# Cognitive impairment in asthmatic Children in Pediatric Department, Zagazig University Hospitals

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## ABSTRACT

**Background:** Asthma is a heterogenous disease, usually characterized by chronic airway inflammation. The variable expression of asthma symptoms has prompted the shift from the concept that asthma is a single disease to the new concept of asthma as a syndrome.

**Objectives:** this study aimed to evaluate and assess cognitive impairment of children with asthma.

**Subjects and methods:** This was a descriptive cross-sectional study of children with asthma that has been approved from Institutional Review Board (IRB). Assuming that the total number of bronchial asthma patients attending to Pediatric Outpatient Clinic Pulmonology Unit, Pediatric Department, Zagazig University Hospital.

**Results:** With 290 asthmatic children in 6 months and prevalence of low Wechsler Intelligence Scale for Children Third Edition (WISC-R) score was 88%, at CI 95%. So, the total sample size was 104 patients (male 58.7% and female 41.3%) calculated by EPI-INFO 7. There was a statistically significant difference between severity of asthma and IQ (verbal, performance and full IQ).i.e., with increasing severity of asthma there was significant decrease in IQ.

**Conclusion:** Cognitive impairment in affected children is related to asthma severity. Asthmatic children have lower cognitive abilities as regarding general intelligence. Children with chronic asthmatic chest troubles represent a population at possible high risk for cognitive and psychological maladjustment.

**Key words:** Asthma, Cognitive impairment, Pediatric.

## INTRODUCTION

Asthma is a heterogenous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheezes, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airway flow limitation [(1)]. It is one of the commonest chronic diseases worldwide. It has been estimated that over 300 million people have asthma, and its prevalence is increasing in both adult and pediatric population [(2, 3)]. Furthermore, asthma imposes a combined considerable personal and social burden, both in terms of direct costs (like emergent/hospital admissions, increased health service utilization, and medications cost) and indirect costs (such as absenteeism of caregivers and patients from work and premature death) [(4)]. Therefore, it is considered as a major public health problem which deserves paying attention to develop cost-effective prevention and management approaches.

There have been few studies of the epidemiology of asthma in Egypt [(5)]. Zedan and his working group determined the prevalence of bronchial asthma in the Nile Delta region of Egypt. They found that the overall prevalence of childhood asthma was 7.7 % in this region [(6)].

The variable expression of asthma symptoms has prompted the shift from the concept that asthma is a single disease to the new concept of asthma as a syndrome. It is now generally accepted that asthma is an umbrella term for several distinct conditions that share common respiratory symptoms [(6)]. Severity of asthma was assessed as mild intermittent, mild persistent, moderate persistent or severe persistent with a range of severity levels represented as 7%, 61%, 24% and 8%, respectively. A variety of psychological and neurodevelopmental findings have been described in children with persistent asthma, including an increased risk of poor school performance, internalizing disorders, such as anxiety and affective disorders, behavior problems, attention deficits and deficient neurocognitive performance[(7)].

Managing asthma effectively involves three critical components, all of which are necessary to maintain normal pulmonary functioning. These components are: 1) consistent use of prophylactic and therapeutic medications; 2) avoidance of environmental irritants and allergens; and 3) accurate recognition, response, and monitoring of symptoms[(8)].

A common explanation behind the effects of asthma on neurocognitive outcomes relates to the asthma medication itself and specifically the inhaled corticosteroids (ICS) due to the reporting of behavioral disturbances, developmental disabilities and psychosis in children using ICS [(9)]. Other explanations suggested that environmental factors are behind this comorbidity, such as parents' smoking habits, low birth weight and low socioeconomic status that could contribute negatively to the child's health and his cognitive development as well [(10)].





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Preliminary evidence suggests that psychosocial interventions can improve the quality of life and medical outcomes for children with asthma. Interventions that combine education with psychosocial interventions, such as behavioral, cognitive-behavioral, and/or family interventions show particular promise [(11)].

## AIM OF THE WORK

The aim of this study was evaluation and assessment of cognitive impairment in children with asthma.

## SUBJECTS AND METHODS

This was a descriptive cross-sectional study of children with asthma that has been approved from Institutional Review Board (IRB).

Study Setting: Pulmonology Unit, Pediatric Department, Zagazig University Hospital

Sample size: Assuming that total number of bronchial asthma patients attending to pediatric outpatient clinic at Zagazig University Hospitals 290 in 6 months. Prevalence of low Wechsler Intelligence Scale for Children Third Edition (WISC-R) score was 88%, at CI 95%. So, the total sample size was 104 patients calculated by EPI-INFO 7.

**Inclusion criteria:**

Patients aged 5-15 years old with asthma according to GINA classification of asthma that are undergoing routine clinical follow up at Pulmonology Unit, Pediatric Department, Zagazig University.

**Exclusion criteria:**

- Patients with chronic systemic diseases, e.g., heart disease, malignancy, liver disease, and diabetes mellitus.
- Patients with other neurological or psychological disorders.
- Patients with visual and auditory impairments.
- ADHD children.
- Mentally retarded children.
- Autistic spectrum disease (Learning disability).
- Uncooperative patients.

**Ethical and patients' approval:**

**An approval of the study was obtained from Zagazig University academic and ethical committee.** Every patient signed an informed written consent for acceptance of the operation.

**Operational Design:**

**Study methods:**

The selected patients were subjected to the following:

**I. Thorough history taking with particular stress on:**

**II. Clinical examination.**

**III. Dynamic spirometry** was performed for forced vital capacity 'FVC', forced expiratory volume in the 1st second 'FEV1' and FEV1/FVC. They were expressed as percentages predicted for age and sex according to the actual recommendations of both the European Respiratory Society (ERS) and American Thoracic Society (ATS)

**IV. Cognitive function assessment using** Wechsler Intelligence Scale for Children Third Edition

**As detailed below:**

**Verbal IQ:**

This was derived from the scores obtained in the following subtests: information, digit span, vocabulary, arithmetic, comprehension, and similarities. The information subtest was a test of general knowledge, including geography and literature. The digit span subtest required the child to repeat strings of digits recited by the examiner. The vocabulary and arithmetic subtests were general measures of the child's vocabulary and arithmetic skills. The comprehension subtest required the child to solve practical problems and explain the meaning of simple proverbs. The similarities subtest expected the child to describe similarities between pairs of different items of the same category, say apples and oranges, both of which belong to the category of fruits**.**

**Performance IQ:**

This was derived from the scores obtained in the following subtests: picture completion, picture arrangement, block design, object assembly, coding, and mazes. In the picture completion subtest, the child was required to complete pictures with missing elements. The picture arrangement subtest consisted in arranging pictures in such an order as to tell a story**.**

The block design subtest required the child to use blocks for making specific designs. The object assembly subtest expected the child to put together pieces in such a way as to construct an object. In the coding subtest, the child had to make pairs from a series of shapes or numbers. The mazes subtest expected the child to solve progressively more complex maze puzzles**.**

Scores on the performance subtests were based not merely on correct answers but also on the speed of response. Administration Time: The administration time for the test was approximately 60 to 90 minutes. The child was allowed to complete the test in 2 separate sessions**.**

**Interpretation of IQ Score:**

The IQ was graded based on the following guidelines**:**

- 130 and higher: very superior
- 120-129: superior
- 110-119: high average
- 90-109: average
- 80-89: low average
- 70-79: borderline
- 69 and lower: extremely low.

**Statistical analysis:**

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures were coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. According to the type of data; qualitative were represented as number and percentage and quantitative were represent by mean ± SD. The following tests were used to test differences for significance. Difference and association of qualitative variable by Chi square test ($X^2$). Differences between quantitative independent groups by t test or Mann Whitney. P value was set at ≤ 0.05 for significant results & < 0.001 for high significant result.

**RESULT**

Table and figures represent the descriptive statistics on demographic characteristics of studied group. The studied group of patients consisted of 104 patients. They included male (58.7% and female 41.3%). There was a statistically significant difference between severity of asthma and IQ (verbal, performance and full IQ).i.e., with increasing severity of asthma there was significant decrease in IQ.

**Table (1):** Socio-demographic data among the studied group.

| Socio-demographic data | Study group (n=104) |
|---|---|
| **Age/ years**<br>Mean ± SD | 8.40±2.71 |
| **Sex**<br>Male<br>Female | <br>61 (58.7%)<br>43 (41.3%) |
| **Order of sibling**<br>Median (Min-Max) | 2 ( 1-6) |
| **Age of diagnosis**<br>Median (Min-Max) | 3 (1-14) |
| **Family smoking**<br>Positive<br>Negative | <br>77 (74%)<br>27 (26%) |
| **Consanguinity**<br>Positive<br>Negative | <br>46 (44.2%)<br>58 (55.8%) |

Table (1) showed positive family smoking (74%), negative family smoking (26%), positive consanguinity (44.2%) and negative consanguinity (55.8%).

**Table (2):** Asthma characteristics among the studied group.

| Asthma characteristics | Study group (n=104) |
|---|---|
| **Severity of asthma**<br>Mild persistent<br>Moderate persistent<br>Severe persistent | <br>35 (33.7%)<br>40 (38.5%)<br>29 (27.9%) |
| **Duration**<br>Median (Min-Max) | 5 (2-12) |
| **Symptoms/week**<br>Median (Min-Max) | 5 (1-10) |
| **Symptoms/night/month**<br>Median (Min-Max) | 4 (2-12) |

Table (2) showed mild persistent (33.7%), moderate persistent (38.5%) and severe persistent (27.9%).

**Table (3):** Wechsler test among the studied group.

| Wechsler test | Study group (n=104) |
|---|---|
| **VIQ (Mean ± SD)** | **102.19±17.59** |
| Superior | 17 (16.3%) |
| High average | 21 (20.2%) |
| Average | 36 (34.6%) |
| Low average | 19 (18.3%) |
| Borderline | 11 (10.6%) |
| **PIQ (Mean ± SD)** | **78.62±11.94** |
| High average | 1 (1.0%) |
| Average | 22 (21.1%) |
| Low average | 24 (23.1%) |
| Borderline | 57 (54.8%) |
| **FIQ (Mean ± SD)** | **90.08±14.05** |
| Very superior | 2 (1.9%) |
| High average | 7 (6.7%) |
| Average | 46 (44.2%) |
| Low average | 27 (26%) |
| Borderline | 22 (21.2%) |

Table (4) showed the severity of VIQ among the studied group. Superior (16.3%), high average (20.2%), average (34.6%), low average (18.3%) and borderline (10.6%).

**Table (4):** Relation between severity of asthma and Wechsler tests.

| Wechsler test | Severity of asthma | | | P1 | P2 | P3 |
|---|---|---|---|---|---|---|
| | Mild (n=35) | Moderate (n=40) | Severe (n=29) | | | |
| **VIQ** | **113.94 ±14.34** | **105.87±13.37** | **82.93±7.99** | 0.014* | <0.001* | <0.001* |
| Superior | 15 (42.9%) | 2 (5%) | - | <0.001* | <0.001* | <0.001* |
| High average | 6 (17.1%) | 14 (35%) | 1(3.4%) | | | |
| Average | 14 (40%) | 18 (45%) | 4 (13.8%) | | | |
| Low average | - | 6 (15%) | 13 (44.8%) | | | |
| Borderline | - | - | 11 (37.9%) | | | |
| **PIQ** | **85.91±11.95** | **79.17±9.56** | **69.06±7.90** | 0.008* | <0.001* | <0.001* |
| High average | 1 (2.9%) | - | - | 0.006* | 0.011* | <0.001* |
| Average | 16 (45.7%) | 6 (15%) | - | | | |
| Low average | 10 (28.6%) | 11 (27.5%) | 3 (10.3%) | | | |
| Borderline | 8 (22.9%) | 23 (57.5%) | 23 (89.7%) | | | |
| **FIQ** | **101.00±12.12** | **91.95±8.29** | **74.34±6.46** | <0.001* | <0.001* | <0.001* |
| Very superior | 2 (5.7%) | - | - | 0.025* | <0.001* | <0.001* |
| High average | 5 (14.3%) | 2 (5%) | - | | | |
| Average | 23 (65.7%) | 22 (55%) | 1 (3.4%) | | | |
| Low average | 5 (14.3%) | 16 (40%) | 6 (20.7%) | | | |
| Borderline | - | - | 22 (75.9%) | | | |

P1: comparison between mild & moderate, P2: comparison between moderate & sever, P3: comparison between mild & sever.

Table (4) showed that there was a statistically significant difference between severity of asthma and IQ (verbal, performance and full IQ).i.e., with increasing severity of asthma there was significant decrease in IQ. Regarding Verbal IQ (VIQ), lower VIQ score was associated with severe asthma, mean score of VIQ in severe asthma was 82.93 ± 7.99 compared to 105.87 ± 13.37 in moderate asthma and 113.94 ± 14.34 in mild asthma. Borderline grade was more frequent in severe asthma represents 37.9% compared to zero in mild and moderate asthma. Low average was higher in severe asthma and represented 44.8% compared to 15% in moderate asthma and zero in mild asthma. Superior grade was

higher in mild asthma and represented 42.9% compared to 5% in moderate asthma and zero in severe asthma. As regards performance IQ (PIQ), lower PIQ score was associated with severe asthma, mean score of PIQ was 69.06 ± 7.90 compared to 79.17 ± 9.56 in moderate asthma and 85.9 ± 11.95 in mild asthma. Bordeline grade was more frequent in severe asthma and represented 89.7% compared to 57.5% in moderate asthma and 22.9% in mild asthma. Also, low average grade was more frequent in severe asthma than mild and moderate asthma. Regarding Full IQ (FIQ), lower FIQ score was associated with severe asthma. Mean FIQ score in severe asthma was 74.34 ± 6.46 compared to 91.95 ± 8.29 in moderate asthma and 101.100 ± 12.12 in mild asthma.

## DISCUSSION

Asthma has been recognized as a syndrome of overlapping, complex diseases or phenotypes rather than a single disease. It is attributed to deranged inflammatory responses to environmental triggers in genetically predisposed individuals [(12)]. Asthma is a chronic disease with significant health burden and socioeconomic and racial/ethnic disparities related to diagnosis and treatment. Asthma primarily affects the lungs, but can impact brain function through direct and indirect mechanisms. Some studies have suggested that asthma negatively impacts cognition, while others have failed to identify asthma-related cognitive compromise [(13)].

Many systemic pediatric illnesses place children at risk for cognitive deficits that can adversely affect functioning in academic and other performance contexts. Chronic hypoxic conditions as chronic lung diseases were proposed to cause cognitive impairment, which affects the quality of various daily activities [(14)].

In our study we aimed to evaluate and assess the cognitive impairment of children with asthma. The study was cross-sectional study included 104 patients aged 5-15 years old with asthma according to GINA classification. They were undergoing routine clinical follow up at Pulmonology unit, Pediatric Department, Zagazig University Hospital. Cognitive function was assessed using Wechsler Intelligence Scale for Children (WISC-R).

Our study showed a statistically significant difference between severity of asthma and IQ (verbal, performance and full IQ).i.e., with increasing severity of asthma there was significant decrease in IQ. Regarding VIQ, lower VIQ score was associated with severe asthma. Mean score of VIQ in severe asthma was 82.93 ± 7.99 compared to 105.87 ± 13.37 in moderate asthma and 113.94 ± 14.34 in mild asthma. Borderline grade was more frequent in severe asthma and represented 37.9% compared to zero in mild and moderate asthma. Low average was higher in severe asthma and represented 44.8% compared to 15% in moderate asthma and zero in mild asthma. Superior grade was higher in mild asthma and represented 42.9% compared to 5% in moderate asthma and zero in severe asthma.

**Ghaffari *et al.*** [(15)] reported that there was a noticeable difference observed in IQ score in asthmatic children aged 6 and 10 years. Also, **Bratek *et al.*** [(16)] reported that patients with mild to moderate asthma exhibit higher levels of cognitive dysfunction than healthy controls. However, in very mild cases, this phenomenon was statistically not significant. This is also reflected in finding that the severity of airflow obstruction is correlated with the level of all measured neuro-psychological factors, which means deterioration of cognitive functions and become even more severe as the pulmonological disease progresses. **Esmaeel *et al.*** [(17)] reported that 54% of the studied group with asthma had cognitive impairment. This is in line with previous studies, which revealed that asthma was associated with increased risk of cognitive impairment that reached up to 78% even when controlling demographic characteristics, self-rated health status, inhaled corticosteroids and FEV1/forced vital capacity. Also, a study conducted by **Verlato and Oliveri** [(18)] reported that reduced lung function can be considered a predictor of cognitive decline. In addition, another study conducted by **Lutsey *et al.*** [(19)] reported that reduced lung function was associated with modestly increased odds of dementia and mild cognitive impairment.

In our study, there was significant negative correlation between frequency of symptoms and the IQ (VIQ_PIQ_FIQ). This is in agreement with **Tulek *et al.*** [(20)] who found that the frequency of COPD symptoms was inversely associated with cognition and potentially implicating symptoms severity in the development of cognitive impairment. In addition, **Roncero *et al.*** [(21)] noted that frequent respiratory symptoms and exacerbations were associated with cognitive impairment. The systemic inflammation seen in severe COPD and during acute exacerbation may participate in neurocognitive impairment via direct neurotoxic effect by affecting cerebral atherosclerosis.

## CONCLUSION

Cognitive impairment in affected children is related to asthma severity. Asthmatic children have lower cognitive abilities regarding general intelligence. Children with chronic asthmatic chest troubles represent a population at possible high risk for cognitive and psychological maladjustment.

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