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Research Article

Erythrocyte sedimentation rate and C-reactive protein as inflammatory markers in children with attention –deficit hyperactivity disorder

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Abstract

Background: Attention deficit–hyperactivity disorder (ADHD) is one of the most frequent neuropsychiatric disorders present in children, it is characterized by inattention, hyperactivity and lack of impulse control. Inflammation is a biological condition characterized by increased levels of acute-phase proteins and complement factors, cytokine cascades, and cellular immune responses as ESR and CRP From this study we 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 is a case-control study, carried out at the Pediatric Department and Clinical Pathology Department, Minia University Children and Maternity Hospital, it was conducted on 60 children during the period 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 from children 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**: included 20 newly diagnosed children to had ADHD before taking any medical treatment for ADHD, they were (90% male, 10% female) with an age range (6-15), and (Mean ± SD = 8.15 ± 2.62). **Group 1B**: included 20 previously diagnosed children to have ADHD and they were under treatment with non-stimulant ADHD medication for at least 6 months they were (70% male, 30% female) with an age range (6-12), and (Mean ±SD = 8.15 ± 1.62). **Group 2:** 20 healthy children with matched age and sex to group **I** children. they were (65% male, and 35% female) with an age range (6-12), and (Mean ± SD= 9.15 ± 1.59). **Results**: There was a statistically significant difference as regards (1st hour ESR) in the un-medicated and medicated ADHD groups compared with a healthy control group with **P values (0.0001, 0.0001 respectively),** but there was no statistically significant difference regarding CRP between the studied groups with **p value= (0.121). Conclusion:** ESR is used as an inflammatory marker in follow-up of ADHD children.

Keywords; Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) as inflammatory markers in children with attention–deficit hyperactivity disorder.

Introduction

Attention deficit–hyperactivity disorder (ADHD) is one of the most frequent neuropsychiatric disorders present in children, it is characterized by a lack of impulse control, inattention, and

hyperactivity.[1] ADHD may have a substantial influence on children's school performance, familial relationships, and social interactions.[2] The estimated prevalence of ADHD in childhood worldwide, has been reported to be 5.3%. [3]

Inflammation is a biological condition characterized by increased levels of acute phase proteins and complement factors, cytokine cascades, and cellular immune responses. Inflammatory events induce cytokines, which may directly pass the blood–brain barrier or be carried into the brain via cytokine-specific transporters.[4] The most widely used indicators of the acute phase response are the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels.[5]

Subjects and Methods

The study is a case control study, carried out at the Pediatric Department and Clinical Pathological Department, Minia University Children Hospital. It was conducted on 60 children during the period from (April 2021 to April 2022). The hospital ethics committee approved this study and a written consent was obtained from each patient caregiver.

Subjects

The children included in the study were divided as follows:

Group 1: 40 children, diagnosed as ADHD from children who had regular follow up in the Pediatric Neuropsychiatric Outpatient Clinic of Minia University Children Hospital. Their age ranged from 6 to 18 years.

They were further divided to the following subgroups:

Group 1A: included 20 newly diagnosed children to have ADHD before taking any medical treatment of ADHD, they were (90% male, 10% female) with age range (6-15), and (Mean ± SD = 8.15 ± 2.62).

Group 1B: included 20 previously diagnosed children to have ADHD and they were under treatment with non- stimulant ADHD medication for at least 6 months they were (70% male, 30% female) with age range (6-12), and (Mean ±SD = 8.15 ± 1.62).

Group 2: 20 apparently healthy children with matched age and sex to group **I** children. They were (65% male, 35% female) with age range (6-12), and (Mean ± SD= 9.15 ± 1.59).

Inclusion criteria

- Children age from 6 – 18 years old.
- Children newly diagnosed to have ADHD before taking any ADHD medical treatment or cognitive behavior therapy.
- Children previously diagnosed as ADHD children with at least 6 months duration from starting medical treatment and cognitive behavior therapy.

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 which may cause an increase of the inflammatory markers, masking our results.
- Children suffering from any another psychiatric or neurological co-morbidity.

Study design

The diagnosis of ADHD relies on clinical assessment and it is performed based on diagnostic classification systems, predominantly the Diagnostic and Statistical Manual of Psychiatric Disorders (DSM-5: American Psychiatric Association 2013).

The included children were subjected to the following:

a- Careful history taking including:

Name, age, sex, residence, socioeconomic standard and family history of blood diseases.

b. Full clinical examination: including

1- Vital data: respiratory rate, heart rate, blood pressure, temperature.

2- Systemic examination: full chest, cardiac and abdominal examinations

c-Laboratory investigation: ESR and CRP.

Results

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

Table (1): Comparison among the studied groups regarding the 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 (%)** **Female N (%)**	18 (90%) 2 (10%)		14 (70%) 6 (30%)		13 (65%) 7 (35%		0.155
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) showed 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 ttt (months)	-	-	11 ± 6.88	1 – 24	-
Type of ttt: Risperidone (%) Atomoxetine N (%)	-		10 (50%) 10 (50%)		-
Family history **+ve** N (%) **-ve** N (%)	5 (25%) 15(75%)		1 (5%) 19 (95%)		0.077

The table (II) showed no statistically significant difference regarding the duration of illness in un-medicated group (mean 17.9±10.0) and medicated group with Mean± SD (26.4±10) and **(p value=0.106).**

The family history was positive in 25% of un-medicated children, while in medicated group, family history was positive in 5% only, 50% of the medicated group treated with atomoxetine and the remain medicated children 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	

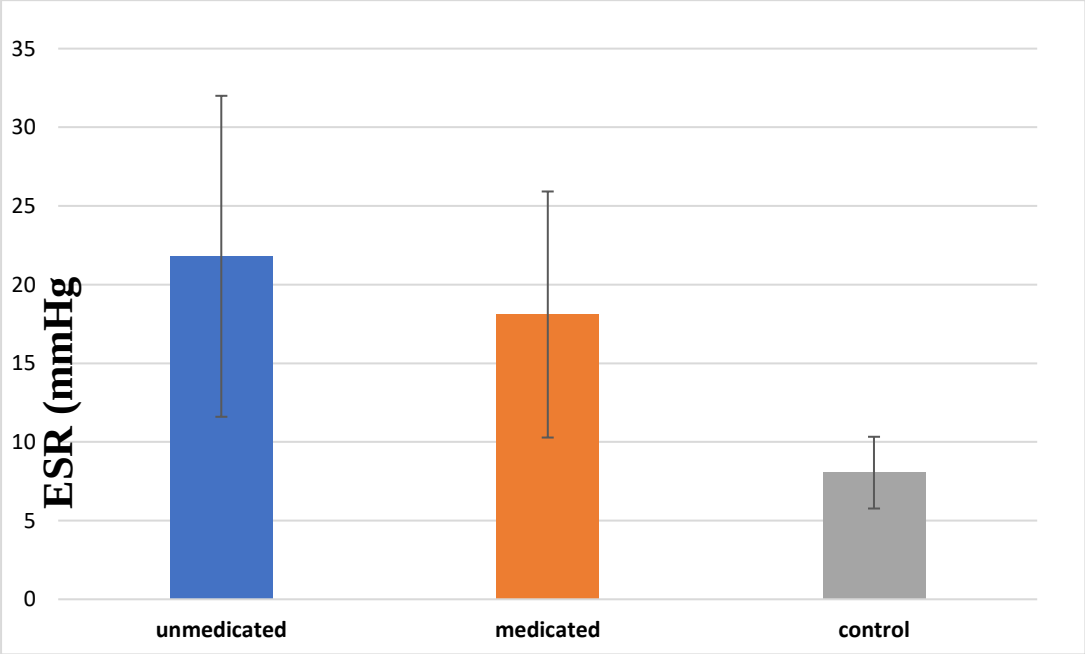

Figure (1): 1st hour ESR level in the studied groups.

Table III and figure 1 showed that there was a statistically significant difference as regard (1st hour ESR) in the un-medicated and medicated ADHD groups compared with control group with **P value= (0.0001-0.0001,** respectively), but there was no statistically significant difference as regard CRP between the studied groups with **P value= (0.121).**

Discussion

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder which cause emotional and behavioral disorders. The three main symptoms of ADHD (inattention, hyperactivity, and impulsiveness) are typically appeared in children before the age of 12 years old and can persist until the child reaches adulthood. [6]

Inflammation is a biological condition characterized by increased levels of acute-phase proteins and complement factors,

cytokine cascades, and cellular immune responses. Inflammatory events induce cytokines, which may directly pass the blood brain barrier or be carried into the brain via cytokine-specific transporters.[7]

This study showed that there is significant higher increase in 1st hour ESR (which is one of acute phase reactant that increases in inflammation) in ADHD un-medicated and medicated groups than 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]

Conclusion and recommendation:

- Further studies on large geographical scale and on larger sample size to emphasize our results.
- Encourage the studies supporting the use of anti -inflammatory drugs as ADHD treatment depending on the inflammatory basis in pathogenesis of ADHD.

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