

Research Article

Erythrocyte Sedimentation Rate and C-Reactive Protein as Inflammatory Markers in Children with Attention – Deficit Hyperactivity Disorder



Mohamed Farouk Afify¹, Asmaa Khalaf Allah Kamel²,
Walaa Esam Mohamed Fathi¹ and Marwa Waly Eldin Ali¹

¹Department of Pediatrics, Faculty of Medicine, Minia University, El-Minia, Egypt.

²Department of Clinical Pathology, Faculty of Medicine, Minia University, El-Minia, Egypt

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Abstract

Background: Attention deficit–hyperactivity disorder (ADHD) is a common neuropsychiatric disorder affecting children marked by inattention, hyperactivity, and lack of impulse control. Inflammation, a biological state, is characterized by elevated levels of acute-phase proteins, complement factors, cytokine cascades, and cellular immune responses (e.g., ESR and CRP). This study aimed to: Evaluate ESR and CRP as indicators of inflammatory processes in the pathogenesis of ADHD. And To evaluate ESR levels in the prediction of treatment response in children with ADHD. **Methods:** The study was a case-control study conducted at the Pediatric Department and Clinical Pathology Department, Minia University Children and Maternity Hospital, from April 2021 to April 2022. The hospital ethics committee approved this study, and written consent was obtained from each patient's caregiver. **Subjects and methods:** The children included in the study were divided as follows: **Group 1:** 40 children diagnosed with ADHD who had regular follow-up in the Pediatric Neuropsychiatric Outpatient Clinic of Minia University Children's Hospital. Their age ranged from 6 to 18 years. They were further divided into the following subgroups: **Group 1A:** 20 newly diagnosed children with ADHD who had not yet taken any medical treatment for ADHD. They were 90% male, 10% female, with an age range of 6-15 years (Mean \pm SD = 8.15 \pm 2.62). **Group 1B:** 20 previously diagnosed children with ADHD who had been under treatment with non-stimulant ADHD medication for at least 6 months. They were 70% male and 30% female, with an age range of 6-12 years (Mean \pm SD = 8.15 \pm 1.62). **Group 2:** 20 healthy children with matched age and sex to the children in group I. They were 65% male and 35% female, with an age range of 6-12 years (Mean \pm SD= 9.15 \pm 1.59). **Results:** There was a statistically significant difference in 1st hour ESR levels between the un-medicated and medicated ADHD groups compared to the healthy control group (**P values = 0.0001, 0.0001, respectively**). **However**, there was no statistically significant difference in CRP levels between the studied groups (**p value = 0.121**). **Conclusion:** ESR is used as an inflammatory marker in the follow-up of ADHD children.

Keywords; Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), Inflammatory markers, Attention–Deficit Hyperactivity Disorder (ADHD), Children.

Introduction

Attention Deficit Hyperactivity disorder (ADHD) is one of the most common neuropsychiatric conditions affecting children. It is characterized by a lack of

self-control, difficulty focusing, and excessive activity.^[1] ADHD can have a significant negative impact on a child's academic performance, family relationships, and social interactions.^[2] The

estimated prevalence of ADHD in childhood worldwide is approximately 5.3%.^[3]

Inflammation is a complex biological response characterized by an increase in levels of acute phase proteins, complement factors, cytokine cascades, and cellular immune responses. Inflammatory stimuli can induce the production of cytokines, which can readily traverse the blood–brain barrier or be transported into the brain via cytokine-specific transporters.^[4]

Common markers used to assess systemic inflammation include the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels.^[5]

Subjects and Methods

This case control study was conducted at the Pediatric and Clinical Pathology Departments of Minia University Children's Hospital. The study took place between April 2021 and April 2022 and involved 60 children. The hospital's ethics committee approved the study, and a written consent was obtained from each child's caregiver.

Subjects

The children involved in the study were categorized into two main groups:

Group 1: This group consisted of 40 who had been diagnosed with ADHD. These children were selected from a pool of patients who regularly attended follow up visits at the Pediatric Neuropsychiatric Outpatient Clinic of Minia University Children's Hospital. Their age ranged from 6 to 18 years.

This group was further divided into two subgroups:

Group 1A: This subgroup comprised 20 who had recently been diagnosed with ADHD and hadn't yet received any medical treatment for the condition. The majority of these children were male (90%) male, with a few females (10%). Their ages ranged from 6 to 15 years, with a mean age of 8.15 years and a standard deviation of 2.62.

Group 1B: This subgroup included 20 children who had previously been diagnosed with ADHD and were currently

undergoing treatment with non-stimulant ADHD medication for at least six months. The majority of these children were male (70%), with a few females (30%). Their ages ranged from 6 years to 12 years with mean \pm SD = 8.15 \pm 1.62.

Group 2: 20 apparently healthy children, matched in age and sex to group I children. 65% were male, and 35% were female. The age range was 6 to 12 years old, with a mean age of 9.15 years (SD=1.59).

Inclusion criteria

- Children aged 6 – 18 years old.
- Children newly diagnosed with ADHD who hadn't yet received any medical treatment or cognitive behavioral therapy.
- Children previously diagnosed with ADHD children who had been receiving medical treatment and cognitive behavioral therapy for at least 6 months.

Exclusion criteria:

Children having the following diseases or conditions were excluded from the study.

- Children with any other chronic diseases.
- Children suffering from any inflammatory or allergic diseases that could increase, potentially masking the results.
- Children suffering from any another psychiatric or neurological co-morbidity.

Study design

The diagnosis of ADHD requires a clinical evaluation and is done using the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013).

Participants

The children participated in this study underwent the following:

- a. Full medical history: including name age, gender, address, socioeconomic status, and family history of blood diseases.
- b. A full physical examination was performed, including measurement of vital signs (breathing rate, heart rate, blood pressure, and body temperature). The chest, heart, and abdomen were thoroughly examined.
- c. Blood tests for erythrocyte sedimentation rate and C-reactive protein were ordered to assess inflammation.

Results

The results of the study are presented in tables (I-III) and figure (1).

Table (1): Comparison among the studied groups regarding demographic data:

Demographic data	Group 1				Group 2 (Control) (n = 20)		P value
	Group 1A (Un-medicated) (n = 20)		Group 1B (Medicated) (n = 20)		Mean ± SD	Range	
	Mean ± SD	Range	Mean ± SD	Range			
Age (yrs.)	8.15±2.62	6 – 15	8.5 ± 1.67	6 – 12	9.15 ± 1.59	6 - 12	0.290
Sex:							
Male N (%)	18 (90%)		14 (70%)		13 (65%)		0.155
Female N (%)	2 (10%)		6 (30%)		7 (35%)		
Weight(kg)	28.3±7.63	19 – 49	27.6 ± 5.86	19 – 46	30.7 ± 5.18	23 - 41	0.273
Height(cm)	130.±11.5	105 – 153	127. ± 8.09	115 – 151	130.35± 5.33	122- 139	0.399
BMI	16.3±1.83	12.7 - 20.9	16.8 ± 1.61	14.3-20.1	17.0 ± 4.41	0.19-22.1	0.745

The table (I) shows no statistically significant difference among all studied groups as regards demographic data.

Table (II): Comparison between un-medicated and medicated ADHD subgroups regarding clinical data:

Data of disease	Group 1A (Un-medicated) (n = 20)		Group 1B (Medicated) (n = 20)		P-value
	Mean ± SD	Range	Mean ± SD	Range	
Duration of illness (months)	17.9 ± 10.0	8 - 36	26.4 ± 10	12 – 36	0.106
Duration of treatment (months)	-	-	11 ± 6.88	1 – 24	-
Type of treatment:					
Risperidone (%)				10 (50%)	-
Atomoxetine N (%)				10 (50%)	
Family history					0.077
+ve N (%)		5 (25%)		1 (5%)	
-ve N (%)		15(75%)		19 (95%)	

Table II shows no statistically significant difference in the duration of illness between the un-medicated group (mean 17.9 ± 10.0) and the medicated group (mean 26.4 ± 10) (**p value = 0.106**).

Twenty-five percent of un-medicated children had a positive family history for ADHD, while only 5% of medicated children did. Among the medicated group, 50 % were treated with atomoxetine, and the remaining 50% were receiving risperidone.

Table (III): Comparison among the studied groups regarding ESR and CRP:

Laboratory data	Group 1		Group 2 (Control) (n = 20)	P value	
	Group 1A (Un-medicated) (n = 20)	Group 1B (Medicated) (n = 20)			
	Mean ± SD	Mean ± SD	Mean ± SD		
ESR 1h (mmHg) Mean ± SD	21.8 ± 10.2	18.1 ± 7.82	8.05 ± 2.28	<0.0001*	
				1A&1B	0.276
				1A&2	0.001*
1B&2	0.001*				
CRP (mg/l) ●Median ●IQR	1.5 1 – 3	2.5 1 - 10.25	2 1.25 - 4	0.121	

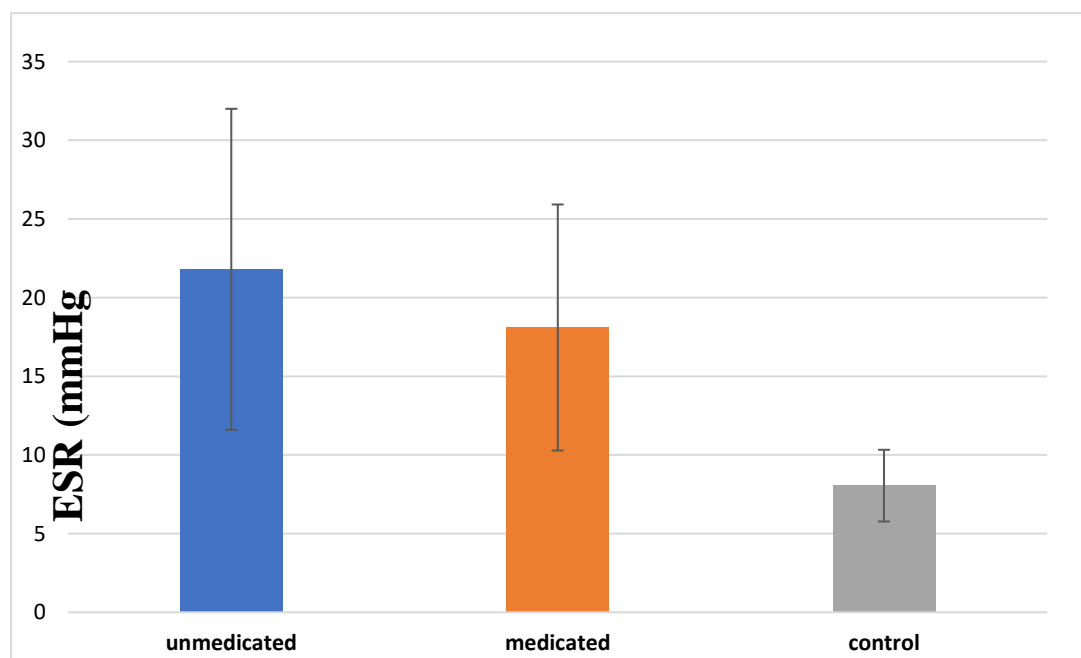


Figure (1): 1st hour ESR level in the studied groups.

Table III and Figure 1 reveal a statistically significant difference in the 1- hour Erythrocyte sedimentation rate (ESR) between the un-medicated and medicated ADHD groups and the control group (**P value = 0.0001**). However, there was no statistically significant difference in C-reactive protein (CRP) levels among the studied groups (**P value = 0.121**).

Discussion

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental condition that can cause emotional and behavioral difficulties. The key symptoms of ADHD, which include trouble paying attention, excessive activity, and impulsive

behavior, often appear in children before the age of 12 and can persist into adulthood.^[6]

Inflammation is a biological response characterized by increased levels of inflammatory markers, such as acute-phase

proteins, complement factors, and cytokines. These inflammatory mediators can directly enter the brain or be transported across the blood-brain barrier through specific transport mechanisms, potentially contributing to neuroinflammation and neurodegenerative diseases..[7]

This study showed that there is a significant increase in the 1st hour ESR (a marker of acute phase reactants that increases in inflammation) in both un-medicated and medicated ADHD groups compared to the control group. This result was supported by study of **Sahu et al.**, who reported that the 1st ESR was significantly high in ADHD group compared to the control group. [8]

Limitations of the study

* Limited Sample Size: The study had a relatively small sample size, which could limit the generalizability of the findings. A larger sample size would have increased the statistical power of the study and provided more robust results.

* Geographical Limitations: The study had been conducted in a specific geographical region, which could limit the generalizability of the findings to other populations. Further research across different geographical regions would be necessary to confirm the observed associations.

* More direct measures of inflammation, such as cytokine levels, would be more informative, accurately reflect the underlying inflammatory processes.

Conclusion and recommendations:

- Further studies on a larger geographical scale and with a larger sample size are needed to emphasize our results.

- We encourage studies supporting the use of anti-inflammatory drugs as an ADHD treatment, depending on the inflammatory basis in the pathogenesis of ADHD.

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