Review

Clinical Profiles in Autism Spectrum Disorder: Enhancing Diagnosis, Treatment, and Overall Health Outcomes

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Clinical Profiles in Autism Spectrum Disorder: Enhancing Diagnosis, Treatment, and Overall Health Outcomes

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Abstract: Autism Spectrum Disorder (ASD), a neurodevelopmental disorder, is increasingly diagnosed and significantly affects communication, behavior, and social interaction. The current diagnostic framework, guided by the DSM-5, has limitations that may lead to clinical gaps due to overlapping symptoms of ASD and other disorders. This study proposes a comprehensive approach to enhance ASD diagnosis through clinical stratification based on comorbidities. We applied precision medicine techniques to identify and categorize ASD into ten clinical profiles. Our findings contribute to a more profound understanding of ASD, including its varied clinical manifestations and comorbidities, and facilitate the development of personalized therapeutic strategies.

Keywords: autism spectrum disorder; precision medicine; clinical profiles; mitochondrial dysfunction; nutritional strategies; genetic variants; integrative care; comorbidities; personalized treatment; neuroinflammation

1. Introduction

The global incidence of Autism Spectrum Disorder (ASD) reflects an escalating public health issue, with the latest estimates from the Centers for Disease Control and Prevention (CDC) indicating that ASD affects 1 in 36 children at eight years of age in the United States [1]. This increase underscores the urgent need for enhanced diagnostic and therapeutic approaches in various healthcare systems.

Traditional methods for diagnosing ASD have predominantly focused on behavioral assessments based on the Diagnostic and Statistical Manual of Mental Disorders criteria [2]. Despite the widespread use of conventional methods to address autism, these approaches frequently fail to consider the diverse range of individual characteristics and comorbidities associated with the condition. This can result in inadequate treatment strategies that do not fully address the complexities of ASD. Moreover, reliance on narrow diagnostic criteria can result in incomplete diagnoses, affecting the timely implementation of interventions that could improve outcomes [3].

A significant concern in the management of autism is the prevalence of polypharmacy, in which individuals are often prescribed multiple medications to manage a wide array of associated symptoms and comorbidities. Studies indicate that individuals with ASD are much more likely to receive prescriptions from multiple medication classes. This not only complicates clinical management but also increases the risk of adverse drug interactions and side effects. [4].

Furthermore, the life expectancy of individuals with Autism Spectrum Disorder is significantly affected. Recent research indicates that the average life expectancy of those with ASD can be up to 16 years shorter than that of the general population, mainly because of a combination of health comorbidities, such as epilepsy and mental health conditions, and external factors, including inadequate healthcare responses to their unique needs.

The necessity for personalized approaches to the diagnosis and treatment of autism is becoming increasingly apparent. These approaches must account for the diverse clinical profiles and intricate interplay of the genetic, neurological, and environmental factors that characterize ASD. By tailoring

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strategies to individuals, it is possible to significantly enhance the quality of life and health outcomes of those affected by this complex condition [5].

2. Methods

This study synthesizes existing knowledge and introduces a novel stratification model for Autism Spectrum Disorder through an extensive review and critical analysis of the current literature. The foundation of this approach lies in a comprehensive examination of peer-reviewed articles, clinical trials, and meta-analyses that focus on the diagnosis, treatment, and management of ASD.

The methodology involves thematic analysis to identify and categorize standard clinical profiles of autism, as described in existing research. This process includes extracting data on the efficacy of various diagnostic and therapeutic strategies, their limitations, and the outcomes of precision medicine applications for neurodevelopmental disorders.

To establish the proposed stratification model for ASD, a detailed analysis of the existing genetic, neurological, and psychiatric research was conducted. This analysis involved a thorough review of empirical studies that documented the differences in ASD presentation and their association with specific genetic markers, neurophysiological patterns, and psychiatric profiles.

The model was constructed to categorize ASD into distinct clinical profiles supported by a combination of empirical evidence and clinical observations from a wide range of patient data. These profiles were formulated to align closely with variations in symptomatology and the underlying biological mechanisms, facilitating more targeted and effective treatment strategies. This approach utilizes traditional diagnostic criteria and incorporates advanced biomarkers and behavioral assessments to determine the precision of the diagnostic process.

As part of this methodology, we developed the Integrative Mapping (IMAP) tool, a rigorous framework to differentiate ASD profiles. The IMAP tool facilitates the categorization of ASD into distinct clinical profiles by aligning variations in symptomatology with underlying biological mechanisms, thereby enabling more targeted and effective treatment strategies. This structured methodology aims to improve therapeutic outcomes by addressing specific challenges and requirements inherent to each ASD subtype.

The validity of the proposed model was evaluated against established clinical guidelines and current best practices for autism. This involved comparing the outcomes derived from traditional diagnostic methods with those suggested by precision medicine approaches [6]. This discussion is based on scientific evidence and aims to provide a clear rationale for adopting a personalized approach to ASD management.

3. The Personalized and Integrated Approach to ASD

Recent data from the Centers for Disease Control and Prevention (CDC) indicate the prevalence of Autism Spectrum Disorder in 1 out of every 36 children aged eight years, representing approximately 2.8% of this age group in the United States [1]. This prevalence underscores the critical need for a personalized and integrated approach to managing autism, including medical, psychological, educational, and therapeutic interventions, each uniquely tailored to the individual needs of the patient. Traditional diagnostic methods for ASD, primarily based on behavioral observations and questionnaires, often fail to provide a comprehensive clinical picture, emphasizing the need for more nuanced diagnostic tools.

The advent of precision medicine has emerged as a pivotal tool for unraveling the complexities inherent in neurodevelopmental disorders, notably autism. This approach is characterized by a thorough evaluation encompassing medical history, physical examination, and an array of biomarkers, facilitating the identification of unique clinical profiles and enabling the classification of individuals based on symptomatology [7]. A critical aspect of this methodology is the systematic and comprehensive assessment of simple and complex comorbidities to identify the root causes of presenting symptoms.

Implementing this approach in diagnosing and managing comorbidities among individuals with ASD, especially within the framework of ten clinical profiles, offers substantial advantages.

 doi:10.20944/preprints202406.0856.v1

These include enhanced symptom management, increased effectiveness of treatments and behavioral therapies, disease prevention, and potential reductions in healthcare costs and medication usage. This process is essential for gathering extensive phenotypic data and biomarkers, including epigenetic markers, transcriptomics, proteomics, metabolomics, and neurobehavioral metrics. Such detailed profiling facilitates the differentiation of distinct clinical profiles, leading to improved prognoses and, ultimately, a significant enhancement in the quality of life of these individuals across short-, medium-, and long-term [8].

4. Clinical Profiles in ASD

Genetics plays a critical role in the development of disorders such as Autism Spectrum Disorder. However, complex interplay with other factors shapes the unique phenotypic expression of each individual, even among those sharing the same diagnosis [9]. The utility of precision medicine in this context lies in its ability to integrate genomic insights into an extensive understanding of biological processes and environmental influences. This approach facilitates the development of personalized therapies tailored to individual patient-specific needs while exploring a variety of triggers to understand the root cause of symptoms, including internal and external factors. For example, metabolic disruptions can lead to various symptoms, whereas genetic variations can affect neurotransmitter synthesis and mitochondrial functions [10]. Additionally, the composition of the gut microbiome significantly influences the microbiome-gut-brain axis, which can cause inflammation, autoimmune reactions, or pain [11–13].

Individuals with autism typically exhibit unique symptoms and comorbidities that are frequently exacerbated by external factors such as infections or diet, which often lead to metabolic disruptions. Such disruptions can trigger immune dysregulation, inflammation, and oxidative stress. Approximately 70% of individuals with autism have some form of metabolic dysfunction, while almost 90% face gastrointestinal difficulties. However, these symptoms are often misinterpreted as behavioral problems, overlooking clinical comorbidities' potential origins [14–17]. The coexistence of psychiatric signs and clinical comorbidities offers critical insights for clinicians, which can be obtained through comprehensive physical examinations, detailed medical histories, and laboratory tests. These insights are instrumental in identifying distinct clinical profiles within the autism spectrum and facilitating the development of customized treatment plans and interventions for effective and targeted care [18].

The following ten clinical profiles have been meticulously developed to assist in diagnosing and treating various conditions in ASD.

1. Syndromic
2. Gastrointestinal
3. Metabolic
4. Mitochondrial
5. Endocrine
6. Infectious
7. Bioaccumulative
8. Immunological
9. Inflammatory
10. Neurological

It is vital to acknowledge that the presentation of these profiles may vary. A particular profile may be more evident during the initial evaluations, whereas further assessments may reveal additional associated profiles. This dynamic and evolving process is crucial for accurately understanding each individual's unique factors and allowing for tailored treatment strategies. Initially, patients may present with multiple profiles due to untreated comorbidities. The persistent presentation of symptoms helps clinicians stratify and refine clinical profiles over time. Identifying and differentiating particular clinical profiles and subtypes of autism is achieved using a multi-tiered

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approach that includes observing characteristic signs and symptoms, following progression from primary to complex treatment protocols, and utilizing targeted laboratory examinations. Each profile presents unique features, and understanding these nuances is pivotal for tailoring interventions according to individual needs [19].

4.1. Syndromic Profile

The Syndromic Profile within the autism spectrum is mainly observed in individuals with pre-established genetic syndromes such as Down Syndrome, Fragile X Syndrome, and Rett Syndrome [20–22]. In such cases, the primary focus is often on genetic syndromes, which can lead to specific physical characteristics, such as low-set ears.

A critical aspect of this profile is the potential for a delayed or overlooked diagnosis of autism. The symptoms and challenges associated with genetic syndromes can overshadow the behavioral and developmental signs of autism. Therefore, autism, as a co-occurring neurodevelopmental condition, may not be promptly recognized or adequately addressed [23]. This trend highlights a significant diagnostic oversight, in which the primary genetic syndrome manifestations might be exclusively attributed to the syndrome, neglecting the possibility of autism [24].

Therefore, healthcare professionals must be vigilant about the signs of autism in individuals with genetic syndromes and not attribute all symptoms and behaviors solely to the primary syndrome.

4.2. Gastrointestinal Profile

The gastrointestinal profile is a significant aspect of the autism spectrum. It is particularly prevalent in those who have not received nutritional interventions for allergies, intolerance, or food sensitivities that impact the microbiota-intestine-brain axis [5,11,12,17]. Notably, a significant proportion of individuals with autism experience gastrointestinal symptoms. These symptoms are often characterized by chronic conditions such as diarrhea, which is prevalent in up to 45% of individuals with ASD, and constipation, which is reported in approximately 30-45% of cases. Additional frequently observed symptoms include abdominal distension, skin rashes, and persistent diaper rashes [12,25,26]. Furthermore, conditions such as Small Intestinal Bacterial Overgrowth (SIBO) and Gastroesophageal Reflux Disease (GERD) may contribute to this profile, causing discomfort and affecting the overall well-being of affected individuals [27].

Addressing the Gastrointestinal Profile requires a comprehensive approach, starting with a thorough assessment to identify the underlying causes. This includes laboratory tests for nutritional deficiency, immune dysfunction, and gastrointestinal inflammation [28,29]. Personalized treatment plans for this profile often involve dietary modifications and supplements.

It is crucial to recognize that gastrointestinal symptoms in autism, such as chronic diarrhea or constipation, may be misinterpreted as purely behavioral issues. Effective management requires a deep understanding of each patient's medical history, including gastrointestinal symptoms, dietary habits, and responses to prior treatment [30].

4.3. Metabolic Profile

A complex interplay between genetic and non-genetic factors shapes the metabolic profiles of individuals with autism [31]. Genetic variants such as single nucleotide polymorphisms (SNPs) can significantly affect critical metabolic pathways, including the one-carbon metabolism pathway. This pathway is integral to various biological functions and illustrates the influence of genetic factors on metabolism.

In addition to genetic influences, non-genetic and epigenetic factors play a substantial role in shaping metabolic profiles, including enteropathies and deficiencies in essential nutrients such as zinc, iron, and calcium [32,33]. The combined effects of these genetic and non-genetic elements contribute to various metabolic challenges, leading to increased oxidative stress, diminished energy production, and altered metabolic pathways [34].

 doi:10.20944/preprints202406.0856.v1

Moreover, the interaction between nutrition, environmental factors, and genetic predispositions is pivotal in determining the metabolic function in individuals with autism. This dynamic underscores the importance of personalized nutrition and environmental management approaches for metabolic health.

4.4. Mitochondrial Profile

Individuals with autism often experience mitochondrial dysfunction, which can manifest in various ways, such as facial hypotonia, speech delay, suspected apraxia of speech, epilepsy, and cognitive challenges. Mitochondrial dysfunction can be linked to inborn errors of metabolism, such as polymorphisms in the MCAD gene, which are crucial for beta-oxidation of medium-chain fatty acids and mitochondrial energy production [35,36]. Deficiencies in essential nutrients, such as the vitamin B complex, can also lead to mitochondrial dysfunction. Patients with mitochondrial dysfunction may also exhibit increased allergy and atopic conditions. Environmental allergens and toxins can exacerbate this dysfunction, leading to increased production of reactive oxygen species (ROS) and impairment of the electron transport chain, causing mitochondrial damage, mast cell degranulation, and triggering inflammatory and allergic responses [37].

A comprehensive approach encompassing genetic and environmental factors is essential to address mitochondrial dysfunction in autism. Nutritional support is crucial for optimizing mitochondrial function, highlighting the importance of a tailored dietary strategy for managing this aspect of autism [38].

4.5. Endocrine Profile

Individuals with ASD may exhibit deficiencies in hormone production, particularly steroids and thyroid hormones, which can manifest as endocrine profiles [39–41]. This profile is characterized by symptoms of hormonal imbalances that may present as either insufficient or excessive hormone production.

A key concern within this profile is the disruption of the hypothalamic-pituitary-adrenal-thyroid (HPA-T) axis, which can significantly affect various bodily systems. Proper regulation of this axis is critical, as imbalances may precipitate more severe psychiatric disorders and chronic illnesses [42–44]. The initial presentation of this profile often involves elevated cortisol levels, which may lead to decreased cortisol levels over time. This dysregulation suggests either hyporeactivity or hyperreactivity of the HPA-T axis [45–47].

Assessing cortisol production is essential to delineate the endocrine profile and to ensure that the adrenal glands are sufficiently robust to support diverse treatments, including those for infections. Individuals with this endocrine profile commonly experience speech delay, significant sensory dysfunction, and hypotonia [44,48].

Individuals with ASD and an identified endocrine profile are commonly diagnosed with attention deficit hyperactivity disorder (ADHD) [45,49]. Treatment strategies typically involve eliminating endocrine disruptors, managing inflammation, and supporting adrenal and thyroid functions as required.

4.6. Bioaccumulative Profile

The phenotypic expression of autism is influenced by the complex interplay between environmental factors, such as exposure to toxins and pesticides, and genetic predispositions [15,50,51]. Various single-nucleotide polymorphisms (SNPs), including MTHFR, CBS, and SUOX, affect detoxification processes in the body, making them genetic factors that influence this profile [52]. These genetic variations significantly affect how the body handles and eliminates the toxins. Individuals with this profile often show clinical signs of systemic intoxication, such as dark circles under the eyes, edema, dermatitis, chronic fatigue, and neurological symptoms. Recognizing and addressing these signs is crucial for effectively managing their conditions [53–55].

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Effective management of the Bioaccumulative Profile involves reducing toxin exposure, utilizing targeted detoxification therapies, and a diet rich in antioxidants, essential nutrients, and phytochemicals to support detoxification [56,57]. Understanding an individual's specific genetic makeup, particularly in genes related to detoxification, is vital for developing personalized therapeutic approaches to enhance detoxification efficiency and alleviate the adverse effects of bioaccumulation [58].

4.7. Infectious Profile

Psychiatric and neurological disorders, including autism, are often intricately linked to the immune and inflammatory responses to various infections [18,27]. Understanding the infectious profile is essential for comprehending these conditions, as it offers insights into the potential underlying causes and guides appropriate treatment strategies. Analyzing the immune system response and cytokine profiles is crucial for clinicians to understand the role of infectious processes in developing the symptoms observed in autism and other psychiatric disorders.

It is essential to recognize the potential overlap and confusion in symptom presentation between conditions such as Pediatric Acute-onset Neuropsychiatric Syndrome (PANS), Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS), and autism [59]. These conditions can be challenging to diagnose, especially in children aged 3-17 years, owing to the similarities in their presentation to autism, which leads to diagnostic complexities. An overactive immune response to infection can trigger autoimmune encephalitis and cause brain inflammation and neuropsychiatric symptoms that may resemble or exacerbate autism symptoms [60–62].

Furthermore, it is essential to acknowledge that anxiety in individuals with autism may be associated with various viral infections [63]. These infections can lead to neuroinflammation and contribute to neuropsychiatric symptoms. The emergence of COVID-19 and the associated neuroinflammatory responses, including in children with autism, underscores the need for pediatricians to be particularly vigilant [64–66]. This vigilance is crucial for detecting neurodevelopmental regression or other changes that may indicate an infectious or an autoimmune response.

Individuals with autism may experience concurrent infections or autoimmune encephalitis of infectious origin, which may affect their clinical presentation. Therefore, a thorough and detailed investigation is vital for the diagnosis and treatment of autism, recognizing that individuals with autism can experience a wide range of health issues, including those related to infections [67].

4.8. Immunological Profile

The Immunological Profile presents significant challenges owing to its complexity and severity, often resulting in a poor prognosis. This profile is influenced by various immunological triggers, including infections, exposure to toxic agents, and comorbidities, all contributing to management difficulties. One of the critical challenges in this profile is the significant overlap and mimicry of symptoms with conditions such as viral encephalitis, leading to potential diagnostic errors. Patients with immunological profiles may exhibit a range of symptoms and conditions, such as Obsessive-Compulsive Disorder (OCD), Disruptive Mood Dysregulation Disorder (DMDD), selective eating, and multiple allergies. Owing to their severity, these patients often require moderate to high levels of support and respond well to treatments, such as antibiotics, corticosteroids, or immunomodulatory drugs [59,67,68].

Additionally, a history of autoimmune diseases, including upper respiratory tract infections (URTI) and atopic dermatitis, is common in these patients. Significantly, conditions such as Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) and Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) are strongly associated with immunological profiles [69]. Both PANS and PANDAS are characterized by sudden-onset neuropsychiatric symptoms following an infection, often leading to significant behavioral changes and exacerbation of autism-related symptoms. Recognizing and addressing these conditions is

 doi:10.20944/preprints202406.0856.v1

crucial for managing the Immunological Profile, as they demonstrate the profound impact of immunological factors on neuropsychiatric presentation in autism. Managing the immunological profile requires a comprehensive approach that focuses on the specific immunological needs of each individual and tailors treatment strategies to effectively address a broad spectrum of symptoms and their underlying triggers [70].

4.9. Inflammatory Profile

The Inflammatory Profile is characterized by chronic inflammation, evident through elevated levels of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α). This profile is frequently observed in patients with gastrointestinal tract disorders and is initially observed in a significant proportion of individuals with autism spectrum disorders [71]. Gastrointestinal symptoms often serve as early indicators of an inflammatory profile originating from gut inflammation, which is common in these patients. The primary sources of inflammation are intestinal and diet-related causes [72]. However, the defining characteristic of the inflammatory profile is persistent inflammation, even after addressing various underlying issues, including intestinal dysfunction, endocrine abnormalities, subclinical infections, and autoimmune diseases.

Despite comprehensive treatment efforts, some patients continue to exhibit clinical and laboratory signs of inflammation, indicating the presence of a chronic inflammatory disease. This persistent inflammation suggests an ongoing role of the inflammasome, a multiprotein complex involved in chronic inflammatory conditions. Identifying specific Single Nucleotide Polymorphisms (SNPs) that contribute to the pro-inflammatory state is crucial for understanding individual variations in inflammatory responses [73]. Notably, SNPs such as those in the MTHFR and the TNF genes, specifically TNF-α -308G>A, have been extensively studied for their roles in inflammatory processes [71].

Addressing this profile requires a comprehensive approach that considers symptoms, underlying causes, and genetic predispositions. Understanding these genetic factors and conducting thorough clinical evaluations are critical for developing effective and personalized treatment plans. Recognizing that inflammation often persists despite extensive treatment highlights the need for targeted strategies to manage chronic inflammation and improve patient outcomes.

4.10. Neurological Profile

The neurological profile of individuals with autism is often identified early in treatment or may have been previously diagnosed with a condition related to the central nervous system (CNS). This profile encompasses conditions such as epilepsy, congenital malformations, and syndromes that result in seizure disorders, including Landau-Kleffner syndrome [74,75]. In some instances, a neurological profile may develop because of a lack of diagnosis and subsequent treatment of chronic neuroinflammation, leading to exacerbation of the overall condition.

An integrative approach is vital for the understanding and management of neurological profiles. For instance, individuals with severe allergies may experience food-reactive epilepsy, or food allergies can lead to adenoid hypertrophy, causing hypoxia and nocturnal epilepsy [76,77]. Identifying and addressing these underlying factors are crucial, especially for treatment-resistant neurological symptoms.

It is also essential to recognize that the CNS interacts with all profiles within the autism spectrum. While the Neurological Profile may predominantly display neurological characteristics and symptoms, these can be influenced by various factors, including gut-related disorders, infections, intoxication, and hypothalamic-pituitary-adrenal (HPA) axis dysregulation.

5. Discussion

Autism spectrum disorder (ASD) is a complex disorder that presents significant challenges in terms of diagnosis and treatment owing to its wide range of symptoms and comorbidities. Despite substantial progress in understanding ASD and its associated conditions, there is a need for extensive

 doi:10.20944/preprints202406.0856.v1

exploration, especially in understanding the variation in symptom presentation among individuals with autism, which complicates the diagnostic process. The current diagnostic criteria for ASD do not fully capture its complexity and heterogeneity. This gap presents a challenge in the development of personalized diagnostic tools and treatments. Focusing on preventive medicine, especially when it comes to comorbidities, is crucial for enhancing the quality of life of individuals with autism. Many symptoms that exacerbate the challenges faced by individuals with autism are either direct manifestations of untreated clinical comorbidities or are worsened by them [19,27]. Moreover, symptoms arising from these comorbidities can often be misinterpreted by professionals as a core aspect of autism, leading to inaccurate diagnosis. Neglecting the treatment of these comorbidities can have negative consequences, including worsening the patient's required support, prognosis, and overall quality of life [78].

Psychiatry can be challenging due to the absence of conventional laboratory findings for the identification of certain disorders. This lack of recognition is partly due to difficulties obtaining meaningful medical histories and conducting physical tests, particularly for non-verbal individuals or those whose behaviors may interfere with the assessments. Hence, it is crucial to accurately subtype and genotype individuals with ASD to enhance treatment and to add various psychiatric and clinical comorbidities [40].

Precision medicine has the potential to refine treatments for psychiatric symptoms in ASD patients. Identifying clinical profiles can provide a more accurate assessment of individuals with autism and, consequently, better treatment options. It also helps monitor and predict symptoms' progression and potential complications and identify future treatment possibilities [7]. However, further research is needed to determine the effectiveness of precision medicine in treating psychiatric symptoms, its potential risks and long-term effects, and the potential of precision medicine for treating patients with ASD.

This study highlights the significance of a personalized and integrated approach to managing autism, emphasizing the integration of the DSM-5 diagnostic criteria based on behavioral observations. Although the DSM-5 provides a standardized framework for ASD diagnosis, the heterogeneity of autism and the presence of both clinical and psychiatric comorbidities often complicate the identification of distinct clinical profiles. By incorporating various clinical profiles, this approach aims to achieve a more comprehensive understanding and diagnosis of autism, addressing its diverse and complex nature more effectively. This approach should integrate various medical, psychological, educational, and therapeutic interventions tailored to individual needs. Considering the complexity of neurodiversity, it is crucial to correlate the core signs and symptoms of autism with the potential clinical comorbidities [19]. This ensures that comorbidities causing or exacerbating symptoms are identified and treated appropriately rather than being mistaken for autism symptoms alone. Embracing an integrative perspective encompassing genetic factors and a broad spectrum of associated conditions will enable professionals to develop precise and effective interventions. This approach improves patient outcomes and the quality of life of individuals with autism and their families.

Advancing our understanding of ASD involves identifying distinct clinical profiles and utilizing epigenetic, transcriptomic, proteomic, and metabolomic markers, along with neurobehavioral measures. This strategy aims for more accurate diagnoses and treatments, potentially reducing the incidence of chronic diseases, improving prognoses, achieving cost efficiency, and enhancing the effectiveness of behavioral therapies. Such holistic approaches signify a significant paradigm shift in autism care, promising a future with better health outcomes and opportunities for individuals with ASD.

6. Limitations and Future Research Directions

The introduction of a novel stratification model for Autism Spectrum Disorder has undergone preliminary validation in a controlled clinical environment. This initial validation supports the model but highlights several areas that require further investigation owing to inherent limitations. Although

 doi:10.20944/preprints202406.0856.v1

the initial validation supports the model, it highlights the need for further studies to address these limitations comprehensively.

The empirical validation of the model was confined to a specific patient cohort within a clinical setting, providing promising preliminary results. However, these findings may not adequately capture the full diversity of ASD as observed in broader clinical practice. The development of the model relied heavily on the existing literature, which, while extensive, may carry inherent biases or limitations that could affect its comprehensiveness and applicability in different clinical contexts. Furthermore, owing to the complex and variable nature of ASD, the model, despite its robust framework, might only partially capture the nuances of the individual cases. This reflects the inherent challenge of creating diagnostic models universally applicable to a broad spectrum of ASD manifestations [79,80].

Several directions for future research are evident. To further validate the model's effectiveness, it is necessary to conduct broader empirical studies that extend beyond the initial clinical settings and include more diverse patient cohorts across different environments. This expansion helps establish the robustness and generalizability of the model. In addition, there is a need to explore how the model can be seamlessly integrated into routine clinical practice. Developing practical implementation tools and guidelines would facilitate their use by a broader range of healthcare professionals, thus enhancing the model's accessibility and utility.

Our research team planned a series of follow-up studies to delve more deeply into the clinical profiles introduced in this preliminary study. Future studies should provide a more detailed characterization of each profile to help clinicians integrate these findings into routine practice. This approach includes laboratory investigations and the identification of clinical symptoms to improve the quality of life and clinical stratification of patients with autism. The goal was to offer more tailored and effective treatments by refining our understanding of each profile and associated comorbidities.

Future research can enhance the effectiveness of the stratification model in diagnosing and treating ASD by validating and refining the model, exploring the suggested research directions, and addressing the limitations. This ultimately results in improved patient outcomes.

7. Conclusions

This research introduces a stratification model for Autism Spectrum Disorder, which significantly enhances the precision of diagnosis and the effectiveness of treatment. By developing a nuanced understanding of ASD's diverse manifestations, the model challenges and extends beyond the traditional diagnostic approaches. Our research demonstrates that accurate identification of specific clinical profiles within ASD enables more personalized and effective interventions tailored to the unique needs of each individual.

Introducing this model in clinical practice can improve diagnostic accuracy, ensuring that interventions align with each patient's characteristics and comorbidities. This approach improves treatment outcomes and reduces the likelihood of side effects by avoiding one-size-fits-all solutions. Additionally, by addressing the often-overlooked comorbid conditions frequently associated with ASD, our model enhances overall patient care and promotes a more comprehensive management strategy that significantly improves the quality of life of individuals with ASD.

The implementation of the stratification model has immense potential to revolutionize the management of Autism Spectrum Disorder in clinical settings. This model involves the integration of personalized medicine into the standard care for individuals with neurodevelopmental disorders. By analyzing an individual's genetic and clinical data, we categorized them into subgroups with distinct clinical features. This categorization allowed us to tailor the treatment plans specific to each subgroup, resulting in more responsive and effective healthcare solutions.

This change is expected to yield substantial benefits in clinical outcomes and lay the foundation for future innovations in ASD treatments. This stratification model can potentially provide insights into the pathophysiology of ASD and identify novel therapeutic targets. By improving our understanding of the underlying mechanisms of ASD, we can develop more targeted interventions personalized to each individual's unique needs.

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