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RESEARCH PAPER

Hereditary Load and Socio-Demographic Determinants of Pediatric Neurodevelopmental Disorders: A Comparative Analysis of Risk Patterns in Pakistan

[1]Nigar Fatima, [2]Maryam Ishfaq and [3]Yusra Aftab

1. MS Scholar, Department of Clinical Psychology, National University of Medical Sciences (NUMS), Islamabad, Pakistan
2. Head of Academics & Student Wellbeing Counselor, UNIPLACE, Rawalpindi, Punjab, Pakistan
3. Lecturer in Psychology, ASTI Academy, Dubai, UAE

Corresponding Author nigarfatima.nf1@gmail.com

ABSTRACT

The etiology of pediatric neurodevelopmental disorders (NDDs) is a complicated set of genetic, hereditary, and environmental factors. The high consanguinity and diverse socioeconomic settings in Pakistan produce a distinct epidemiological picture of NDDs, but there is limited comparative data on how such variables vary between distinct diagnostic groups. These are crucial determinants to consider in the sense of regional genetic counseling and resource allocation within the domain of the population health. The aim of the research was to investigate the socio-demographic variables and the hereditary load of four distinct groups of NDDs among a sample of Pakistani patients in a clinical cohort, which included Autism Spectrum Disorder (ASD), Cerebral Palsy (CP), Down Syndrome (DS), and Intellectual Developmental Disorder (IDD). The epidemiological cross-sectional design was applied and a sample of 80 children and adolescents (11-18 years old) was used. The participants were stratified into four diagnostic groups (n=20 each). Gender, socioeconomic status (SES), and a more detailed family history (consanguinity and hereditary clusters) data were gathered using structured clinical interview and medical record. Chi-square tests of independence and descriptive modeling were used to statistically analyze data to determine significant risk patterns. The correlation between family history and diagnostic category was found to be of a very high significance (p =.007) with the IDD group having the highest hereditary burden (100%) and ASD group having the lowest (60%). Gender differences were also significant with males being dominant in ASD and females dominant in IDD. Conversely, no significant differences were found between socioeconomic status and personal forms of NDDs (p = .690) suggesting that the disorders are distributed across the socioeconomic continuum in this cohort. The findings emphasize the power of genetics in Intellectual Developmental Disorders among Pakistani population which is likely to be related to local marriages arrangements. Even though SES does not appear to be a significant predictor of NDD type, the significant gender and heredity differences imply that there is a need to take certain public health actions. These results underpin the concept of enhanced genetic screening and culturally sensitive family counseling in order to minimize the NDDs burden in Pakistan.

Keywords: Neurodevelopmental Disorders, Family History, Hereditary Load, Socio-Demographic Factors, Consanguinity, Pakistan, Public Health, Epidemiology

Introduction

The proportion of neurodevelopmental disorders (NDDs) in the global disability burden is quite significant, and the etiology of these conditions starts increasingly being viewed as a complicated interaction between a genetic predisposition and environmental exposure (Burgio et al., 2026; Thapar et al., 2025; World Health Organization, 2022). These conditions include Autism Spectrum Disorder (ASD), Intellectual Developmental Disorder

(IDD), Cerebral Palsy (CP) and Down Syndrome (DS). It is also complicated by the late diagnosis, rehabilitation facilities, and absence of epidemiological surveillance systems in low and middle-income countries (LMICs), including Pakistan (Maulik et al., 2011). The socio-cultural and genetic determinants of the epidemiological status of NDDs in the South Asian environment and especially, Pakistan, are quite different, as compared to the population of the Western world. Regularly, the consanguinity rate of marriage is associated with increased prevalence of autosomal recessive diseases and intellectual disability (Hamamy, 2012; Tadmouri et al., 2009). The prevalence of ASD and IDD globally has been increasing over the years but there is a huge disparity in regional-specific epidemiological data of LMICs, which limits the development of culturally appropriate intervention and prevention strategies (Elsabbagh et al., 2012).

The high consanguinity rate that has been linked to increased expression of inherited neurodevelopmental disorders due to high homozygosity of the deleterious alleles is one of the primary causes of prevalence of NDD in Pakistan (Hamamy, 2012). Formation of families has also signified that neurodevelopmental issues are clustered in extended families particularly in a population with high endogamous customs (Xie et al., 2020). However, there has been no extensive comparison of evidence of the difference in hereditary loading in diverse diagnostic groups of ASD, CP and DS across South Asian clinical groups. Socioeconomic status (SES) plays a dual role in the context of the NDD in that is a risk modifier and an access determinant to the diagnostic services. Lower SES is associated with prenatal and perinatal risk factors such as malnutrition, infections and environmental stressors, which cause neurodevelopment vulnerability (Walker et al., 2007). However, in the superior SES groups the diagnostic exposure may be larger due to the higher healthcare access which may lead to a potential referral bias in the clinical data in Pakistan and other LMIC sites.

Another vital dimension of NDD demographic profile is gender differences. It is always reported that males have a higher prevalence of ASD, and it has been suggested that neurobiological vulnerability and protective factors among females explain this difference (Lai et al., 2014; Baron-Cohen et al., 2011). Nevertheless, gender-related differences in healthcare access can also introduce bias in reported prevalence patterns in the South Asian context because female children with disabilities might be underrepresented in clinical samples because of sociocultural constraints in seeking help (Salman et al., 2024). In addition to biological and socioeconomic risk factors, environmental exposures, including prenatal complications, maternal health, and early childhood infections also play a major role in NDD risk. There are indications that cerebral palsy and cognitive impairment are closely linked with perinatal complications such as hypoxia and low birth weight (Blair and Stanley, 1988). These are especially applicable in the LMICs where maternal healthcare infrastructure is not well developed and preventive screening is irregular.

Literature Review

The neurodevelopmental disorders in Pakistan are currently under management because comparative data is unavailable on the socio-demographic and hereditary risk factors that distinguish particular diagnostic groups. Although there are case studies, there is no strong evidence to compare the hereditary load in ASD, CP, DS, and IDD in the local population (Sheraz et al., 2024; Xie et al., 2020). Such incompleteness hinders proper and evidence-based genetic counseling given by clinical psychologists and neurologists to the impacted families. The relationship between socioeconomic status and distribution of NDD in Pakistan is unclear. It is unknown whether some disorders are clustered in particular economic groups because of environmental conditions or the differences in diagnoses are only a result of healthcare access. In the absence of such a clear understanding, the allocation of public health resources to the populations that require them the most may not be applicable and poor families may not be provided with the necessary support (World Health Organization, 20232; Black et al., 2017).

It is important to note that neurodevelopmental disorders are increasingly being conceptualized as a dimensional and overlapping spectrum of diagnosis as opposed to discrete categorical diagnosis. Large-scale cohort and genomic studies suggest significant shared genetic architecture in ASD, ADHD, intellectual disability, and developmental coordination disorders, which demonstrate pleiotropic effects of neurodevelopmental risk genes (Thapar and Rutter, 2017; Smoller et al., 2019). Epidemiological evidence of high comorbidity between ASD and ADHD has supported this dimensional approach, and has led to the need to consider transdiagnostic assessment frameworks in clinical populations (Leitner, 2014). This overlap is especially applicable to LMIC where diagnostic accuracy might be limited and symptom based classification is more in common than neuropsychiatric assessment.

Prenatal, perinatal, and early postnatal exposures are very sensitive to early neurodevelopment and may cause early disruptions in brain maturation pathways, leading to long-term cognitive and behavioral disabilities. Global burden studies have provided evidence on a large scale that the maternal infection, hypoxia at birth and environmental deprivation constitute a significant proportion of developmental disabilities (Mkunyanae et al., 2026). Lancet Commission on child development also observes that children who experience early adversity in low resources settings are disproportionately represented in cumulative developmental risks and consequently have educational and functional disadvantages across the lifespan (Black et al., 2017).

Extending this, massive developmental studies point to the fact that early childhood is a prime neuroplasticity period, with deleterious exposures potentially having enduring impacts on the brain development. The other critical dimension in neurodevelopmental studies is the interaction between the genes and the environment where genetic vulnerability is either manifested or altered by the environment. Modern theories imply that NDDs are not to be perceived as either genetic or environmental, but as the result of dynamic interactions between developmental factors throughout the lifespan (Thapar et al., 2017). This model is particularly applicable to the high-genetic-load and intermittently-exposed populations, including Pakistan. Finally, the issue of NDDs in Pakistan needs a transition away from a single clinical diagnosis and into a combined socio-epidemiological model. Through the study of hereditary history, gender distributions and interplay of socioeconomic stratification, the researchers will be in a better position to appreciate how risks and vulnerabilities are patterned among clinical population. The present study will thus seek to map these determinants in a pediatric cohort of neurodevelopment, which will be relevant in enhancing genetic counseling, early intervention planning, and planning of health at the population level in the area.

The presence of considerable gender disparities in the diagnosis of NDD also implies a possible existence of the so-called identification gap that has not been adequately studied in the Pakistani environment. When the prevalence of NDDs in females is actually huge, but gender-specific cultural biases are affecting the diagnosis, then the actual diagnosis is underestimated by far. These gender patterns should be identified to address equitable access to early intervention services in the country. The extent of familial clustering of Intellectual Developmental Disorders implies a deep hereditary factor that is usually overlooked in normal psychological testing. The inability to measure this hereditary load constrains our knowledge on the etiological understanding of NDDs in Pakistan. This paper will fill these gaps by examining the socio-demographic and hereditary characteristics of a clinical group with the goal of offering a risk-factor map of the Pakistani pediatric population.

Material and Methods

The research design that was used in this study was cross sectional and socio epidemiological research design to conduct etiological profiling. Instead of evaluating the

validity of the tools, this framework was concerned with the patterns of distribution of hereditary and demographic variables within a clinical range. The risk-factor density in particular categories of neurodevelopment was determined using a multi-group comparative approach (e.g., family history) and environmental correlates vary within a Pakistani pediatric clinical population (Mirza et al., 2009; Ibrahim et al., 2023; Sheraz et al., 2024). Evidence from genetic studies enabled the analysis of the clustering of environmental and genetic proxies (such as family history) in the Pakistani pediatric population (Ilyas et al., 2020; Khalid et al., 2020).

Conceptual Framework of the Study

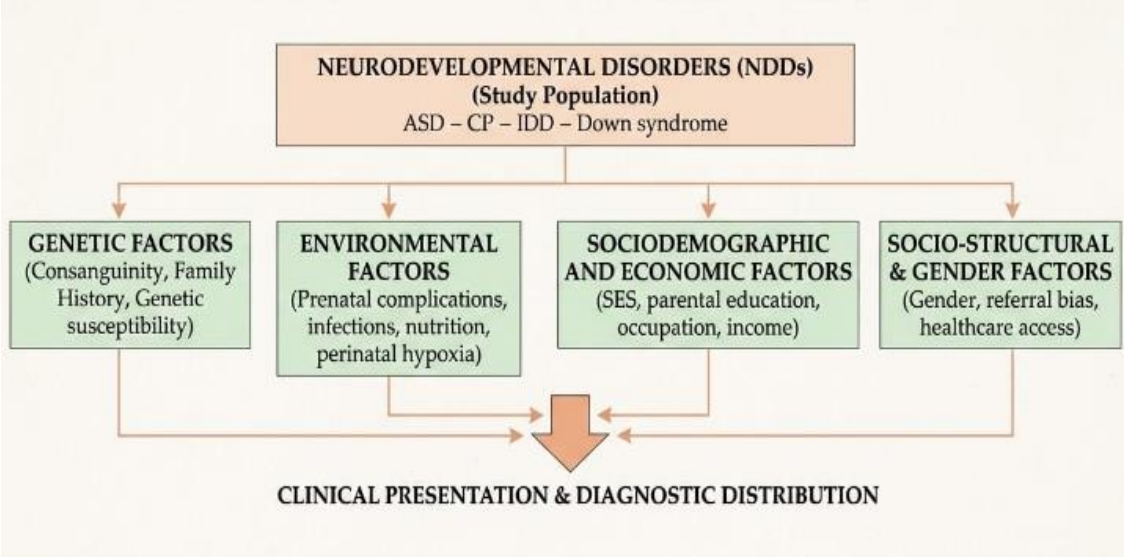

Figure 1. Theoretical model depicting interplay between genetic, environmental, and socio-demographic factors involved in the development of neurodevelopmental disorders in a clinical group of Pakistani population.

Population and Sampling Strategy

Purposive sampling was used to recruit the population sample (80 pediatric cases) among the major tertiary neurology and developmental centers in Rawalpindi, Pakistan. They were classified into four diagnostic group, Autism Spectrum Disorder (ASD), Cerebral Palsy (CP), Down Syndrome (DS), and Intellectual Developmental Disorder (IDD). The demographic mapping was also made up of equal representation (n=20) in groups, which was facilitated by the stratified method of recruitment. Only verified clinical diagnoses were factored according to DSM-5-TR standards, and the socio-demographic data gathered were mapped on to high-confidence clinical phenotypes.

Data Collection Protocols (Risk-Factor Mapping)

Data collection for this study focused on three primary socio-epidemiological axes. Structured parental interviews were carried out to obtain a detailed retrospective family history. This centered on the identification of disabilities in the form of familial clusters, which are considered to be the occurrence of a first- or second-degree relative who has known neurodevelopmental or cognitive disability (Xie et al., 2020). The participants were divided into socioeconomic strata (Low, Middle, High) according to the adapted to the Pakistani context of the Kuppuswamy Socioeconomic Scale (Although originally developed for urban Indian populations, the scale has been widely utilized in South Asian clinical research due to its structured and multidimensional assessment of socioeconomic position), which includes parental education, occupation, and total family income (Kuppuswamy,

1981). The biological gender and the chronological age were noted to determine whether there might be biases in identification or a variation in prevalence in the regional clinical environment.

Analytical Approach

The processing of the data was done with SPSS version 29.0. The leading statistical goal, in contrast to a psychometric emphasis of other earlier studies, was to determine categorical associations. The Chi-Square Tests of Independence were applied to find out the strength of association between diagnostic groups and hereditary load, and socioeconomic distribution. The visualization of the Gender-Diagnosis Intersection was conducted with the help of descriptive modeling and percentage-based frequency distributions that give a clear map of the intersection of demographic variables with particular neurodevelopmental phenotypes (Kirkwood & Sterne, 2010; Field, 2024).

Results and Discussion

Table 1
Frequency Distribution of Demographic Variables across NDD Groups

Variable	ASD	CP	DS	IDD	Total
Gender					
Male	13 (65.0%)	12 (60.0%)	12 (60.0%)	7 (35.0%)	44 (55.0%)
Female	7 (35.0%)	8 (40.0%)	8 (40.0%)	13 (65.0%)	36 (45.0%)

The results show a clear Gender-Phenotype bias. The ASD group has a higher proportion of males (65 per cent) compared to the IDD group (65 per cent). This distribution indicates that gender can affect the nature of neurodevelopmental diagnosis that a child obtains in the Pakistani clinical setting, which may indicate a detection gap in which females are only mostly diagnosed when global intellectual impairments are detected.

Table 2
Association Between Socioeconomic Status (SES) and NDD Type

SES Category	ASD	CP	DS	IDD	Total
Low	9 (45.0%)	7 (35.0%)	11 (55.0%)	6 (30.0%)	33
Middle	8 (40.0%)	9 (45.0%)	6 (30.0%)	8 (40.0%)	31
High	3 (15.0%)	4 (20.0%)	3 (15.0%)	6 (30.0%)	16

SES= Socioeconomic status, ASD= autism spectrum disorder, CP= cerebral palsy, DS= Down syndrome, IDD= intellectual disability disorder Chi-square Test: $\chi^2(6) = 3.90$, $p = .690$

According to chi-square analysis, there is no significant relationship (Chi-square = 4.31, p = .690). These disorders have an economic Neutrality since the highest number of cases in all four categories fit within the Middle and Low SES levels. This implies that neurodevelopmental disorders among this cohort are a global issue in Pakistan with cut off economic backgrounds and is an indication that environmental or biological risks are common.

Table 3
Comparative Analysis of Hereditary Load (Family History)

Family History	ASD	CP	DS	IDD	Total
Yes	12 (60.0%)	16 (80.0%)	18 (90.0%)	20 (100.0%)	66
No	8 (40.0%)	4 (20.0%)	2 (10.0%)	0 (0.0%)	14

Chi-square Test: $\chi^2(3) = 12.12$, $p = .007$

The correlation between hereditary history and diagnostic category is extremely high (p =.007). The 100 hereditary load in the IDD group is an important epidemiological

characteristic which implies that there is a robust association with family clustering and possibly consanguineous marriage in the area. On the other hand, the ASD group has the highest percentage of cases of the type of the etiology known as Sporadic (40%), which suggests a divergent etiological mechanism, which could be either de novo genetic mutations or environmental stimuli.

Discussion

The main aim of the research was to trace the socio-demographic and hereditary factors of pediatric neurodevelopmental disorders (NDDs) in a Pakistani clinical cohort with specific focus on determine patterns in Autism Spectrum Disorder (ASD), Cerebral Palsy (CP), Down Syndrome (DS), and Intellectual Developmental Disorder (IDD). The results offer strong evidence that there is a significant difference in cognitive and epidemiological profiles across the diagnostic categories, and one of the strongest determinants can be hereditary factors. The most interesting is the strong hereditary burden ($p = .007$) found in the diagnostic spectrum with the Intellectual Developmental Disorder (IDD) group having a 100% prevalence of familial clustering. This trend is a great indication of a genetic and hereditary foundation of intellectual developmental disorders within this population.

In the Pakistani context, this result can be partly explained by the fact that the percentage of consanguinity marriages is rather high, and it is known to predispose individuals to autosomal recessive diseases and spread genetic susceptibility across generations (Bittles and Black, 2010; Hamamy et al., 2011). The idea of a hereditary load is thus especially relevant to IDD with the implication that there may be a strong influence of familial and genetic risk factors on its development. Conversely, the ASD group had a relatively lower rate of family history indicating a more heterogeneous and multifactorial etiology. This is in line with the modern findings that autism is a product of inherited susceptibility in genes, a de novo mutation, and environmental exposures (Sandin et al., 2014; Modabbernia et al., 2017). The overlapping of IDD and ASD in hereditary patterns indicates that one should not pay attention to etiological pathways of neurodevelopmental disorders and define them as a single group. This finding is related to the researches that indicate that intellectual developmental disorders often include a major genetic component, including inheritable diseases and family-related risk factors (American Psychiatric Association, 2013; Fombonne, 2005). Such distinctions play a vital role in the process of genetic counseling, early screening and special intervention plans.

The observed gender distribution among the diagnostic groups showed that most of the patients with ASD were male and most of the patients with IDD were female. This is in line with available literature that indicates that ASD is more commonly diagnosed in males though it could be both biologically predisposed and biased in diagnoses where females may be under- diagnosed unless they have more extreme symptoms (Harm, Hope & Household, 2013; Wing, 1981). It is also an important phenomenon and can be conceptualized as a so-called Diagnostic Identification Gap. Although the literature is clear that males are more likely to develop ASD and the overrepresentation of females in the IDD group is frequently explained by cultural bias to seek help and be diagnosed (Loomes et al., 2017), it is possible that the increase in help-seeking and diagnosis among females is culturally mediated. The probability of clinical assessment may depend on gender norms and access to healthcare in a context, as it is in many South Asian settings, such as Pakistan. Professional attention is more likely to be given to female children only in the instances when the impairment is severe, global, and functional as is common in IDD. Conversely, less severe or socially insensitive deficits, e.g., typical of ASD, can be neglected or incorrectly explained by personality traits in girls (Ratto et al., 2018). This results in a possible failure to identify ASD in females and intervention delays. The results thus highlight the importance of gender sensitive diagnostic frameworks and screening programs capable of identifying the entire range of neurodevelopmental manifestations, especially those who are under-identified.

The other significant results of the study are the non-significant difference in the socioeconomic status (SES) and the type of neurodevelopmental disorder which is an indication that NDDs are not limited to any economic level in this cohort. This observation concurs with previous studies that neurodevelopmental disorders, such as ASD and intellectual disabilities, exist at all socioeconomic levels albeit with potential differences in the access to diagnosis and treatment (World Health Organization, 2022). Though the three aspects of environmental disadvantages related to lower SES, including inability to access health services, poor nutrition and disadvantages in education, are often viewed as risk factors of developmental disorders, the current data shows that biological and hereditary factors can work comparatively independently of the socioeconomic status. The trend promotes the notion of economic neutrality, where neurodevelopmental disorders spread across the socioeconomic spectrum, although inequalities may exist in the aspects of diagnosis, awareness, and service availability. Past studies have also established that the prevalence might not vary considerably by SES but the timing of diagnosis and access to intervention tend to vary (Durkin et al., 2010; Emerson, 2012). The Pakistani contextual meaning of this finding is significant in the context of public health, implying that intervention plans need to be more universal than targeted, such that screening and support services are available to all children irrespective of their economic status.

Conclusion

This study concludes that hereditary load is a primary determinant of the neurodevelopmental landscape in Pakistan, particularly for intellectual disabilities. The current research offers a subtle insight into the neurodevelopmental disorders within a Pakistani clinical setting, with the emphasis on the interaction between genetic, demographic, and cognitive factors. The results provide significance to the need to utilize differentiated etiological frameworks, gender-sensitive diagnosis, and universal intervention strategies, thus adding to the literature on pediatric neurodevelopment in the local and global context.

Recommendations

The results of the current research have important clinical, research, and policy implications. To start with, the high rates of hereditary occurrence of IDD underscores the importance of genetic counseling and community education, especially in areas where consanguinity is common in marriages. Second, the existence of a diagnostic gender gap necessitates the creation of culturally sensitive and gender-sensitive screening instruments that ought to be seen as a means to the prompt and correct identification of every child. Third, the reality of the economic neutrality of NDDs implies that health promotion efforts should be large-scale and inclusive instead of only focused on certain groups of people in terms of socioeconomic status. Future studies are advised to build on these results by using bigger and more heterogeneous samples, and longitudinal designs to follow developmental patterns over time. Also, the neuropsychological subdomains and biological markers would be added to a better insight into the underlying mechanisms of neurodevelopmental disorders.

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