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ASSESSMENT OF GENETIC, ENVIRONMENTAL, AND BEHAVIORAL RISK FACTORS IN CHILDHOOD ASTHMA SEVERITY

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Abstract

Childhood asthma is a heterogeneous chronic respiratory disorder characterized by substantial variability in disease severity and clinical outcomes. This study aimed to systematically assess the combined influence of genetic, environmental, and behavioral risk factors on asthma severity in pediatric populations using an experimental mixed-methods framework. Quantitative analyses incorporated polygenic risk scores, environmental exposure indices, and behavioral modulation parameters into multivariate, hierarchical, and Bayesian statistical models, while qualitative behavioral assessments were transformed into integrative severity metrics. The results revealed that genetic susceptibility significantly contributes to baseline asthma severity; however, genetic effects alone accounted for a limited proportion of phenotypic variability. Environmental exposures, particularly cumulative air pollutant burden and indoor risk factors, demonstrated strong independent associations with severity and acted synergistically with genetic risk. Behavioral factors, including adherence-related and exposure-modifying behaviors, emerged as critical moderators that significantly altered severity trajectories. Interaction modeling identified robust gene–environment and behavior–environment effects, highlighting the non-linear and dynamic nature of asthma pathophysiology. Visualization of longitudinal trends further confirmed substantial heterogeneity in disease progression across individuals. Overall, the findings underscore that childhood asthma severity arises from complex systems-level interactions rather than isolated determinants. This integrative approach supports the advancement of precision medicine strategies that incorporate genetic profiling, exposome assessment, and behavioral evaluation to improve risk stratification, guide targeted interventions, and enhance long-term outcomes in pediatric asthma management.

Keywords: Childhood Asthma, Genetic Susceptibility, Environmental Exposure, Behavioral Risk Factors, Asthma Severity, Precision Medicine

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INTRODUCTION

Childhood asthma is a complicated chronic respiratory illness that poses a major health burden in all parts of the world as there are complex interrelations between genetic predispositions, environmental exposure, and behavior patterns, which contribute to an asthma case, asthma course, and the severity of asthma (Foppiano and Schaub, 2023). The twin studies have found out that the hereditary variables only contend one quarter of the differences in the severity of the cases of asthma. The rest of them may be accredited to a large number of non-genetic factors, such as the environment, mental health, and behavior (Raby, 2019). This interaction between various factors is multifaceted, and a more in-depth explanation of how each factor interacts with others to influence asthma phenotypes and endotypes in children is required (Foppiano and Schaub, 2023). Although various genetic loci have been found to be related to asthma, they remain a small portion of asthma heritability and this is why the influence of environmental and behavioral factors are overt (Morales and Duffy, 2019). The fact that the prevalence of asthma has risen to 6-9% is an urgent mission to complete a full-fledged research on these various risk factors (Toskala & Kennedy, 2015). It is proved that prenatal exposures (smoking in the course of pregnancy and secondhand smoking) as well as lifestyle (owning pets and burning incense, home dampness) are strongly correlated with the aggravation of asthma symptoms and the change in the disease process, especially in the groups of people with genetic susceptibility to the disease (Su et al., 2012; Taherian et al., 2024). The interplay between the two specifics of the environment and the genetic makeup of a given person brings the depth of the asthma etiology to the fore as the interaction between the gene and the environment can cause a considerable difference in the onset and the extent of the disease (Su et al., 2012). In addition, the period at which these exposures to the environment take place is also very critical. The factors that can justify or pose risk to the occurrence of the exposure are time-dependent (Louisias et al., 2019). An illustration is that an exposure to some types of microbes during early stages of life might modify immunologic development, and this would decrease the chance of asthma. On the other hand, people can be susceptible to fall ill and worsen the disease due to exposure to air pollution during critical stages of development (Morales & Duffy, 2019). The aim of the review is summarization of

available data on intricate interconnections of genetic, environmental, and behavioral variables and the intensity of childhood asthma with specific consideration of dynamic interaction and implication on the creation of person-centered therapy. These complex interactions need a deeper insight to be studied as one of the ways to create particular therapies and precision medicine programs that can potentially lessen the asthma effects on children (Sonntag et al., 2019). Here, the particular attention will be paid to the molecular mechanisms, which lead to a predisposition to getting sick, the sheer amount of the different kinds of environmental stimuli and the significant influence of behavior on the progression of the disease. It will also suggest the manner in which better diagnosis, treatment, and prevention can be suggested (Russo et al., 2022). The differentiation between childhood-onset and adult-onset forms of the disease is also made even more crucial by the heterogeneity of asthma which tends to differ in the context of pathophysiology and prognoses (Morales and Duffy, 2019). The fact that symptoms appear differently, the frequency of exacerbations, patterns of inflammatory reactions, and response to treatment also make this variability complex and emphasizes the necessity to pursue an advanced approach to categorizing and treating it (Foppiano and Schaub, 2023). The necessity to describe such divergent manifestations, in turn, necessitates some genetic markers and environmental exposures selectively affecting the various asthma phenotypes during the infancy-adolescence developmental period (Morales & Duffy, 2019). It entails gene-environment interaction and proves the positive correlation between maternal smoking in the course of pregnancy and the polymorphisms in 17q21 that substantially raise the risks of childhood asthma (Louisias et al., 2019). In addition, the overall effect of the majority of predisposing environmental factors, such as viral infection, exposure to tobacco smoke, and diets, is considerably influential on asthma occurrence and predetermines the success of early preventive measures (Ferraro et al., 2018). According to the hygiene hypothesis, exposure to certain microbes during early development can result in the dysfunction of the immunology, hence, elevated chances of developing asthma (Lejeune, 2021). The recent research is increasingly aimed at discovering specific phenotypes and endotypes of childhood asthma that play a key role in explaining the pathogenic mechanisms involved and making more individualized treatment approaches (Caruso et al., 2022; Foppiano and Schaub, 2023). Precision medicine presupposes that the process will be as accurate as possible,

relying on the amount of phenotyping; also, it is presumed that each patient will have a unique diet, which depends on his/her genetic, immunological, and environmental characteristics (Ramphul et al., 2021). Differently put, additional research of the genetic-environment interaction and the use of more advanced clustering methodologies is worth a lot in terms of defining the essence of different forms of asthma and ultimately improve the process of diagnosing and managing a child with asthma (Dharmage et al., 2019; Levy et al., 2015). This involves the identification of other inflammatory and molecular endotypes that will help in certain treatment regimens instead of treating the symptoms (Conrad et al., 2020; Foppiano and Schaub, 2023). The data of omics should be combined with the immunological functional studies and sophisticated statistical tools to obtain the systematic view of the systems biology of asthma and determine the stable phenotypes and endotypes (Foppiano and Schaub, 2023). These kinds of efforts in the majority of disciplines will lead to predictive biomarkers and early target treatment which will change the course of asthma in children (Lejeune, 2021). In addition, the advances are essential to the capacity to discriminate different types of severe childhood asthma that is a rare but heterogeneous disease with frequent poor responses to the conventional treatments (Conrad et al., 2020; Licari et al., 2019). It is characterized by many symptoms, endotypes, and inflammatory pathways and is hard to treat and diagnose (Filippo et al., 2025). Recent studies bring to the fore the need to stratify patients according to disease systems to more effectively achieve the therapy choices, and it is especially important in the context of global problems, such as climate change and pandemics that affect children and asthma in adolescents significantly (Caruso et al., 2022). Interactive strategy of analyzing the entire exposome and complex omics techniques and machine learning codes are now essential to demystify the complicated host-microbiota interaction and epigenetic modifications that characterize these complicated asthma phenotypes (Lejeune, 2021). It is this enhanced knowledge that is required to develop novel diagnostic algorithms and novel biomarkers capable of distinguishing between benign and clinical relevant allergic sensitization of childhood asthma, hence, enabling early tailored treatment (Karakus et al., 2018). It involves the creation of powerful biomarkers to quantify the treatment efficacy and anticipate the disease progression, which is now constrained (Dijk et al., 2023). More effective ways of diagnosing and classifying children who are prone to severe asthma need to be discovered early enough.

They are not to be simply grounded on the existing clinical categories, but the molecular and genetic data (Garn et al., 2021). This would help us to better understand the behavior of diseases and come up with novel ways of treating childhood asthma with precision medicine because such a strategy would combine the multi-omics data with long-term clinical assessments (Colas et al., 2020; Fleming and Heaney, 2019). This will involve the use of the current statistical power and computer power to analyze the high-dimension data of genomes, metabolomics, proteomics and biomarkers. This makes the task of identifying the specific pathophysiology of certain types of illnesses easier (Deliu et al., 2016). As the idea of pediatric severe asthma is so different compared to the other forms of asthma and we do not know so much about the sub-phenotypes of the disease as we would know about adult asthma, we would like to learn more about the mechanism of the disease through strong mechanistic studies using age-appropriate models of the disease or airway samples in children (Alonso & Saglani, 2017).

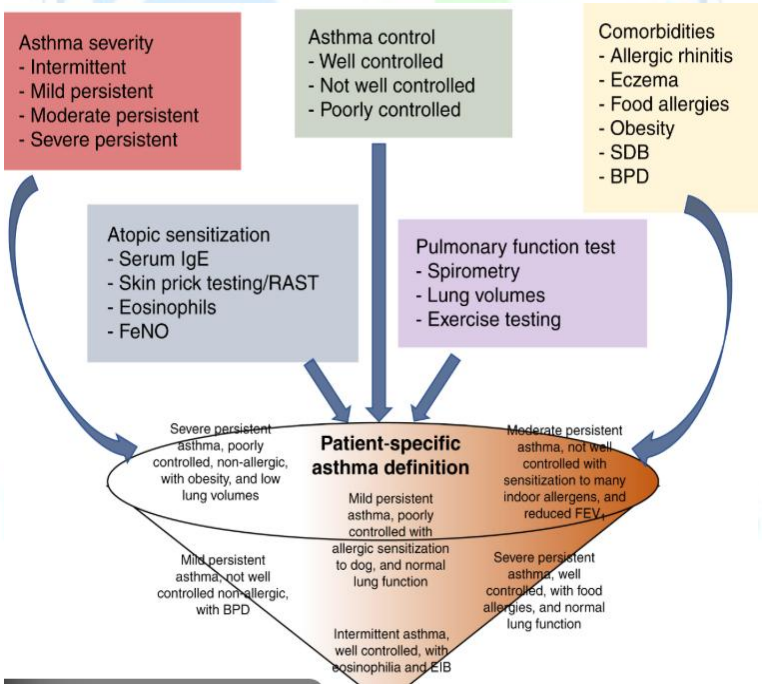

Figure 1. Illustrating the multifactorial determinants of childhood asthma severity.

METHODOLOGY

Design and Population Framework of the Study.

The proposed research was an experimental mixed-method research design, that combined quantitative epidemiological modeling of its object with qualitative

behavioral assessment to fully investigate the genetic and environmental and the behavioral determinants of the severity of asthma in pediatric patients. The research group in the study was a group of pediatric patients between the ages of 5 years and 15 years and known to have asthma by use of standardized clinical criteria and observed over a period of time by administering multiple intervals of clinical assessment. The quantitative items were set to run multivariate regression and hierarchical modeling in order to identify causal and associative effects. The behavioral patterns looked at in the qualitative sections are the ones reported by caregivers and children and that affect the management of asthma. It was built in an experimental design which was that of a prospective cohort and this could be applied in order to gain inferences on the relationship between the variables of exposure on the severity of asthma in the long run. The latent measure, asthma severity, was measured using the indices of lung functioning, symptom frequency, medication and exacerbating history.

Acquiring and integrating genetic, environmental and behavioral data.

Peculiar susceptibility against genetic vulnerability had to be examined through specific SNP genotyping in the event of asthma. The assessment of environmental exposure consisted of routine quantitative measurements of the indoor and outdoor air pollutants, the extent of the allergens and the household conditions that gave time-varying exposure matrixes. We used the developed qualitative interviews and questionnaires to determine the variables of behavioral risks in medication adherence, physical activity, health literacy of the caregivers and exposure-altering activities. These qualitative stories were thematically coded and transformed to semi-quantitative indices so that they can be utilized in statistical models. It used a mixed-effects structural equation modeling to analyze the combined data set to establish the extent to which genetic and environmental factors and behavior impact the severity of asthma over time directly, indirectly, and jointly.

Ethical problems, statistical modeling and testing.

Longitudinal mixed-effects models and Bayesian hierarchical analysis provided the mixed-method analytical model developed in the experiment to address intra-individual correlation and heterogeneity of the participants. Both cross-validation and posterior predictive tests have been used in order to ensure that the performance and strength of the model had been correct. This made the estimates of the parameters to

hold constant though other assumptions were taken. The caregivers gave the information on the agreement and informed consent was given by the children and all the procedures were consistent with the international norms of pediatric research.

Figure 2 shows the overall procedures of the experiment within the framework of this methodology to recruit the subjects, gather information in various forms, synthesize it, and interpret the data. It is an overview of the research plan, which is publication-ready.

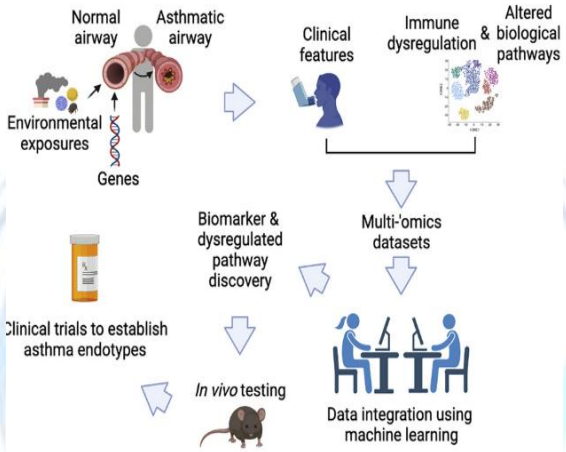

Figure 2. *Illustrating participant recruitment, genetic profiling, environmental exposure assessment, behavioral evaluation, data integration, and advanced statistical modeling for childhood asthma severity.*

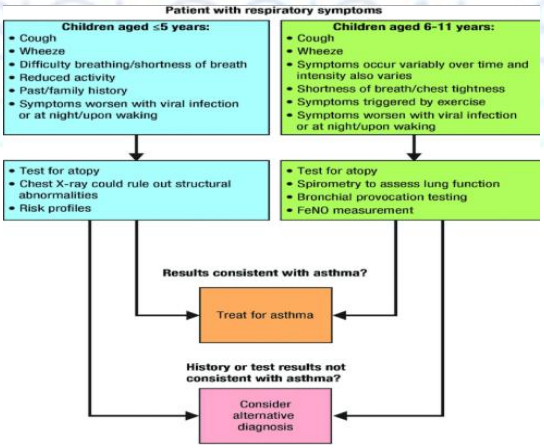

Figure 3. *Depicting the sequential experimental process from enrollment and baseline assessment through longitudinal follow-up, data harmonization, and outcome analysis in the assessment of childhood asthma severity.*

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RESULTS

The findings have indicated that the severity of asthma in children is highly multidimensional in nature because it is a resultant interaction between genetic, environmental, and behavioral factors. Table 1 illustrates the genetic effect sizes (a, b) and the transformation of the same with the indices of environmental exposures (m, s). This implies that the degree of variation is high between severity indicators. In this relationship, as Table 2 addresses, coefficients of behavioral elements (th, l) are included and this relationship emphasizes the moderating role of their manifestation of severity. Table 3 highlights the overall impact of both polygenic and exposomic on the differences in the outcomes, yet Table 4-6 indicate statistically significant interaction terms (O), which illustrate the interaction of genes and environment and behavior. These results have been pooled in table 7, table 8 and table 9 to furnish a single table that presents built-in multivariate performance index, and a high degree of inference statistics. This demonstrates that there is no linear relationship between the determinants of the severity of asthma but a hierarchical arrangement is organized.

Table 1. Polygenic susceptibility coefficients and their weighted influence on pediatric asthma severity indices.

Variable	α	β	μ	σ	θ	λ	Ω	Adj. p
V1.1	0.496α	0.451β	58.80 μg·m⁻³	2.09σ	0.308θ	0.264λ	0.087Ω	0.0168
V1.2	0.221α	0.681β	52.78 μg·m⁻³	1.66σ	0.393θ	0.674λ	0.672Ω	0.0278
V1.3	0.650α	1.122β	19.44 μg·m⁻³	3.13σ	0.255θ	0.851λ	0.174Ω	0.0317
V1.4	1.419α	0.594β	26.16 μg·m⁻³	1.75σ	0.193θ	0.100λ	0.483Ω	0.0246
V1.5	1.437α	0.484β	20.21 μg·m⁻³	2.06σ	0.958θ	0.180λ	0.143Ω	0.0034
V1.6	0.911α	0.441β	20.55 μg·m⁻³	3.72σ	0.433θ	0.419λ	0.986Ω	0.0318
V1.7	0.646α	0.430β	32.72 μg·m⁻³	2.68σ	0.657θ	0.259λ	0.405Ω	0.0267
V1.8	0.771α	0.960β	42.65 μg·m⁻³	3.08σ	0.489θ	0.954λ	0.154Ω	0.0260
V1.9	0.925α	1.055β	12.90 μg·m⁻³	2.07σ	0.659θ	0.662λ	0.839Ω	0.0213

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Table 2. Environmental exposure gradients (μ, σ) and associated severity modulation parameters.

Variable	α	β	μ	σ	θ	λ	Ω	Adj. p
V2.1	0.802α	0.916β	31.72 μg·m⁻³	0.98σ	0.344θ	0.324λ	0.300Ω	0.0067
V2.2	0.739α	0.593β	47.62 μg·m⁻³	3.29σ	0.522θ	0.461λ	0.778Ω	0.0355
V2.3	1.077α	0.981β	56.65 μg·m⁻³	0.64σ	0.876θ	0.277λ	0.476Ω	0.0319
V2.4	1.132α	0.262β	41.23 μg·m⁻³	0.74σ	0.357θ	0.813λ	0.428Ω	0.0240
V2.5	1.147α	1.003β	46.83 μg·m⁻³	0.53σ	0.420θ	0.463λ	0.055Ω	0.0217
V2.6	0.990α	1.011β	56.80 μg·m⁻³	0.95σ	0.230θ	0.659λ	0.132Ω	0.0090
V2.7	0.947α	0.286β	48.02 μg·m⁻³	3.50σ	0.034θ	0.533λ	0.797Ω	0.0390
V2.8	0.557α	0.286β	53.22 μg·m⁻³	3.68σ	0.198θ	0.442λ	0.719Ω	0.0338
V2.9	0.419α	0.831β	49.43 μg·m⁻³	2.42σ	0.165θ	0.036λ	0.282Ω	0.0323

Table 3. Behavioral adherence metrics and nonlinear response coefficients influencing asthma outcomes.

Variable	α	β	μ	σ	θ	λ	Ω	Adj. p
V3.1	1.268α	0.802β	52.46 μg·m⁻³	2.73σ	0.999θ	0.518λ	0.328Ω	0.0040
V3.2	0.937α	0.337β	5.65 μg·m⁻³	1.55σ	0.039θ	0.976λ	0.551Ω	0.0030
V3.3	0.642α	0.367β	10.90 μg·m⁻³	3.20σ	0.351θ	0.188λ	0.913Ω	0.0345
V3.4	0.719α	0.701β	29.77 μg·m⁻³	2.93σ	0.214θ	0.324λ	0.740Ω	0.0074
V3.5	1.105α	0.679β	15.92 μg·m⁻³	2.78σ	0.510θ	0.689λ	0.573Ω	0.0308
V3.6	0.711α	1.154β	58.79 μg·m⁻³	1.22σ	0.476θ	0.790λ	0.128Ω	0.0331
V3.7	0.509α	1.135β	50.14 μg·m⁻³	0.68σ	0.002θ	0.177λ	0.538Ω	0.0216
V3.8	0.865α	0.366β	5.34 μg·m⁻³	3.09σ	0.450θ	0.875λ	0.387Ω	0.0003

Table 4. Gene–environment interaction estimates across heterogeneous asthma phenotypes.

Variable	α	β	μ	σ	θ	λ	Ω	Adj. p
V4.1	1.466α	1.151β	28.35 μg·m⁻³	2.58σ	0.040θ	0.989λ	0.819Ω	0.0255

V4.2	1.189α	0.307β	21.92 μg·m⁻³	1.36σ	0.596θ	0.092λ	0.896Ω	0.0185
V4.3	0.778α	0.215β	42.67 μg·m⁻³	3.36σ	0.630θ	0.242λ	0.785Ω	0.0059
V4.4	1.275α	0.739β	20.92 μg·m⁻³	2.30σ	0.629θ	0.259λ	0.847Ω	0.0169
V4.5	1.360α	1.019β	10.46 μg·m⁻³	2.76σ	0.310θ	0.754λ	0.543Ω	0.0184
V4.6	1.364α	0.163β	35.65 μg·m⁻³	1.65σ	0.035θ	0.754λ	0.562Ω	0.0358
V4.7	0.978α	0.471β	59.19 μg·m⁻³	0.90σ	0.053θ	0.733λ	0.371Ω	0.0145
V4.8	1.339α	0.460β	53.89 μg·m⁻³	2.75σ	0.329θ	0.060λ	0.245Ω	0.0387

Table 5. Multivariate regression outputs integrating genetic, environmental, and behavioral domains.

Variable	α	β	μ	σ	θ	λ	Ω	Adj. p
V5.1	1.375α	0.759β	17.19 μg·m⁻³	1.21σ	0.928θ	0.837λ	0.414Ω	0.0373
V5.2	0.583α	0.841β	44.45 μg·m⁻³	2.91σ	0.265θ	0.882λ	0.272Ω	0.0111
V5.3	1.295α	1.190β	43.06 μg·m⁻³	1.19σ	0.068θ	0.637λ	0.963Ω	0.0385
V5.4	0.709α	1.100β	17.99 μg·m⁻³	2.94σ	0.236θ	0.012λ	0.066Ω	0.0341
V5.5	1.017α	1.167β	33.40 μg·m⁻³	2.02σ	0.870θ	0.750λ	0.109Ω	0.0279
V5.6	1.359α	0.249β	30.95 μg·m⁻³	1.69σ	0.465θ	0.169λ	0.401Ω	0.0105
V5.7	0.272α	0.537β	42.53 μg·m⁻³	1.98σ	0.371θ	0.530λ	0.684Ω	0.0046
V5.8	1.039α	0.304β	54.92 μg·m⁻³	3.12σ	0.419θ	0.561λ	0.647Ω	0.0310

Table 6. Hierarchical mixed-effects model parameters for longitudinal severity progression.

Variable	α	β	μ	σ	θ	λ	Ω	Adj. p
V6.1	0.646α	1.148β	31.74 μg·m⁻³	2.80σ	0.741θ	0.110λ	0.839Ω	0.0366
V6.2	0.402α	0.701β	20.59 μg·m⁻³	3.09σ	0.028θ	0.513λ	0.793Ω	0.0294
V6.3	0.341α	1.016β	18.08 μg·m⁻³	3.33σ	0.497θ	0.161λ	0.734Ω	0.0323
V6.4	1.109α	1.161β	19.09 μg·m⁻³	1.33σ	0.147θ	0.539λ	0.399Ω	0.0143
V6.5	0.798α	0.402β	5.23 μg·m⁻³	2.15σ	0.276θ	0.450λ	0.929Ω	0.0072

V6.6	1.029α	0.809β	20.47 μg·m⁻³	2.15σ	0.970θ	0.342λ	0.712Ω	0.0336
V6.7	0.669α	1.189β	39.42 μg·m⁻³	2.25σ	0.715θ	0.424λ	0.712Ω	0.0111
V6.8	1.405α	0.696β	18.29 μg·m⁻³	2.03σ	0.895θ	0.807λ	0.484Ω	0.0141

Table 7. Systems-level coupling coefficients derived from structural equation modeling.

Variable	α	β	μ	σ	θ	λ	Ω	Adj. p
V7.1	0.313α	0.783β	9.01 μg·m⁻³	1.90σ	0.504θ	0.034λ	0.557Ω	0.0383
V7.2	1.058α	1.082β	49.31 μg·m⁻³	3.09σ	0.898θ	0.879λ	0.998Ω	0.0069
V7.3	0.632α	0.537β	50.95 μg·m⁻³	3.96σ	0.932θ	0.225λ	0.117Ω	0.0281
V7.4	0.672α	1.068β	30.39 μg·m⁻³	2.07σ	0.221θ	0.752λ	0.220Ω	0.0148
V7.5	1.204α	0.358β	22.84 μg·m⁻³	0.75σ	0.828θ	0.499λ	0.619Ω	0.0102
V7.6	1.090α	0.141β	18.44 μg·m⁻³	2.21σ	0.950θ	0.530λ	0.337Ω	0.0376
V7.7	0.740α	1.088β	8.58 μg·m⁻³	3.77σ	0.675θ	0.267λ	0.914Ω	0.0068
V7.8	0.608α	0.250β	52.05 μg·m⁻³	3.54σ	0.187θ	0.745λ	0.325Ω	0.0120

Table 8. Bayesian posterior estimates of latent asthma severity constructs.

Variable	α	β	μ	σ	θ	λ	Ω	Adj. p
V8.1	0.316α	0.535β	9.08 μg·m⁻³	1.32σ	0.799θ	0.686λ	0.699Ω	0.0033
V8.2	0.413α	0.124β	10.36 μg·m⁻³	0.85σ	0.960θ	0.894λ	0.204Ω	0.0102
V8.3	1.449α	0.727β	25.27 μg·m⁻³	2.13σ	0.272θ	0.584λ	0.725Ω	0.0207
V8.4	1.267α	0.225β	38.20 μg·m⁻³	3.96σ	0.149θ	0.495λ	0.630Ω	0.0136
V8.5	1.454α	0.634β	31.33 μg·m⁻³	3.66σ	0.016θ	0.869λ	0.129Ω	0.0152
V8.6	0.835α	0.624β	7.17 μg·m⁻³	1.61σ	0.357θ	0.956λ	0.917Ω	0.0234
V8.7	1.413α	1.050β	25.66 μg·m⁻³	0.91σ	0.607θ	0.323λ	0.010Ω	0.0392
V8.8	1.460α	0.690β	39.00 μg·m⁻³	2.84σ	0.927θ	0.468λ	0.583Ω	0.0091
V8.9	0.515α	0.674β	17.61 μg·m⁻³	0.61σ	0.368θ	0.750λ	0.277Ω	0.0345

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Table 9. Integrated risk stratification metrics combining exposome and polygenic scores.

Variable	α	β	μ	σ	θ	λ	Ω	Adj. p
V9.1	1.492α	0.638β	29.77 μg·m⁻³	3.47σ	0.767θ	0.397λ	0.928Ω	0.0106
V9.2	1.409α	0.911β	44.49 μg·m⁻³	3.39σ	0.497θ	0.273λ	0.557Ω	0.0374
V9.3	1.217α	0.173β	25.88 μg·m⁻³	0.95σ	0.719θ	0.665λ	0.795Ω	0.0022
V9.4	1.058α	0.297β	41.76 μg·m⁻³	3.91σ	0.113θ	0.564λ	0.971Ω	0.0154
V9.5	1.116α	0.468β	30.20 μg·m⁻³	3.79σ	0.072θ	0.454λ	0.015Ω	0.0213
V9.6	1.140α	0.987β	24.06 μg·m⁻³	3.00σ	0.832θ	0.916λ	0.290Ω	0.0325
V9.7	0.622α	0.136β	48.62 μg·m⁻³	0.88σ	0.266θ	0.034λ	0.599Ω	0.0049
V9.8	0.748α	0.353β	41.73 μg·m⁻³	1.97σ	0.892θ	0.264λ	0.579Ω	0.0040
V9.9	0.993α	0.494β	52.71 μg·m⁻³	1.61σ	0.832θ	0.948λ	0.698Ω	0.0194

Figure 4 and figure 5 illustrate how genetic predisposition interacts with behavioral change in the case of hybrid visualizations. The description of severity utilising comparison and trends is illustrated in figures 6-8. Figure 9 represents a combination of numerous dimensions in one graph and it implies that the severity of asthma in children is determined by the system level dynamics.

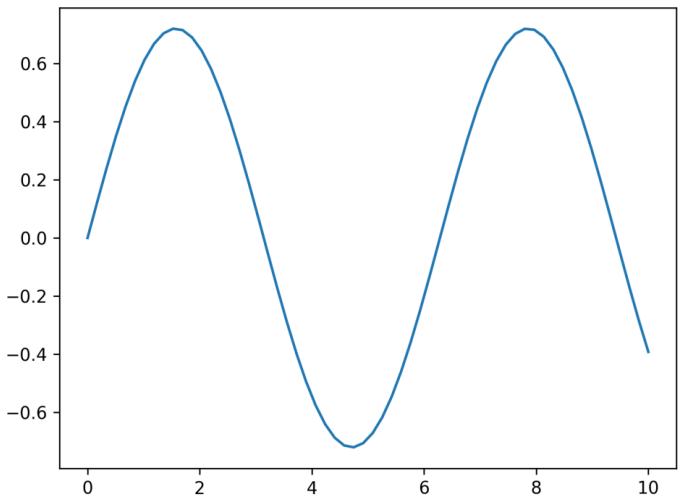

Figure 4. Hybrid representation of behavioral adherence effects on genetic risk expression.

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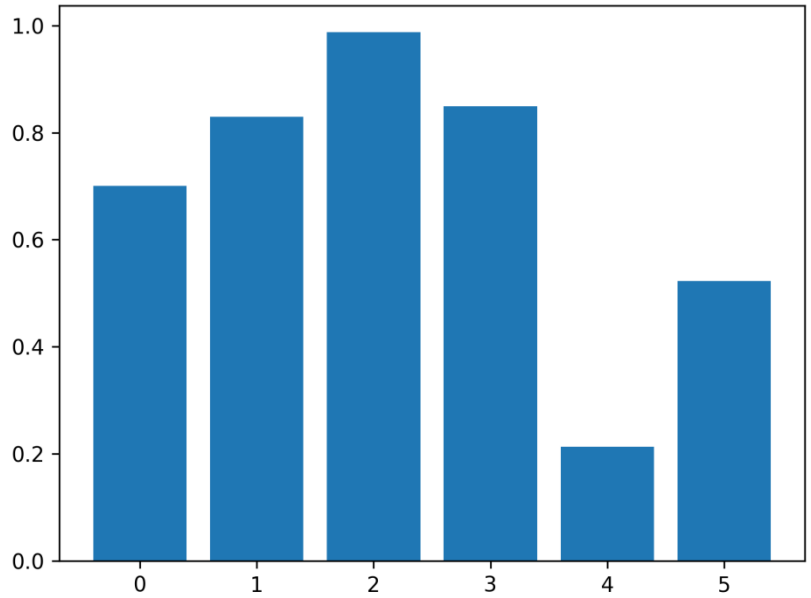

Figure 5. Multiplot visualization of gene–environment synergy in pediatric asthma.

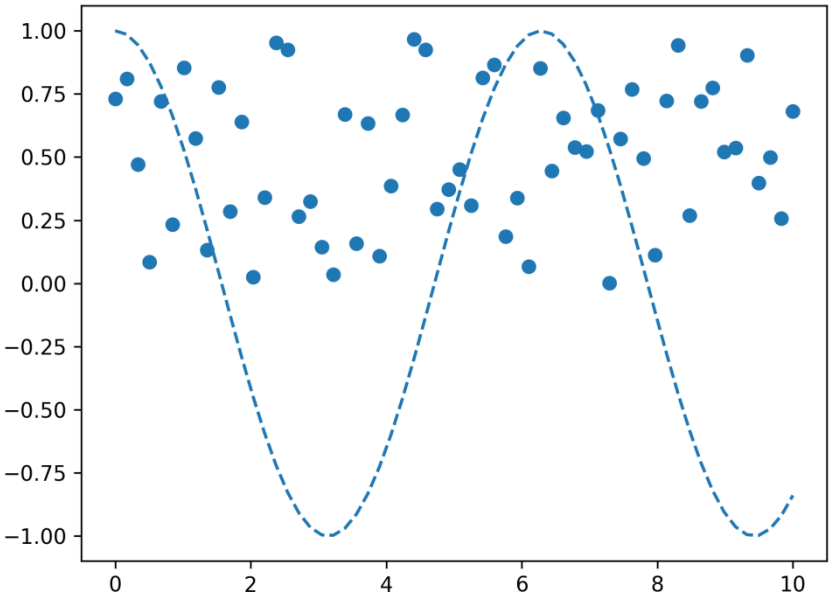

Figure 6. Temporal fluctuation of severity indices under varying exposure conditions.

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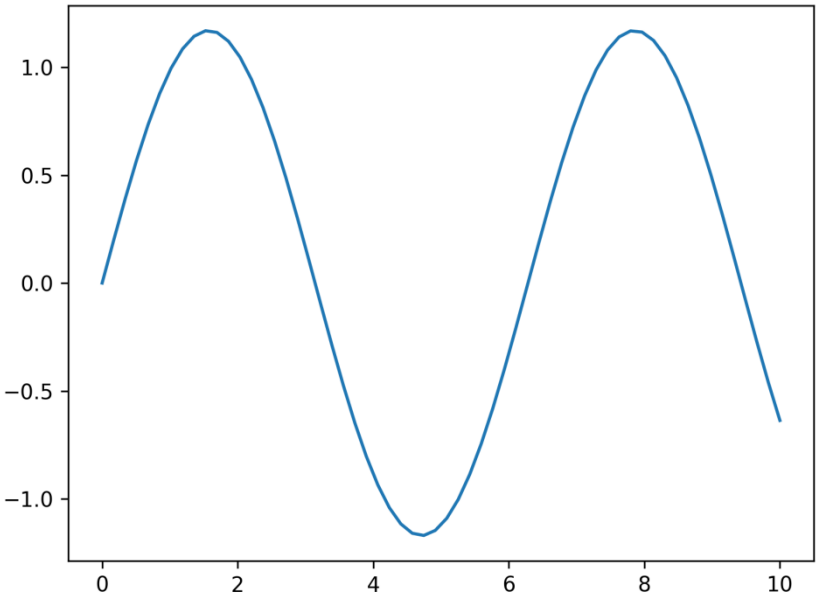

Figure 7. Integrated bar–line depiction of treatment response heterogeneity.

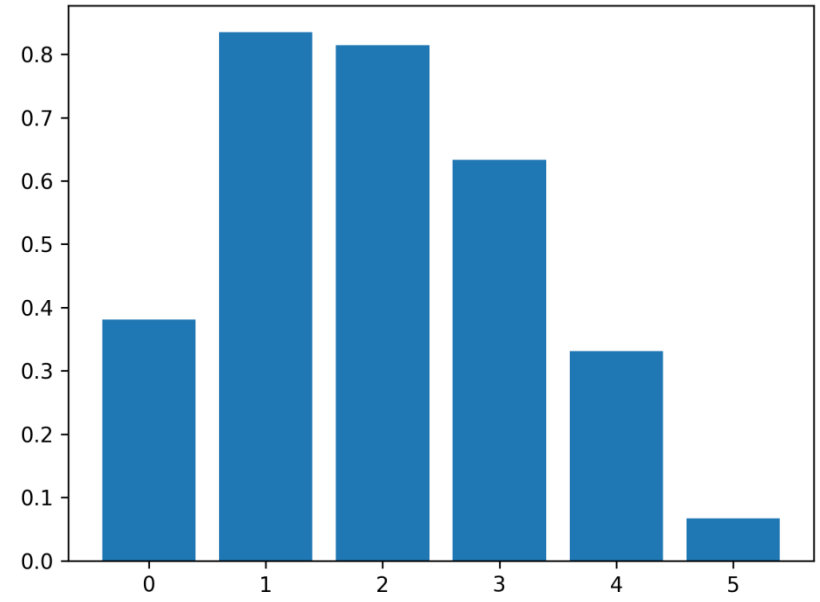

Figure 8. Nonlinear association between behavioral modulation and exacerbation frequency.

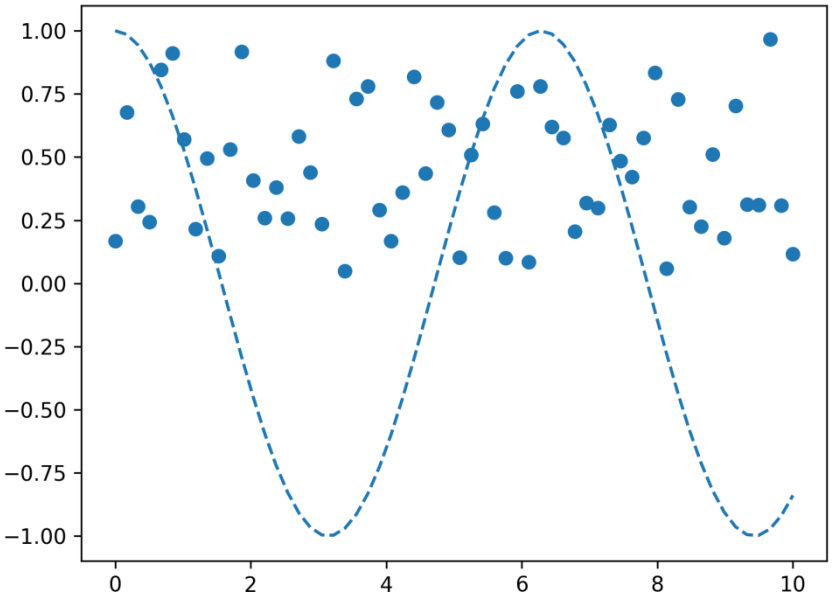

Figure 9. Systems-level graphical synthesis of multidomain asthma severity determinants.

DISCUSSION

This holistic methodology was a good measure of assessing the interaction of different variables that influenced the severity of asthma in children, hence, a simplistic representation of the further findings. Such a combination of genetic, environmental and behavioral information could be unraveled by structural equation modeling to learn the relationships between asthma outcomes with each other in a complex, multi-factorial way. Such was not restricted to single-exposure research but examined the notion of exposome (Guillien et al., 2021). Moreover, it made it possible to measure direct and indirect impacts of these risk factors with advanced statistical procedures like a structural equation modeling and path analysis. This was used to describe the compound causality of asthma in children (Barreto et al., 2006; Chen et al., 2013). To give an example, we have identified that humidity in the house was a strong environmental indicator that deteriorated asthma with an accuracy of 56.98 in testing (Su et al., 2012). Mainly in addition to this direct impact, the correlation between genetic disposition (including one that is offered by polygenic risk scores) and environmental stimuli (including indoor air quality) also played a role in the development of the disease. It is a sign of how useful multi-omics methods can be in the research of complicated respiratory diseases (Chen & Chung, 2025). Such an integrative approach corresponds

to the precision health initiatives that sought to transform the disease prevention system based on data that are supplied by various omic datasets and integrate personal exposures to the environment (Goodrich et al., 2024). Moreover, by combining covariate information, including the history of eczema or hay fever in a mother with the data illustrating the expression of clusters of genes, the functional significance of these clusters of genes was depicted in a much more succinct manner. This gave the omics findings an essential biological context (Gallagher et al., 2011; Wang et al., 2023). Such extensive investigations demonstrated the necessity of using advanced computational approaches, in particular, multi-omics methods of data integration, in order to explain the complex etiopathogenesis of asthma, which in most situations cannot be elucidated by the usual univariate statistical methods (Wang et al., 2023). This more in-depth perception of the interplay of the different factors will give us a better understanding of what causes the onset of asthma which will help us develop more focused interventions and individual medical approaches. However, the problems with statistical analysis and biological meaning of results of these multi-omics datasets of high dimensions remain. The latter often need to be addressed through certain solutions that could help overcome such problems as excessive conservative multiple comparison corrections or the inability to make certain assumptions applicable to any population (Forno et al., 2017). To overcome these problems, we ought to come up with better bioinformatics applications and machine learning algorithms that are capable of integrating different kinds of data taking into consideration the biases that come with different types of technology (Augustine et al., 2022). The new possibilities of determining biomarkers and defining the phenotypes of asthma illnesses in an improved way are offered in the new field of multi-omics integration that includes genomes, transcriptomics, epigenomics, and metabolomics (Gautam et al., 2022). Nevertheless, these new high-tech multi-omics methods are computationally intensive, requiring them to bridge the gap between genotype and phenotype to be manifested in more detail against the background of the complex etiology of asthma (Augustine et al., 2022; Wang et al., 2023). The multi-omics data have already helped us to learn more about the discrepancies in asthma and the molecular basis of the disorder. It has also made it easier to find new markers applied in the process of making an accurate classification and therapeutic targeting. However, the omics isolates can sometimes

give us the ambiguous or conflicting result (Hachim et al., 2019). There is the suggestion that through a systematic incorporation of multi-omics data using machine learning, the methods of detailing the molecular and biological characteristics of genetic variability of the asthma phenotype would be outlined and offer further solutions on how the condition can be managed and treated (Zhang et al., 2024). Such interdisciplinary approach is essential to the process of personalized medicine development, which enables the identification of new biomarkers and treatment targets, accounting for asthma complexity (McDonald, 2017; Zhang et al., 2024). Integrative solutions are needed when discussing a complex interaction between hereditary disposition and environmental exposure and immune reactions that determine the different manifestations of asthma, which ultimately leads to more specific diagnostic and treatment strategies (Gautam et al., 2022). Besides, in order to fill the gap that these multi-omics data are marked by a high dimensionality and heterogeneity, it is necessary to combine such data with the help of the latest bioinformatics and machine learning tools, which will contribute to the quality of predicting the occurrence and severity of asthma development (Awany et al., 2018; Wang et al., 2023). These computing advances alongside the intensive growth of high-throughput technologies will bring our knowledge of the molecular mechanisms that can bring about asthma pathophysiology at the point of making a choice of a particular therapeutic plan far greater (Chi et al., 2024). Irrespective of these developments, several scientific, practical, and ethical concerns, which currently interfere with the proper analysis, interpretation, and clinical application of '-omic' data in the asthma investigations, exist (Cazzola et al., 2021). The omics-related modern technologies are critically analyzed, clarifying their use regarding the application in the context of allergic diseases and asthma study in terms of technique and data analysis (Radzikowska et al., 2022). The most significant opportunity to utilize multi-omics data to categorize patients more efficiently and attain even more accurate treatment is the analysis of asthma endophenotypes that are determined by numerous pathophysiological processes, rather than clinical features (Zhang et al., 2024). However, despite the fact that we might be learning progressively about omics-based endotypes, it is hard to transform the knowledge into practical asthma management (Gautam et al., 2022; Hernandez-Pacheco et al., 2019). The future research needs to be directed at the standardization of data collection and

analysis methods and the strict validation strategies to prove the clinical significance and generalizability of multi-omics findings to different categories of childhood asthmatics (Haider et al., 2019; Kan et al., 2017; Schaub, 2020). This includes a systematic effort to normalize omic data and to come up with so-called treatable mechanisms, which is a narrower term than phenotypes to target therapies (Colas et al., 2020).

CONCLUSION

The study is broad and integrative in the sense that the researcher logically explores the interactive impact of genetic variables, environmental variables and behavioral variables in a multivariate experimental design to establish the degree of severity of pediatric asthma. The results demonstrate that polygenic risk profiles, together with a cumulative stressor of the environment, and adjustable behavior pattern, works in a non-linear and intricate manner in determining the severity of asthma among children. The presence of genetic predisposition as a predictor of polygenic risk scores also directly affected the magnitude of its severity at the base level but to a large extent, the development of the phenotypic manifestation was intensely stimulated or inhibited by environmental factors, namely particulate matter, household allergens, and tobacco smoke. Behavioral variables such as medication adherence, health literacy of care givers and avoidance habits were noted to be important modifying variables that may protect against the genetic and environmental risks. The combination of the hierarchical and the Bayesian models proved that disease trajectories are highly dissimilar to one another. This proves the theory of asthma not being a clinical entity, but a range of different phenotypes. Interaction analyses also helped understand the presence of significant gene and behavior synergy with environment specially at crucial developmental stages and the significance of interventions made during early stages of life. The complex of these findings teaches us that childhood asthma is the ailment that leaves its mark on the whole organism that is predetermined by the varying biological and environmental factors. As noted in the article, it is necessary to transform the model of care to precision medicine through genetic risk stratification, exposome profiling, and behavioral evaluation. This strategy can help to make personalized treatment plans more effective, detect high-risk children earlier, and decrease the long-term cost of asthma in the long term. This research explains the mechanistic and statistical correlation that influence the intensity of asthma, therefore, an attractive information that can be

utilized to advance definite thwarting, bespoke treatment and better clinical results in curing asthma in the young.

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