PFC function in ADHD patients. It is less likely to be abused than stimulants, though, because it has no effects in the striatum and takes at least 4 to 6 weeks to have full effect. As a result, it might be favoured in patients who have a problem with or fear about substance misuse, however the atomoxetine time lag highlights the need to advise patients and carers to be patient with this medication. It may also lessen tics and anxiety, making it effective for people who also have these comorbid conditions (Upadhyaya *et al*., 2013).

It is possible to give atomoxetine in divided dosages twice day or once daily in the morning. There are more gastrointestinal adverse effects with once daily administration, despite the fact that therapy compliance is improved. Because side effects are reportedly less troubling than with stimulants, atomoxetine is typically well tolerated (Ledbetter, 2006).

Tricyclic Antidepressants have been the most frequently utilised off-label treatments for ADHD in monotherapy; the extended duration of action (due to the long half-life), lack of addiction potential, and capacity to treat depression and tics were hailed as key advantages over stimulants (Budur *et al*., 2005). However, they are rarely used

nowadays due to their numerous adverse cardiovascular, neurological, and anticholinergic effects, medication interactions, and lower efficacy than stimulants (Daly and Wilens, 1998). Therefore, these are only prescribed to people who are resistant to stimulants or other treatments, who are unable to tolerate them, or who have a history of misuse, tics, or depression. The drugs that have been utilised are imipramine, desipramine, and nortriptyline, but desipramine is the least recommended due to instances of rapid death (Prince *et al*., 2000).

It is unexpected that the treatment recommendations are not well defined given the substantial literature on the pathophysiology, aetiology, and therapy of ADHD that is currently available. Therefore, medical professionals could have to rely on their clinical expertise, the patient's or their family's preferences, the existence of comorbid diseases, and any other health issues that might prevent the use of the preferred drugs (Silva *et al.*, 1996).

The present study aimed to investigate the co-occurrence of ADHD in Autistic children and to categorize the children into subtypes by evaluating their symptoms having ADHD or not. Additionally, this study will assess the role of parents and clinicians in managing neurodevelopmental disorders of children.

1.2.12. Aims and Objectives

This study aims to study the co-occurrence of ASD and ADHD in pediatric population and the role of clinicians and parents in the management of neurodevelopmental disorders.

Objectives

- To investigate the co-occurrence of ADHD in Autistic children.
- To categorize the children into subtypes by evaluating their symptoms having ADHD or not
- To assess the role of parents and clinicians in managing the neurodevelopmental disorder of children.

CHAPTER 2

METHODOLOGY

2. METHODOLOGY

2.1. Study Design

A multi-center prospective observational study was conducted in which Autistic children were assessed after taking their consent.

2.2. Study Setting / Data Sources

Study setting was patients in different Autism centers and two hospitals located in Islamabad, Pakistan.

2.3. Study Duration

Study duration was one year from June 2022 to June 2023.

2.4. Study Population

- The children that are being diagnosed with ASD
- Parents of the suffering children.
- The clinicians involved in the treatment of patients.

2.5. Inclusion Criteria

- Patients with age >6 years
- Clinically stable patients
- Patients that give the consent to conduct research on them
- Clinicians and parents of affected patients

2.6. Exclusion Criteria

- Patients with age <6 years
- Clinicians and patients who are not willing to be the part of research.

2.7. Ethical Considerations

The consent of patients is the first priority. The participants, before enrolment in the study, are briefly elaborated with the study. The patients' personal data was kept confidential. No invasive intervention was given to the patients. An informed consent Pro forma was filled by the participants before the start of the study. For this study,

ethical approval has been obtained from the Bioethics Committee of Quaid-i-Azam University, Islamabad (vide letter no. BEC-FBS-QAU2022-381).

2.8. Sample Size and Sampling Technique

The non-probability convenience sampling method was used. Patients diagnosed with ASD, their parents and clinicians that meet the inclusion/exclusion criteria were included in study. Data was collected from total 50 autistic children, their parents and 13 clinicians for further analysis.

2.9. Study Tool

The study was conducted in 3 phases/parts. The first part was focused on 50 study subjects, children who are already diagnosed with autism for which screening tool of ADHD has been employed. This was used to evaluate the children either they have the co-morbidity or not. This part has been achieved by using the questionnaire comprising of NICHQ Vanderbilt Assessment Scale. This questionnaire was filled by interviewing the parents of autistic children because the parent's informant questions has been used. Health care practitioners utilize the NICHQ Vanderbilt Assessment Scales to evaluate ADHD in children between the ages of 6 and 12 years old. Both teachers and parents can fill out a number of forms. For signs of ADHD and inattention, both versions are used. The parent evaluation scale features a distinct part for conduct disorder or antisocial behavior, whereas the teacher assessment scale has an additional item for learning problems. Second part is the evaluation of parents for their knowledge and impact on improving the symptoms of the diseases on their children. This part was completed by using self-structured questions and the response is recorded using the binary scale. The final part is the assessment of clinicians, as how they deal with their patient's condition and what treatment methods they use. Additionally, all these questions have worked as training of parents, it had helped them comprehend the many behaviors and symptoms that their child displays. As a result, parents are better equipped to cope with a range of behavioral issues that arise in young children. Their understanding of how to handle their child's symptoms at home has increased.

2.10. Data Collection

Structured questionnaire with variable like socio-demographics was made. ADHD is screened (through parents) using the NICHQ Vanderbilt Assessment Scale screening tool. Parents were evaluated by means of structured questionnaire. Clinicians were also evaluated by using the self-structured questionnaire. Face-to-face interviews were done to administer the questionnaire. Also, the session will be voice recorded too to cross-check; validate the collected data. Data was collected from approximately 6 centers in Islamabad.

2.11. Statitical Analysis

Data entry was done in MS Excel followed by data cleaning and exporting to statistical software. The IBM SPSS Statistics Standard v26 software was used to do all data analysis. Continuous variables were presented as mean and standard deviation or median and inter-quartile range, and one-way analysis of variance (ANOVA) was used to evaluate differences between study variables, while independent t-test or Mann-Whitney test was used to compare two categorical variables. The Chi-square test was used to determine the significance of categorical data, and the results were given as numbers and percentages. A 0.05 p-value is deemed statistically significant.

2.12. Coordination, Monitoring, and Quality Control

The whole project was done in stages i.e., planning the data collection visits, preparing the Data Collection forms needed for field visits, preparing information materials and tools for data collectors in case any ambiguity exists and arranging regular communications with the key participants.

CHAPTER 3

RESULTS

3. RESULTS

3.1. Demographic Characteristics of Patients

The demographic characteristics of patients are summarized in table 3.1 showing distribution of participants across different age groups and genders, along with the associated p-values that indicate the statistical significance of these distributions. Overall, for the 6-10 years group, there were 25 (31.2%) cases, while for the 11-14 years age group, there were 55 (68.8%) cases which were in significantly higher proportion ($p < 0.0001$). Within the 6-10 years age group, there were 15 male (30% of the male population) and within the 11-14 years age group, there were 35 male participants (70% of the male population) which are significantly higher in proportion ($p = 0.0006$). Within the 6-10 years age group, there were 10 female participants (33.3% of the female population) and within the 11-14 Years age group, there were 20 female participants (66.6% of the female population) which are significantly higher in proportion ($p = 0.0098$).

Table 3.1. Gender and age distribution of ADHD patients (n = 80).

	6-10 Years	**11- 14 Years**	**p-value**
Total	25 (31.2)	55 (68.8)	< 0.0001
Male	15 (30)	35 (70)	0.0006
Female	10 (33.3)	20 (66.6)	0.0098

3.2. ADHD Subtype

The patients were categorized into ADHD subtypes and the data is summarized in table 3.2. The data showed that 63 participants (78.7%) were positive for PIS, and 17 (21.2) were negative. A significantly higher proportion of cases were positive for PIS ($p < 0.0001$). For PHS, 59 (73.7%) were positive, and 31 (37.5%) were negative. A significantly higher proportion of cases were positive for PHS ($p < 0.0001$). For CS, 65 (81.2%) were positive, and 15 (18.8%) were negative. A significantly higher proportion of cases were positive for PHS ($p < 0.0001$). For ODD, 70 (87.5%) were positive, and 15 10 (12.5%) were negative. A significantly higher proportion of cases were positive for PHS ($p < 0.0001$). For CD, 78 (97.5%) were positive, and 2 (2.5%) were negative. A significantly higher proportion of cases were positive for PHS ($p <$

0.0001). For depression, 79 (98.7%) were positive, and 1 (1.3%) were negative. A significantly higher proportion of cases were positive for PHS ($p < 0.0001$).

Table 3.2. ADHD subtypes in children with ASD.

ADHD Subtype	Positive	Negative	p-value
PIS	63 (78.7%)	17 (21.2%)	<0.0001
PHS	59 (73.7%)	31 (37.5%)	0.1096
CS	65 (81.2%)	15 (18.8%)	<0.0001
ODD	70 (87.5%)	10 (12.5%)	<0.0001
CD	78 (97.5%)	2 (2.5%)	<0.0001
Depression	79 (98.7%)	1 (1.3%)	<0.0001

3.3. Gender and Age distribution in ADHD Subtype

As shown in Table 3.3, 80% of participants with the PIS were male, and 20% of participants with the PIS were females. Among, PHS, 66% were males and 44 % were females. Subtype CS had 77% males and 23 % females. In ODD, 78% were males and 22% were females, IN CD 66% were males and 44% were females. Overall, 62% males had depression and 38% females had depression. The male gender significantly dominated in all subtypes of ADHD with a p-value of < 0.0001.

Table 3.3. Gender distribution in different subtypes of ADHD.

ADHD Subtype	Male (%)	Female (%)	p-value
PIS	50 (80)	13 (20)	< 0.0001
PHS	39 (66)	20 (44)	0.0004
CS	50 (77)	15 (23)	< 0.0001
ODD	55 (78)	15 922)	< 0.0001
CD	52 (66)	25 (44)	< 0.0001
Depression	49 (62)	30 (38)	0.0025

Age wise distribution showed that in 6-10 years of age, the prevalence of PIS was 20%, PHS 34%, CS 30%, ODD 34%, CD 39%, and depression was 44%. While in 11- 14 years of age, the prevalence of PIS was 80%, PHS 66%, Cs, 70%, ODD 66%, CD 61%, and depression was 56%. The prevalence of PIS ($p < 0.0001$), PHS ($p = 0.0004$), CS, ($p < 0.0001$), ODD ($p = 0.0002$), and CD ($p = 0.0039$) was significantly higher in 11-14 year of age group. However, depression was not statistically significant ($p = 0.1527$) between the two groups as shown in Table 3.4.

Table 3.4. Age wise prevalence of ADHD sub types.

ADHD Subtype	6-10 Years	11- 14 Years	p-value
PIS	13 (20)	50 (80)	< 0.0001
PHS	20 (34)	39 (66)	0.0004
CS	20 (30)	45 (70)	< 0.0001
ODD	24 (34)	46 (66)	0.0002
CD	30 (39)	48 (61)	0.0039
Depression	35 (44)	44 (56)	0.1527

3.4. Demographic Characteristics of Parents

Demographic characteristics of parents are summarized in table 3.5. The table shows that 29 participants were male, which accounts for 36.2% of the total participants and 51 participants were female, constituting 63.7% of the total participants as show in Figure 3.5. The p-value associated with this distribution is < 0.0001, indicating a significantly higher proportion of female participants. The data for age distribution showed that there were 28 participants (35%) were of 23-32 years of age, 30 participants (37.5%) were from 33 - 42 years of age, and 22 participants (275%) were from 42 - 52 years of There was no statistically significant difference in the age group of parents as shown in Figure 3.6. There were 54 participants (67.5%) categorized as illiterate, and 24 participants (31.5%) were literate. The p-value associated with this distributions p = 0.0003 indicating a statistically significant higher proportion of parents from illiterate category as shown in Figure 3.7.

Table 3.5. Demographic characteristics of Parents.

Parents's demographics	Category	Total cases	Frequency	p-value
Gender	**Male**	29	36.2	<0.0001
	Female	51	63.7	
Age	**23 - 32 Years**	28	35	0.7278
	33 - 42 Years	30	37.5	
	42 - 52 Years	22	27.5	
Socioeconomic Status	**Upper Class**	20	25	0.0008
	Middle Class	22	27.5	
	Lower Class	38	47.5	
Qualification	**Illiterate**	54	67.5	0.0003
	Literate	24	31.5	

3.5. Management of ASD and ADHD

The Figure 3.1 provides data related to the frequency of certain practices and approaches in the assessment and management of ASD and ADHD patients taken by the clinicians. The responses were categorized by different levels of frequency, ranging from "Never" to "Very Often and were scored from a scale of 0 to 3.

The data showed that the observed differences in the frequency of using scoring standard scoring scales by the clinicians were not statistically significant ($p = 0.0561$). The observed differences in the frequency of using drug therapy and speech therapy as the initial treatment of choice were not statistically significant ($p = 0.0767$ and 0.523, respectively). However, the observed differences in the frequency of using behavioral therapy as the initial treatment of choice was statistically significant ($p = 0.0384$). Additionally, it was not a common practice to screen such patients for other condition that might co-exist ADHD and ASD ($p = 0.3270$) or treat ADHD as 1st priority in patient suffering from both ADHD and ASD ($p = 0.3376$). A significantly higher proportion of clinician involved the parents during the management of ADHD and ASD patients ($p = 0.0005$).

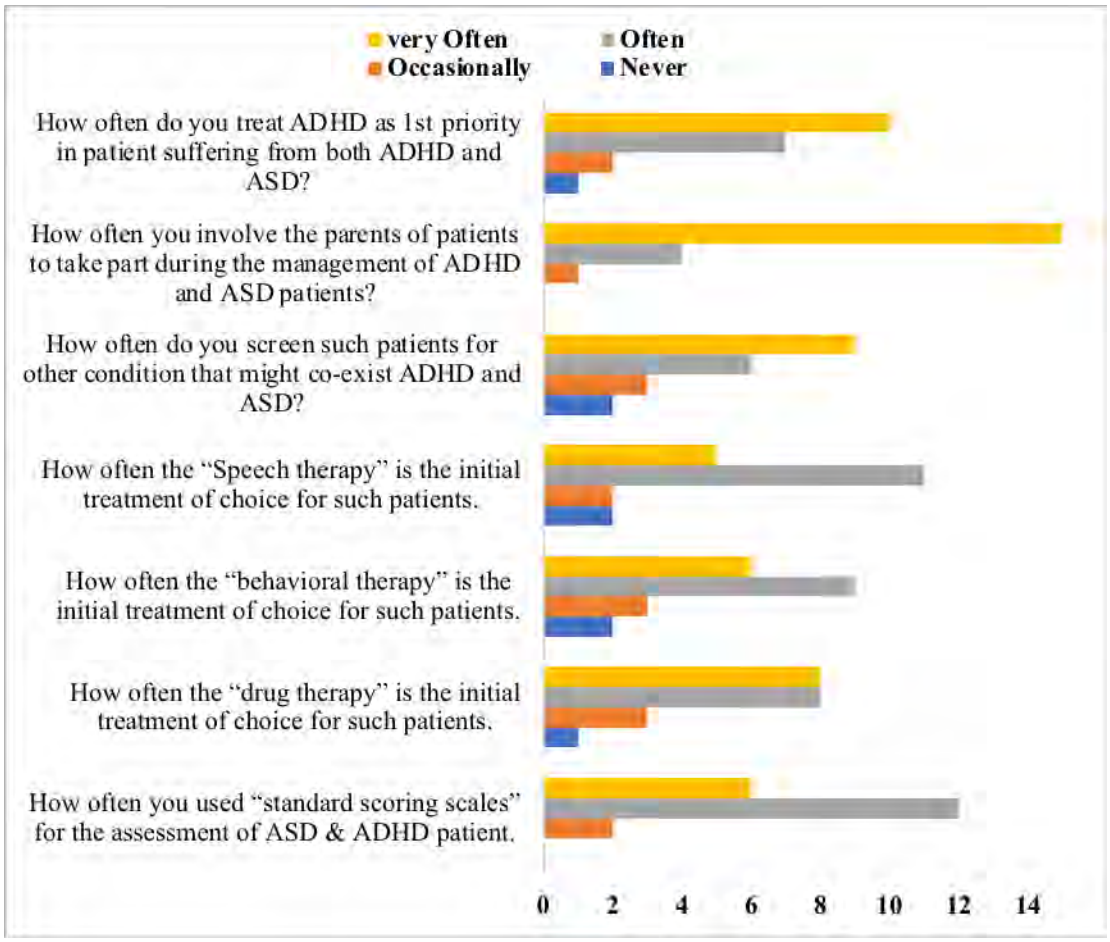

Figure 3.1. Management of ADHD and ASD.

3.6. Effect of Parent's Age on Prevalence of ADHD Sub types in Children

Effect of parent's age on Prevalence of ADHD sub types in children is shown in Table 3.2. A significantly higher proportion of patients with PIS (54%; p= 0.002), PHS (60%; p = 0.042), CS (68%; p = 0.004), ODD (65%; p = 0.005), CD (65%, p < 0.0001), and depression (71%; p < 0.0001) were prevalent in parents with 42-52 years of age group as compared to 23 years and 33-42 years of age group.

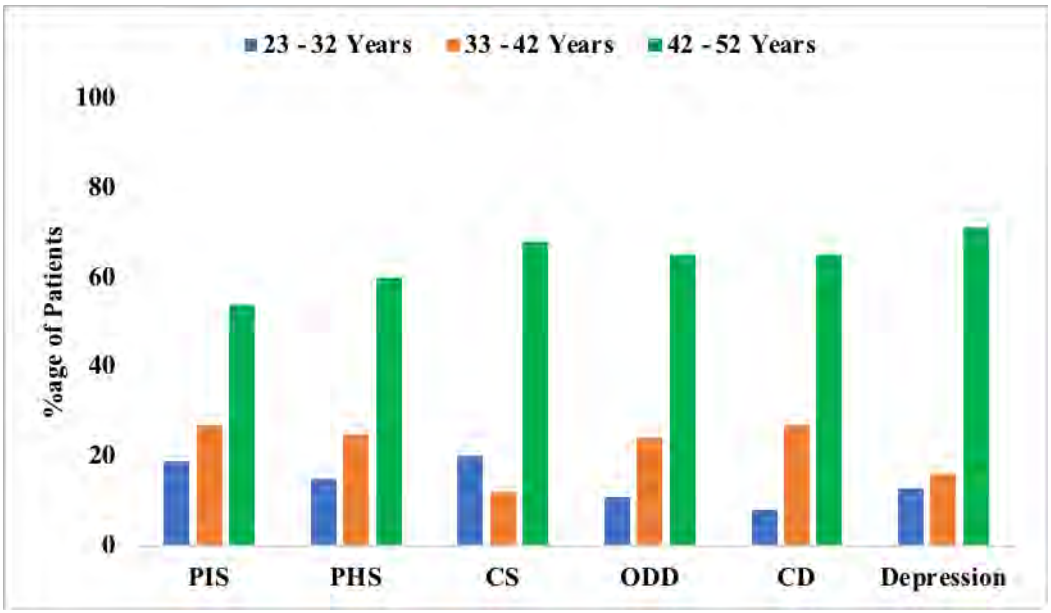

Figure 3.2. Effect of Parent's Age on Prevalence of ADHD Sub types in Children.

The socio-economic status of ADHS parents is shown in Table 3.6 which shows that a significantly higher proportion of patients with PIS (44%; p= 0.0067), PHS (68%; p < 0.0001), CS (75%; p < 0.0001), ODD (65%; p < 0.0001), CD (62%; p < 0.0001), and depression (48%; p < 0.0001) belonged to lower class parents.

Table 3.6. Parent's socio-economic status of ADHD patients.

ADHD Subtype	Upper Class	Middle Class	Lower Class	p-value
PIS	10 (16)	19 (30)	34 (44)	0.0067
PHS	7 (12)	12 (20)	40 (68)	< 0.0001
CS	15 923)	18 (12)	32 (75)	< 0.0001
ODD	10 (14)	15 (21)	45 (65)	< 0.0001
CD	12 (15)	18 (23)	48 (62)	< 0.0001
Depression	16 (20)	18 (22)	45 (48)	< 0.0001

Parent's qualification data is shown in Table 3.7 which indicated that a significantly higher proportion of patients with PIS (63%; p= 0.0024), PHS (64%; p = 0.0017), CS (69%; p < 0.0001), ODD (82%; p < 0.0001), CD (78%; p < 0.0001), and depression (62%; p = 0,0025) were from illiterate parents.

Table 3.7: Qualification of Parents of ADHD patients.

ADHD Subtype	Illiterate	Literate	p-value
PIS	40 (63)	23 (37)	0.0024
PHS	38 964)	21 (36)	0.0017
CS	45 (69)	20 (31)	<0.0001
ODD	58 (82)	12 (18)	<0.0001
CD	61 (78)	17 (22)	<0.0001
Depression	49 (62)	30 (38)	0.0025

3.7. Parent's Knowledge about ASD and ASHD

Parents of ASD and ADHD children were interviewed to access their knowledge about the condition of their child and the results are summarized in Figure 3.3. A significantly higher proportion of parents (75%) did not have any awareness about ASD and ADHD (p = 00046). However, a significantly higher proportion of parents (78%) had the awareness about the importance of treatment of the condition of their child (P < 0.0001). Parents (62.5%) had the awareness about the importance of diagnosis of the condition of their child, while 32.5% did not consider this as important as other parents (P = 0.0258). After or during the treatment, a significant higher proportion of parents (81.2%) were satisfied with the treatment their child was receiving after diagnosis (P < 0.0001). In addition to treatment, 51.2% parents said that their child need special attention for treatment (P = 0.0107). 55% parents believed that the condition or the disease of their child is curable while 45% did not believe this as curable disorder (P = 0.0891).

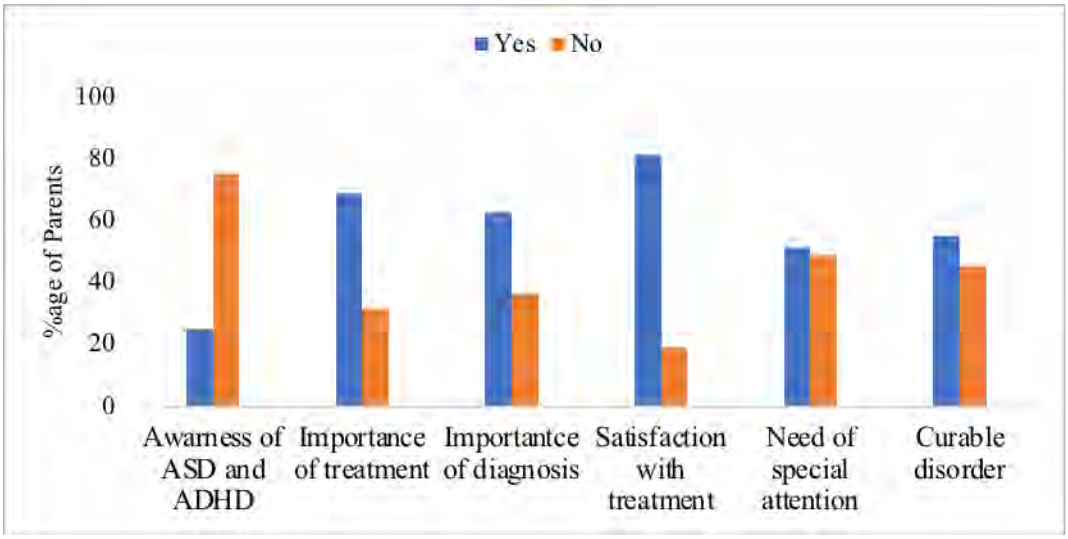

Figure 3.3: Parent's knowledge about ASD and ADHD

3.8. Symptoms of PIS Experienced by Chidren

Parents of children having PIS were interviewed about the symptoms of their child and it was observed that 56.25% of children were often unable to pay attention to details and were making careless mistakes including their homework, which was significantly higher than other responses (P = < 0.0001). It was very often for 55% of children that they had difficulty sustaining attention to tasks or activities which was significantly higher than other responses. It was often (42.5%) observed by parents that their child does not seem to listen when the spoke to him directly which was significantly higher than other responses (p =0.037). 66.2% of the parents responded that it was very often that their child does not follow the instructions which was significantly higher than other responses (p < 0.0001). In addition, 58.7% parents often observed that their child has difficulty organizing tasks and activities which was significantly higher than other responses (p = 0.0001). A significantly higher proportion of parents (62.5%) responded that it is often that their child avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort which was significantly higher than other responses (p = 0.0001). However, it was not significantly observed that children are losing things necessary for tasks or activities (p = 0.865). Additionally, it was very often (40%) that children were easily distracted by extraneous stimuli and (53.57%) were often forgetful in daily activities. The response of the parents to each question are shown in Figure 3.4.

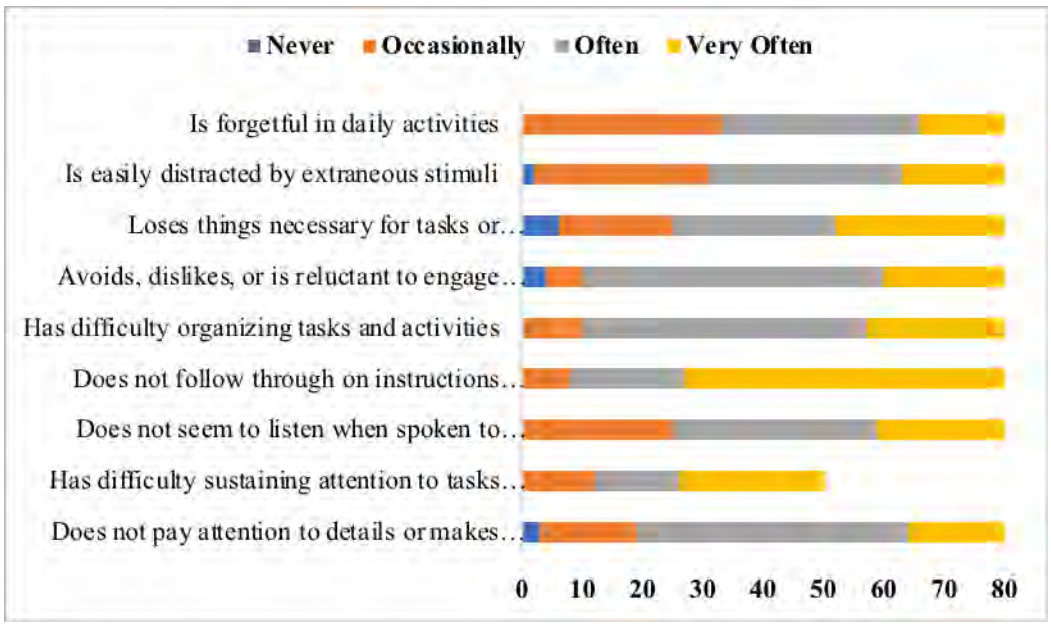

Figure 3.4. Symptoms of PIS experienced by Children.

3.9. Symptoms of PHS experienced by Children

Parents of children having PHS were interviewed about the symptoms of their child and it was observed that 66.2% of parents responded that was “often” for their child to have fidgets with hands or feet or squirms in seat which was significantly higher than other responses ($p < 0.0001$). 47.5% of parents observed that is often that their child leaves the seat when remain seated is expected while 61.2% parents observed that often their child runs about or climbs excessively in situations when remaining seated is expected and this observation was significantly higher that others ($p < 0.0001$). Additionally, 57.5% parents responded that it was often that their child has difficulty playing or engaging in leisure/play activities quietly and this observation was significantly higher that others ($p < 0.0001$). It was often observed that children felt they are driven by motors (50%), and this observation was significantly higher that others ($p < 0.0001$). Parents responded that it was often that their child blurts out answers before questions have been completed (48.75%), have difficulty waiting for their turn (45%), and Interrupts or intrudes on others (46.2%) and these observations were significantly higher that others ($p < 0.0001$). The response of the parents to each question are shown inFigure 3.5.

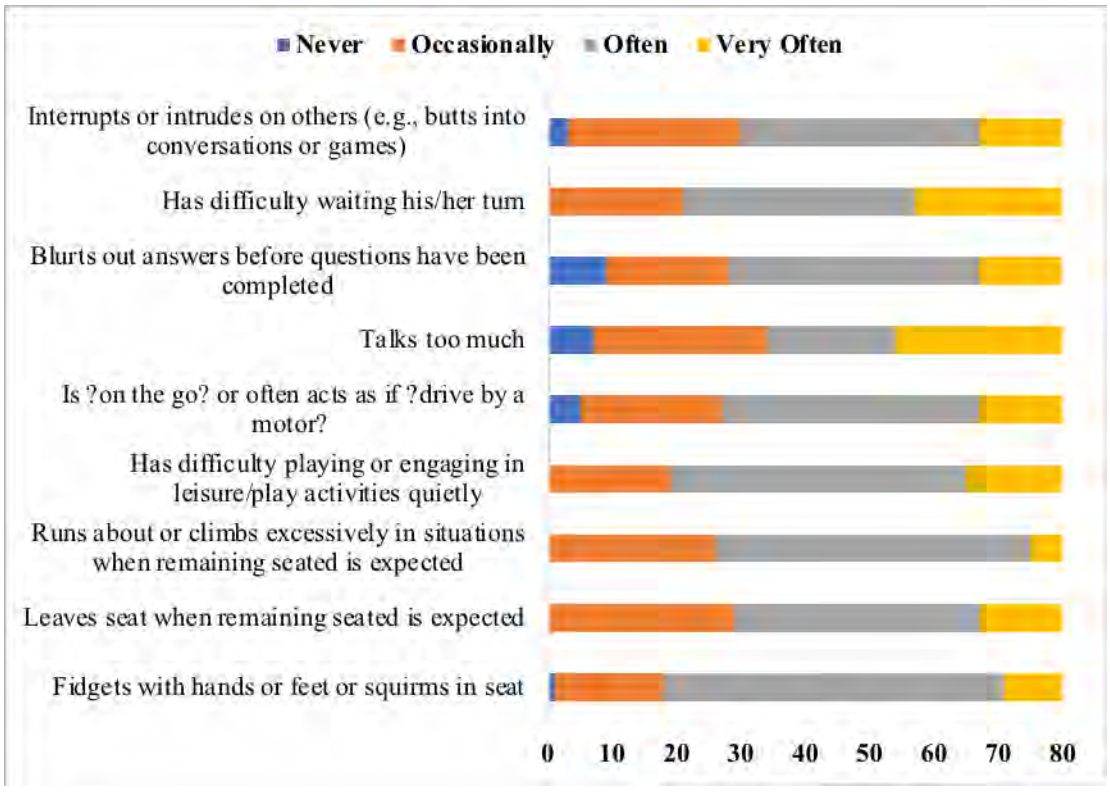

Figure 3.5. Symptoms of PHS experienced by children.

3.10. Symptoms of CS Experienced by Children

Parents of children having CS were interviewed about the symptoms of their child and it was observed often that 52.7% of children were often unable to pay attention to details and were making careless mistakes including their homework, which was significantly higher than other responses ($P < 0.0001$). It was very often for 55% of children that they had difficulty sustaining attention to tasks or activities which was significantly higher than other responses. It was often (42.5%) observed by parents that their child does not seem to listen when the spoke to him directly which was significantly higher than other responses ($p = 0.037$). 66.2% of the parents responded that it was very often that their child does not follow the instructions which was significantly higher than other responses ($p < 0.0001$). In addition, 58.7% parents often observed that their child has difficulty organizing tasks and activities which was significantly higher than other responses ($p = 0.0001$). A significantly higher proportion of parents (62.5%) responded that it is often that their child avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort which was significantly higher than other responses ($p = 0.0001$). However, it was not significantly observed that children are losing things necessary for tasks or activities ($p = 0.865$).

Additionally, it was very often (40%) that children were easily distracted by extraneous stimuli and (53.57%) were often forgetful in daily activities. 66.2% of parents responded that was “often” for their child to have fidgets with hands or feet or squirms in seat which was significantly higher than other responses ($p < 0.0001$). 47.5% of parents observed that is often that their child leaves the seat when remain seated is expected while 61.2% parents observed that often their child runs about or climbs excessively in situations when remaining seated is expected and this observation was significantly higher that others ($p < 0.0001$). Additionally, 57.5% parents responded that it was often that their child has difficulty playing or engaging in leisure/play activities quietly and this observation was significantly higher that others ($p < 0.0001$). It was often observed that children felt they are driven by motors (50%), and this observation was significantly higher that others ($p < 0.0001$). Parents responded that it was often that their child blurts out answers before questions have been completed (48.75%), have difficulty waiting for their turn (45%), and interrupts

or intrudes on others (46.2%) and these observations were significantly higher that others ($p < 0.0001$). The response of the parents to each question are shown in Figure 3.6.

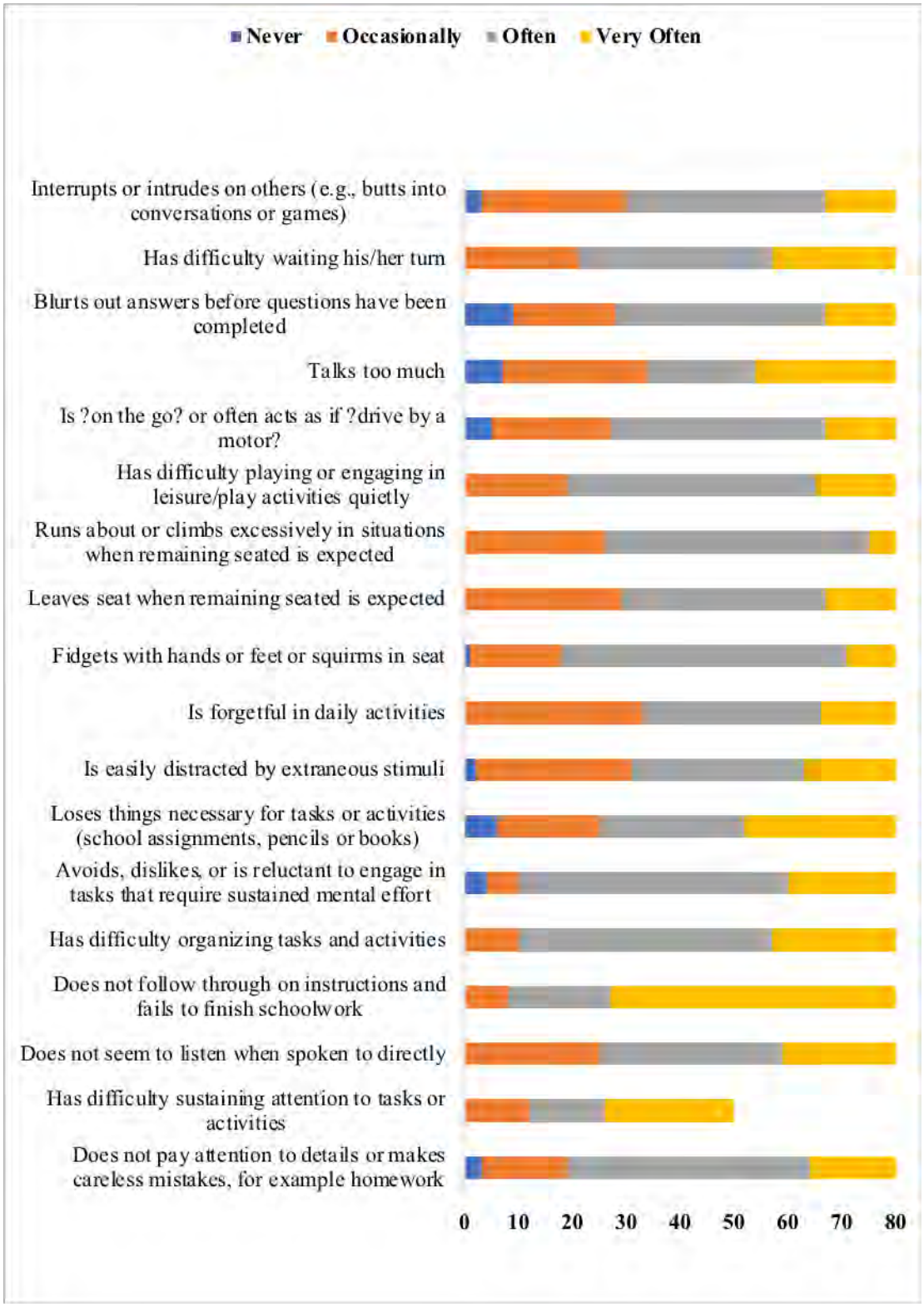

Figure 3.6. Symptoms of CS on experienced by children.

3.11. Symptoms of ODD Experienced by Children

Parents of children having ODD were interviewed about the sympotoms of their child and it was observed often that 42.5% children argued with adults ($p = 0.0001$) and 55% loose temper ($p < 0.0001$), (63.7%) blames others for his or her mistakes or misbehaviors ($p < 0.0001$), 55% were angry or resentful ($p < 0.0001$), and 65% were spiteful and vindictive ($p < 0.0001$). Additionally, 55% were angry or resentful ($p < 0.0001$) and 65% were spiteful and vindictive ($p < 0.0001$). The response of the parents to each question are shown in Figure 3.7.

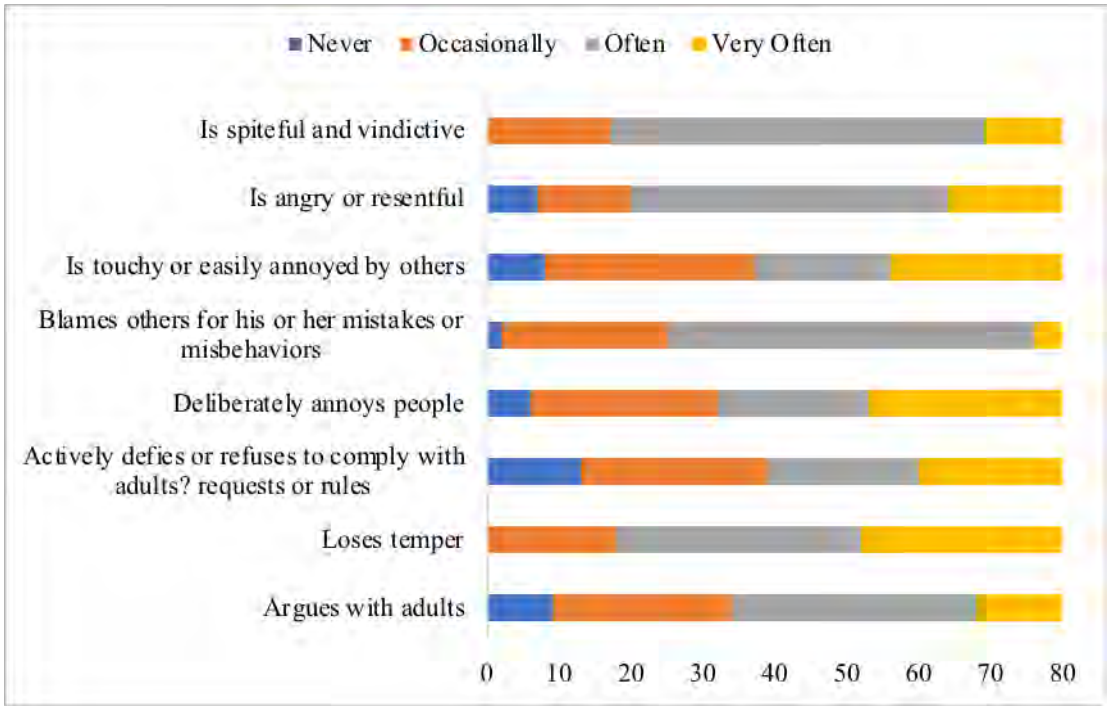

Figure 3.7. Symptoms of ODD experienced by children.

3.12. Symptms of CD Experienced by Children

Parents of children having CD were interviewed about the symptoms of their child and it was observed often that 52.5% children were Bullying, threatening, or intimidating others ($p = 0.0006$), 48.7% were often initiating fights ($p = 0.0001$), 52.5% were lying to obtain goods for favors or to avoid obligations ($p = 0.0003$), 65% were truant from school (skips school) without permission ($p < 0.0001$), 51.2% were physically cruel to people ($p = 0.0021$), 53.7% had the habit of stealing items of nontrivial value ($p =0.0001$), 60% were deliberately destroying others properties ($p < 0.0001$), 53.7% were used a weapon that can cause serious harm (p 0.0007), 55%

were physically cruel to animals ($p = 0.0024$), 46.2% deliberately set fires to cause damage ($p < 0.0001$), 57.5% broke into someone else's home, business, or car ($p < 0.0001$), 65% stayed out at night without permission ($p < 0.0001$), 67.5% ran away from home overnight ($p < 0.0001$), and 52.5% forced someone into sexual activity ($p = 0.0384$). The response of the parents to each question are shown in Figure 3.8.

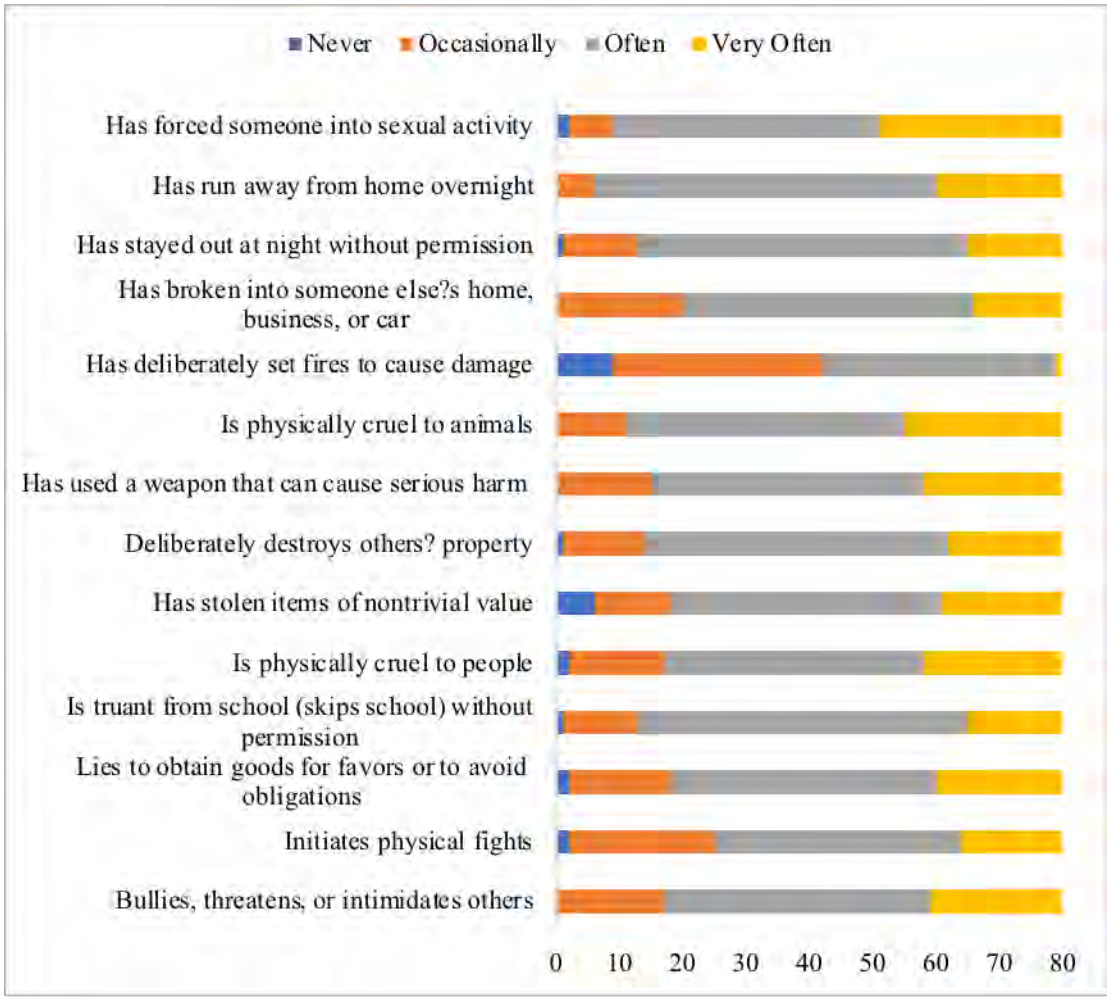

Figure 3.8. Symptoms of CD experienced by children.

3.13. Symptoms of Depression Experienced by Children

Parents of children having CD were interviewed about the symptoms of their child and it was observed often that 66.2% children were fearful, anxious, or worried ($p < 0.0001$), 66.2% were afraid to try new things for fear of making mistakes ($p < 0.0001$), 61.2% were feeling worthless or inferior ($p < 0.0001$), 40% felt lonely, unwanted, or unloved ($p < 0.0001$), and 61.2% were sad, unhappy, or depressed and

self-conscious ($p < 0.0001$). The response of the parents to each question are shown in Figure 3.9.

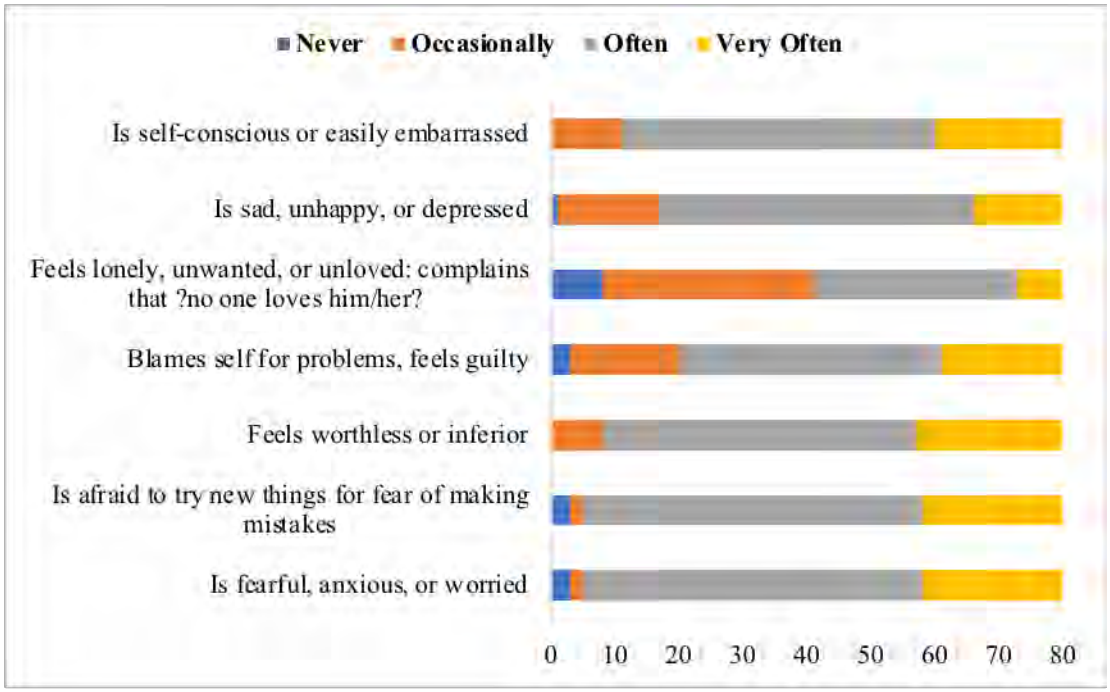

Figure 3.9. Symptoms of Depression experienced by children.

CHAPTER 4

DISCUSSION

4. DISCUSSION

In this study, we have investigated the co-occurrence of ASD ad ADHD in pediatric population and the role of clinicians and parents in the management of neurodevelopmental disorders. We assessed 80 ADHS children with ASD and interviewed their parents and clinician who were treating them to investigate the impact of ASD and ADHD on quality of life and management of the disease with various neurodevelopmental disorders.

We observed that co-occurrence of ASD and ADHD was more prevalent in male children and in the school gong age of 6-13 years. The impact of age and gender on pediatric Attention-Deficit/Hyperactivity Disorder (ADHD) and autism spectrum disorder (ASD) has been the subject of extensive research. Both age and gender play significant roles in the prevalence, presentation, and diagnosis of these neurodevelopmental disorders. The presentation and manifestations of ADHD symptoms can evolve with age. Younger children may exhibit more hyperactive and impulsive behaviors, while older children might display more inattention symptoms as cognitive demands increase.

ADHD symptoms show moderate continuity over time, and the impairment associated with ADHD can vary across different developmental stages (Barkley *et al*., 2002). ASD symptoms typically emerge in early childhood, often by the age of two. However, the severity and manifestation of these symptoms can change as children age, and interventions can lead to improvements in certain areas. It has been found that core ASD symptoms remained relatively stable over time, but adaptive functioning improved in some children (Fountain *et al*., 2011). ADHD and ASD is more commonly diagnosed in males than females. However, research suggests that the presentation of symptoms might differ by gender. Females with ADHD may display more inattentive symptoms, which could contribute to underdiagnosis or misdiagnosis (Lai *et al*., 2015). It has been reported that gender-related differences in ADHD symptoms could lead to gender biases in clinical diagnosis (Gershon and Gershon, 2002).

Additionally, we observed that among major subtypes of ADHD, the prevalence of PIS, PHD, and CS was 78.7%, 73.7%, and 81.2%, respectively. The prevalence of CS was the highest which has been reported in the literature. The overall prevalence of

ADHD is well-studied, the prevalence of individual subtypes can differ across populations and studies. PIS of ADHD is characterized by significant difficulties with attention and focus, but not hyperactivity-impulsivity. The prevalence of PIS varies, with estimates ranging from around 25% to 65% of individuals diagnosed with ADHD. A study reported a prevalence of 25% for the PIS in a sample of children with ADHD (Faraone *et al*., 2006a). PHS of ADHD is characterized by significant hyperactivity and impulsivity, but not the same degree of inattention as the combined subtype.

Prevalence estimates for PHS can vary, with some studies reporting lower prevalence rates compared to other subtypes. It has been reported that the PHS had the lowest prevalence rate among the subtypes in a large sample of children (Willcutt et al., 2012). The CS of ADHD is characterized by significant symptoms of both inattention and hyperactivity-impulsivity. his subtype tends to have the highest prevalence rate among the three subtypes of ADHD. It has been reported that the combined subtype to be the most prevalent, accounting for approximately 62% of diagnosed cases (Polanczyk *et al*., 2007).

Clinicians play a critical role in the management of Attention-Deficit/Hyperactivity Disorder (ADHD), contributing to accurate diagnosis, comprehensive assessment, personalized treatment planning, and ongoing sonitoring. Their expertise ensures that individuals with ADHD receive the appropriate interventions and support to optimize their functioning and well-being. Clinicians are trained to assess and diagnose ADHD using standardized criteria from diagnostic manuals such as the DSM-5. Their expertise allows them to differentiate ADHD from other conditions that may present with similar symptoms (American Psychiatric Association and Association, 2013). Clinicians conduct thorough assessments to gather information about an individual's history, symptoms, functioning in various settings, and potential comorbid conditions. This assessment helps tailor interventions to the specific needs of the individual (Wolraich *et al*., 2019a). Clinicians collaborate with individuals with ADHD, their families, and other professionals to develop individualized treatment plans. These plans often include a combination of behavioral interventions, psychoeducation, and, if necessary, medication (Perrin *et al*., 2001).

Clinicians provide guidance on evidence-based behavioral interventions, such as parent training and school-based interventions, to help individuals with ADHD develop skills for managing symptoms and improving functioning (Pelham Jr and Fabiano, 2008). Clinicians regularly monitor the progress of individuals with ADHD, adjusting interventions and treatment plans based on their evolving needs. This ongoing relationship ensures that interventions remain effective over time. In conclusion, clinicians play a multifaceted role in the management of ADHD, contributing to accurate diagnosis, individualized treatment planning, medication management, and ongoing monitoring. Their expertise is essential in providing effective interventions and support to individuals with ADHD and their families.

We observed in this stud that co-occuring of ADHD and ASD has impacted the life significantly. ADHD and ASD can have a significant impact on various aspects of an individual's quality of life, affecting academic, social, occupational, and emotional well-being. Understanding these effects is crucial for developing appropriate interventions and support strategies. Children and adolescents with ADHD often experience difficulties in academic settings, including poor concentration, organizational challenges, and difficulties completing tasks. Barkley et al. (2008) highlighted the negative impact of ADHD on academic performance and educational attainment, which can lead to lower self-esteem and reduced future opportunities (Barkley *et al*., 2006). Individuals with ADHD may struggle with social interactions due to impulsivity, inattention, and difficulties with self-regulation. This can lead to strained relationships with peers and family members. Kofler *et al.* (2011) found that social impairment in children with ADHD is related to both ADHD symptoms and comorbid conditions, further impacting their overall quality of life (Kofler *et al*., 2013).

ADHD is associated with increased emotional dysregulation, anxiety, and depression. Individuals with ADHD may experience low self-esteem and emotional distress. Biederman *et al.* (2006) found that adults with ADHD are at increased risk for mood and anxiety disorders, which can further reduce their overall quality of life (Biederman *et al*., 2000). The cumulative impact of ADHD-related challenges on academic, social, occupational, and emotional domains can result in a reduced overall quality of life. Nøvik *et al*. (2006) assessed quality of life in children with ADHD and found that impaired psychosocial functioning significantly contributed to their

diminished well-being (Nøvik *et al*., 2006). In conclusion, ADHD can have wide-ranging effects on various aspects of an individual's quality of life, including academic, social, occupational, and emotional well-being. These effects highlight the importance of early intervention, tailored support, and a comprehensive approach to addressing the challenges associated with ADHD.

CONCLUSIONS

- The use of standardized assessment tools is a critical component in accurately assessing and diagnosing the co-occurrence of ASD and ADHD.
- The research shows that ADHD and ASD co-exist together, and clinicians are mostly well informed on contrary to that the parents of patients are less aware of the fact that their child might be suffering from ADHD.
- Another important aspect of managing the co-occurrence of ASD and ADHD is providing support for the parents of affected individuals. Parent training programs, such as the Parent-Child Interaction Therapy (PCIT) and the Incredible Years program, have been shown to be effective in improving parent-child interactions and reducing problem behaviors in children with co-occurring conditions.
- In addition to parent training programs, providing education and support to parents can also be beneficial in helping them navigate the challenges of raising a child with co-occurring conditions. This can include providing information on community resources and support groups, as well as connecting parents with other families who have children with similar conditions.
- Overall, managing the co-occurrence of ASD and ADHD can be challenging, but through the use of appropriate interventions and supports, individuals with co-occurring conditions can make significant improvements in their quality of life.

FUTURE PROSPECTIVES

- By identifying the incidence of mental disorders and the coexistence of multiple mental disorders within patients, symptoms can be identified more easily, hence reducing the number of undiagnosed cases in society.
- The results of this study will benefit Clinicians and healthcare workers by getting better insight into the diagnostic criteria of the disease, which in turn will result in better treatment outcomes.
- The better clinicians are able to understand the behavioral aspects of a patient suffering from these disorders, the more they are able to design an effective treatment plan tailored for the specific needs of each patient.
- Raising the necessary awareness of these disorders through such research will help policymakers understand the importance of incorporating policies tending to these issues. Only through awareness and concrete evidence can a significant change be made in the policies and regulations of our community.
- This study hopes to give ground for future studies to stem from and open new doors for new possibilities.

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Annexure I: Data Collection Form/Questionnaire

Demographics:

I. Full Name:

II. Gender:

○ Male ○ Female

III. Date of Birth:

IV. Age:

Evaluation of ADHD

Each rating should be considered in the context of what is appropriate for the age of your child.

Frequency Code: 0 = Never 1 = Occasionally 2 = Often 3 = Very Often

1. Does your child not pay attention to details or makes careless mistakes, for example homework?
   0 1 2 3
2. Has difficulty sustaining attention to tasks or activities
   0 1 2 3
3. Does not seem to listen when spoken to directly
   0 1 2 3
4. Does not follow through on instructions and fails to finish schoolwork (not due to oppositional behavior or failure to understand)
   0 1 2 3
5. Has difficulty organizing tasks and activities
   0 1 2 3
6. Avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort
   0 1 2 3
7. Loses things necessary for tasks or activities (school assignments, pencils or books)
   0 1 2 3
8. Is easily distracted by extraneous stimuli
   0 1 2 3
9. Is forgetful in daily activities
   0 1 2 3
10. Fidgets with hands or feet or squirms in seat
    0 1 2 3
11. Leaves seat when remaining seated is expected
    0 1 2 3

12. Runs about or climbs excessively in situations when remaining seated is expected
    0 1 2 3

13. Has difficulty playing or engaging in leisure/play activities quietly
    0 1 2 3

14. Is "on the go" or often acts as if "drive by a motor"
    0 1 2 3
15. Talks too much
    0 1 2 3
16. Blurts out answers before questions have been completed
    0 1 2 3
17. Has difficulty waiting his/her turn
    0 1 2 3
18. Interrupts or intrudes on others (e.g., butts into conversations or games)
    0 1 2 3
19. Argues with adults
    0 1 2 3
20. Loses temper
    0 1 2 3
21. Actively defies or refuses to comply with adults' requests or rules
    0 1 2 3
22. Deliberately annoys people
    0 1 2 3
23. Blames others for his or her mistakes or misbehaviors
    0 1 2 3
24. Is touchy or easily annoyed by others
    0 1 2 3
25. Is angry or resentful
    0 1 2 3
26. Is spiteful and vindictive
    0 1 2 3
27. Bullies, threatens, or intimidates others
    0 1 2 3
28. Initiates physical fights
    0 1 2 3
29. Lies to obtain goods for favors or to avoid obligations (i.e., "cons" others)
    0 1 2 3
30. Is truant from school (skips school) without permission
    0 1 2 3
31. Is physically cruel to people
    0 1 2 3
32. Has stolen items of nontrivial value
    0 1 2 3

33. Deliberately destroys others' property
    0 1 2 3
34. Has used a weapon that can cause serious harm (bat, knife, brick, gun)
    0 1 2 3
35. Is physically cruel to animals
    0 1 2 3
36. Has deliberately set fires to cause damage
    0 1 2 3
37. Has broken into someone else's home, business, or car
    0 1 2 3
38. Has stayed out at night without permission
    0 1 2 3
39. Has run away from home overnight
    0 1 2 3
40. Is fearful, anxious, or worried
    0 1 2 3
41. Is afraid to try new things for fear of making mistakes
    0 1 2 3
42. Feels worthless or inferior
    0 1 2 3
43. Blames self for problems, feels guilty
    0 1 2 3
44. Feels lonely, unwanted, or unloved: complains that "no one loves him/her"
    0 1 2 3
45. Is sad, unhappy, or depressed
    0 1 2 3
46. Is self-conscious or easily embarrassed
    0 1 2 3

Evaluating Clinicians:

1. How often you used "standard scoring scales" for the assessment of ASD & ADHD patient.

   0 1 2 3

2. How often the "drug therapy" is the initial treatment of choice for such patients.

   0 1 2 3

3. How often the "behavioral therapy" is the initial treatment of choice for such patients.

   0 1 2 3

4. How often the “Speech therapy” is the initial treatment of choice for such patients.

   0 1 2 3

5. How often do you screen such patients for other condition that might co-exist ADHD and ASD?

   0 1 2 3

6. How often you involve the parents of patients to take part during the management of ADHD and ASD patients?

   0 1 2 3

7. How often do you treat ADHD as 1st priority in patient suffering from both ADHD and ASD?

   0 1 2 3

Evaluating Parents:

1. How do you score yourself regarding the information of ASD and ADHD?

   0 1 2 3

2. Do you think the treatment of neurodevelopmental disorder is important?

   0 1 2 3

3. Do you think an early diagnosis of ADHD and ASD is important?

   0 1 2 3

4. Are you satisfied with the treatment that your child is getting?

   0 1 2 3

5. Do you think that you child needs your special attention

   0 1 2 3

6. Do you think that ADHD and ASD is curable?

   0 1 2 3

Annexure II: Approval form Bioethics Committee

قائداعظم یونیورسٹی
QUAID-I-AZAM UNIVERSITY
Faculty of Biological Sciences
Bioethics Committee

No. #BEC-FBS-QAU2022-391 Dated: 27-06-2022

Dr. Amjad Khan
Department of Pharmacy,
Faculty of Biological Sciences,
Quaid-i-Azam University, Islamabad
45320, Pakistan

Subject: - **"The Co-Occurance of ASD and ADHD in Pediatric Population and the Role of Clinicians and Parents in the Management of Neurodevelopmental Disorders."**

Dear Dr. Amjad Khan,

We wish to inform you that your subject research study has been reviewed and is hereby granted approval for implementation by Bio-Ethical Committee (BEC) of Quaid-i-Azam University, Your study has been assigned protocol **#BEC-FBS-QAU2022-391**.

While the study is in progress, please inform us of any adverse events or new, relevant information about risks associated with the research. In case changes have to be made to the study procedure, the informed consent from and or informed consent process, the BEC must review and approve any of these changes prior to implementation.

Sincerely,

Prof. Dr. Sarwat Jahan
Department of Zoology

cc:
Dean, F.B.S

Annexure III: Turnitin Similarity Index Report

05/09/2023, 12:15 Turnitin - Originality Report - Dua Thesis

Turnitin Originality Report

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