Genetic Predisposition of Language Disorders Among Different Independent Factors in Bronchial Asthma

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Original Article

ABSTRACT

Background: Bronchial asthma is the most common cause of chronic illness in childhood, reflecting on children's psychosocial behavior, cognition, and school performance. The asthmatic children have severe difficulties with concentration, behavior, and emotions. The genetic predisposition element of delayed language development (DLD) is highly suggested to be one of the important independent factors for asthmatic children to have DLD.

Aims: The current work aimed to determine the independent factors that develop DLD in children. 366 asthmatic children were enrolled in this study; their ages ranged from 2-5 years. Modified preschool language scale- four (Arabic edition) was applied to evaluate language age and the Stanford-Binet Intelligence Scale 5th edition (SB-5th) was used to assess Intelligence Quotient (I.Q.). The X-ray and hematological examination were done.

Results: Sixty-six asthmatic children had DLD (18%). X-ray findings, medical treatments, Hemoglobin level, and oxygen saturation showed non-significant differences between the DLD children and the typically developed children's groups. The family history (for both Bronchial asthma and DLD), TLC, PLT, full-scale I.Q., and recurrent attacks of otitis media showed significant differences between the two groups.

Conclusion: The asthmatic children had different independent factors considered as risk factors for delayed language development such as family history (for both bronchial asthma and delayed language development), recurrent otitis media, as well as TLC, PLT, full-scale I.Q, and sleep disturbances. This necessitates the evaluation of the language age in those children to accelerate their management.

Key Words: Asthmatic children, Bronchial asthma, Cognition, Delayed language development, Family history.

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INTRODUCTION

Language is communication that has understandable meanings within a group or community (**Law *et al.,* 2017**). Although language acquisition is spontaneous (**Simms *et al.,* 2011**), the incidence of primarily delayed language development is 2-7% of children (**Strom and Silverberg, 2016**). The study by **Gad-Allah *et al.,* (2012)** reported that 19.7% of their patients had DLD, and their ages ranged from 3-6 years. Genetic predisposition is highly suggested to play a role in most language disorders especially the primarily delayed language development (**Mountford *et al.,* 2022; van Wijngaarden *et al.,* 2024**). In contrast, child language development- in other cases- is like a mirror reflection of the overall development and cognitive ability. Early investigation and intervention are better at a younger age (**Schuster *et al.,* 2000**).

Bronchial asthma is the most common cause of chronic illness in childhood, reflecting on children's psychosocial behavior, cognition, and school performance (**Samuel *et al.,* 2011**). Bronchial asthma adversely affects their healthy growth and quality of life (**Yoshihara *et al.,* 2016**). **Al-Qerem *et al.,* (2015)** revealed that the prevalence rate of bronchial asthma in Egypt ranged between 6.8-7.5%.

Blackman and Gurka, (2007) reported comorbid behavioral, emotional, and developmental problems besides physical symptoms like coughing, breathing difficulty, and wheezing. The asthmatic children struggle greatly with concentration, behavior, and emotions (**Blackman and Gurka, 2007**). **Parry *et al.,* (2009)** reported that a person's ability to think is crucial to their linguistic abilities. Our

study aims to determine the independent factors that enhance delayed language development among asthmatic Egyptian children aged 2-5 years apart from other major contributors like social isolation or sensory impairment.

MATERIAL AND METHODS:

Subjects:

This cross-sectional investigation was conducted between February 2018 and January 2023. The study was approved by ethical committee of faculty of postgraduate childhood studies (FPGCS), Ain Shams University (ID: RHDIRB2020110401). 366 asthmatic children were included in this study, ranging from 2-5 years. All parents agreed to undergo the assessment and had informed consent.

1.1 Inclusion criteria:

• In this trial, children with asthma received follow-up care for at least a year. The children received adequate environmental stimulation and the same socioeconomic (S.E.) status.

1.2 Exclusion criteria:

• Children with mental retardation.

• The presence of any medical illness (except bronchial asthma), psychological illness, or sensory impairment.

Methods:

The children who were fulfilling the criteria mentioned above were subjected to the protocol for objective and subjective assessment:

• A formal pediatric examination was done, including general and local chest examinations.

• Diagnosis of bronchial asthma was confirmed by reviewing the laboratory and radiological findings of the patients.

• Complete blood count and oxygen saturation testing by digital pulse oximetry were assessed for all children.

• Audiological assessment.

• The Stanford-Binet Intelligence Scale 5th edition (SB-5th) (**Farag, 2011**) was applied; it is an intelligence test and an individual cognitive ability to diagnose developmental or intellectual deficiencies. The SB-5th assesses both verbal and non-verbal skills.

• Complete phoniatric evaluation for children with asthma, done by a phoniatrician, and assessment of language abilities using Modified Preschool Language Scale- four (Arabic Edition) (**Abou Hassiba *et al.,* 2011**). This test aimed to divide the asthmatic children who have an average mentality and do not suffer from hearing impairment into two groups; a group without DLD and another with DLD.

Statistical analysis:

SPSS version 24, was applied to tabulated data. Data were explored for normality using the Kolmogorov-Smirnov test and the Shapiro-Wilk test. Comparisons between the two groups were done using the independent *t*-test. For categorical variables, analyzed differences with (chi-square) tests. *P* values ≤0.05 indicate significance.

RESULTS

Three hundred sixty-six kids who met the previously listed requirements were added to the study. After applying the modified preschool language scale-four (Arabic edition) (**Abou Hassiba *et al.,* 2011**), the asthmatic children were divided into two groups:

Group1: Three hundred asthmatic children with normal language development, their mean age was 40.7 months±11.2 (±SD); boys were 175(41.7%), girls were 125(58.3%) and their mean age of onset of asthma was 17.1 months±8.7.

Group2: sixty-six allergic asthmatic children with delayed language development, their mean age was 36.6 months±11.5 (±SD), boys were 44(66.7%), girls were 22(33.3%) and their mean age of onset of asthma was 17.1 months±8.7.

Chi-Square Test:

Chi-Square test in table (1) shows the distribution of x-ray findings among both groups and revealed a non-significant difference between them. 65.2% of group 2 are normal findings; there was a difference between both groups but not detected statistically.

Chi-Square Test :

Chi-Square test in table (2) shows a significant difference between children in both groups as regards sleep disturbance.

Independent samples T:

Independent samples T in table (3) shows the distribution of variable factors among both groups and significant differences only in the family history of asthma (Figure 1), Family history of delayed language (Figure 2), total leucocytic count, platelet count, total I.Q, non-verbal I.Q, and verbal I.Q. The levels of hemoglobin and oxygen saturation were within normal levels; however, the difference was not statistically significant.

Table (4) shows a highly significant difference between the 2 groups regarding the recurrent otitis media.

Table 1: Radiological findings in asthmatic children in both groups:

Item		Asthmatic children		*p*-value
		Group 1 (*n*=300)	Group 2 (*n*=66)	
		n (%)	*n* (%)	
X-Ray finding	Normal	159(53%)	43(65.2%)	0.340 (N.S.)
	Bronchovascular Markings	105(35%)	18(27.3%)	
	Overinflated chest	22(7.3%)	3(4.5%)	
	Pneumonic patches	14(4.7%)	2(3%)	

Table 2: Distribution of frequency of sleep disturbances (according to the history given by the parents regarding their children's frequency of affected regularity and duration of sleep as well as breathing difficulties):

		Asthmatic children		*P*-value
		Group2 (*n*=300)	Group2 (*n*=66)	
		n (%)	*n* (%)	
frequency of sleep disturbances	<2 times/month	216(72%)	38(57.6%)	0.018 (S)
	2-4/month	18(6%)	11(16.7%)	
	>5/month	58(19.3%)	14(21.2%)	
	Frequent	8(2.7%)	3(4.5%)	

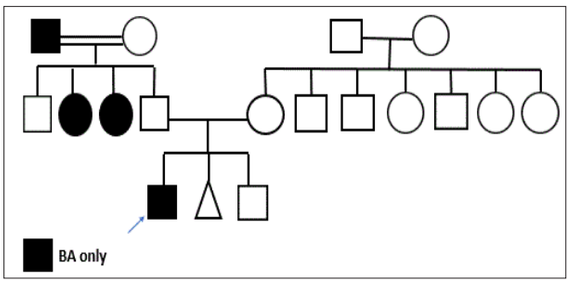

Figure 1: An example in our study of a 3-generation pedigree of a family of an asthmatic male child without DLD (black-colored symbol in the 3rd generation) who has similarly affected family members -BA without DLD- (black-colored male and female symbols in the 1st and 2nd generations).

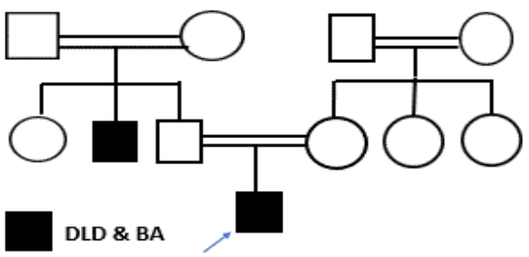

Figure 2: An example in our study of a 3-generation pedigree of a family of an asthmatic male child affected with DLD (black-colored symbol in the 3rd generation) showing consanguinity of his parents and a similarly affected family member - with DLD and BA - (black-colored male symbol in the 2nd generation).

Table 3: Comparison between both groups through independent variable factors:

Item		Asthmatic children		*P*-value
		Group 1 (*n*=300)	Group 2 (*n*=66)	
		n (%)	*n* (%)	
Family history of asthma	Positive	62(20.6%)	28(42.4%)	<0.001(H.S.)
Family history of delayed language	Positive	16(5.3%)	26(39.4%)	<0.001(H.S.)
Positive consanguinity		35(11.7%)	12(18.2%)	0.04(S)
Oxygen saturation		97.1±1.4	96.7±1.6	0.066(N.S.)
Hb g/dl		13.3±2.3	13.6±2.3	0.447(N.S.)
TLC X103/mm^3		11.6±2.7	12.4±3.2	0.032(S)
PLT X103/mm^3		294.3±78.4	323.2±103.6	0.011(S)
Full-Scale I.Q.		99.8±9.9	85.3±9.2	<0.001(HS)
Non-Verbal I.Q.		101.4±10.6	88.6±9.2	<0.001(HS)
Verbal I.Q.		97.7±10.4	81.6±9.5	<0.001(HS)

Table 4: Correlation between both groups and occurrence of recurrent otitis media:

Item		Asthmatic children		*p*-value
		Group 1 (*n*=300)	Group 2 (*n*=66)	
		n (%)	*n* (%)	
Recurrent OM	Positive	54 (18.2%)	47 (71.2%)	0.001 (HS)

DISCUSSION

In the current study, three hundred and sixty-six asthmatic children met the requirements. They were diagnosed by clinical examination, x-ray findings, and receiving medical treatment for at least 12 months. The problem is mainly with the culture of thinking of their parents who were not evaluating their children, often waiting until they were three years old (**Feldman *et al.*, 2005**).

In this study, the boys: girls' ratio was 2:1 in group 2 in concordance with **Law and Frances, (2000)** which estimated the male: the female ratio between 1.3:1 and 2.3:1. Their age range and mean (36.6 months±11.5) was considered a star age of language acquisition. Those children spend their time in hospital and managing bronchial asthma, which is deemed life-threatening for their parents. So those children are exposed to environmental deprivation in their society.

Sleep problems harm health, cognitive functioning, behavior, and school performance (**Van Maanen *et al.,* 2012**). Behavioral problems increase in the case of asthmatic children (**Van Maanen *et al.,* 2012**). This association could be explained by early stressful conditions that affect their quality of life indirectly and affect the proper acquisition of normal language development.

Reilly *et al.,* (2014) found that family history has a significant correlation with DLD. A family history of DLD increases the chances of learning difficulties in children (**Henrichs *et al.,* 2011**). Agreeing to some extent, the current study found that 39.4% of children with a family history of DLD tend to be at a greater risk than those with no family history (5.3%) to have DLD. **Rusconi *et al.,* (1999)** explained a significant correlation between parental history of asthma and early-onset persistent asthma in children. **Strom and Silverberg, (2016)** reported that a history of asthma was positively correlated with language disorders.

In the current study, a statistically significant association between DLD and consanguinity between parents was reported; this is in agreement with previous research reporting that positive consanguinity was an important risk factor for DLD (**Ahmed *et al.,* 2022**). The asthmatic children with DLD in our study having statistically significant consanguinity between their parents in addition to the family history of previous cases with DLD suggest a strong genetic predisposition independent factor of DLD in the asthmatic children apart from major contributors like hearing impairment and environmental deprivation.

Determination of oxygen saturation by pulse oximetry helps monitor the severity of asthma or wheezing. This was not a factor affecting language acquisition, but it has a predictive value for bronchial asthma.

Hemoglobin level showed a non-significant correlation in this study, which could be explained by the fact that our patients are controlled asthmatic children. This is in contrast to **Hailemaryam *et al.,* (2018)** which showed a significant hematological profile among the asthmatic children. **Elsayed and Essa, (2017)** reported that iron deficiency increases with the severity of asthmatic attacks. Iron insufficiency produces nutritional anemia, which delays language development and results in poor attention span, emotions, IQ, behavior, and sensory perception. The brain is vulnerable to iron depletion, which impacts cognition (**Elalfy *et al.,* 2022**).

Total leukocyte count (TLC) has a significant difference between the 2 groups in our study. **Dihingia and Jahan, (2013)** revealed that there was slight leukocytosis among asthmatic patients compared to the control group. **Hendy and Elawady, (2019)** reported that no significant difference was found in total leukocyte count (TLC).

The current study results revealed a significant difference in platelet counts between both groups, although both were in a normal range. This is in contrast to **Hailemaryam et al., (2018)** which revealed that the mean platelet count was lower in asthmatic children than in the control group, although the difference was insignificant. Other studies reported significantly high thrombocytosis in asthmatic patients (**Kemona-Chetnik *et al.,* 2007**).

Table (4) revealed that the recurrent otitis media diagnosed through history and tympanometry showed significant differences between both groups. Recurrent otitis media occurred in (71.2%) of children with delayed language development compared to (18.2%) of the other group, which is a logical result of the increasing occurrence of conductive hearing loss, which is considered the main cause of DLD.

Childhood asthma with language disorder is multifactorial. Asthma is associated with increased immunologic mediators such as cytokines and IgE (**Barnes, 2001**). These inflammatory cytokines may cross the BBB (**Banks *et al.,* 1995**) and affect behavioral, executive, and emotional neurocircuitry. **Rosenkranz *et al.,* (2005)** reported that (f MRI) shows increased activation of the anterior cingulate cortex (ACC), which is active during everyday speech. The repeated inflammatory insults to neurocircuitry lead to an increased risk of language disorders in children with allergies (**Buske-Kirschbaum *et al.,* 2013**).

Allergic diseases affect the quality of life (**Cummings *et al.,* 2010**). They are accompanied by sleep disturbance and associated with language disorders (**Strom and Silverberg, 2016**). Many studies have reported the adverse neurocognitive outcomes of various chronic diseases of childhood, associated with poor language and verbal performance in children (**Hooper *et al.,* 2011**). It was recently found that children with eczema showed higher contact with therapists, including speech and language therapists (**Strom and Silverberg, 2016**). Children with eczema have multiple risk factors for language disorders, including sleep disturbance (**Dionne *et al.,* 2011**), especially in the first three years of life which are critical for language development.

CONCLUSION

We hypothesized that the asthmatic children had different independent factors as risk factors for delayed language development, such as recurrent otitis media, family history (for both BA and DLD) as well as TLC, PLT, full-scale I.Q, and sleep disturbances. Consequently, it must be necessary to evaluate language age in asthmatic children -especially those showing positive family history and evident sleep disturbances- to accelerate their management if they are found to be affected by DLD.

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CONFLICT OF INTEREST

There are no conflicts of interest.

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