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Evaluation of Salivary Insulin Like Growth Factor 1 on Gingival Health Condition of Children with Attention Deficit and Hyperactivity Disorder

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Abstract

Background: hyperactivity disorder is one of the most public neurodevelopmental conditions in juvenile. Insulin-like growth factor 1 define as a polypeptide hormone basically resembling to insulin. It is signing is an important element to the early development of the brain. And its axis plays a significant role in oral tissue regeneration such as gingiva.

Objective: The aim of this study to evaluate the salivary levels of insulin like growth factor 1 and gingival health among children with Attention deficit/hyperactivity- disorder.

Material & method: this is a cross-sectional comparative study included 500 student aged 11-13 years in the primary school of AL-Shamiya sector in Al-Diwaniya. The questioner of the disorder was introduced into student's parent to fill the checklist. The spitting method was used for the collection of Unstimulated saliva, then laboratory analysis was done using ELIZA test. The data was collected, summarized and statistically analyzed. WHO CPI probe was used to assess the bleeding condition using the gingival index of WHO 2013.

Result: the result of current study shows that salivary insulin like growth factor 1 level was less significantly among the student with disorder, while the bleeding index was not significantly higher them as no significant relation correlation was found between salivary insulin like growth factor 1 and gingival in positive direction.

Conclusion: This study around the correlation of insulin like growth factor 1 with Attention-deficit/hyperactivity disorder. Insulin like growth factor 1 level was more in control than study group.

Introduction:

Attention deficit/hyperactivity disorder (ADHD) known as the common public behavioral complaint and the second most communal chronic complaint in childhood , and categorized by a mixture of stage unsuitable points of inattention, impulsive behavior and hyperactivity [1]Many children identified with ADHD having difficulties associated to education , communal functioning , and/or other mental disorder as adolescents and young adults[2]. Evidence suggests that there is no single factor that determines the expression of ADHD[3]. ADHD have three subtypes: hyperactive, inattentive, and a combined type characterized by a mixture of them [4].About (60% - 80%) of this symptoms keep on into adulthood[5] . ADHD symptoms may seem unexpectedly after a traumatic brain injury [6] .The complaint is diagnosed in children commonly, and about 70% of childhood cases or symptoms persist into adulthood [7] .ADHD have a multiple etiologies like genetic , neurological, and environmental factors may donate to its heterogeneous phenotype and pathogenesis [8] . Influences of hormonal on the behavior organization are obvious to neuro endocrinologists ,but it's still under-examination in relation to mental disorders in children and adolescent [9] .The insulin-like growth factor (IGF) system consist from three receptors (the insulin receptor [IR], the IGF-I receptor [IGF-IR], and the mannose phosphate IGF-II receptor [M6P/IGF-IIR]), three ligands (insulin, IGF-I, and IGF-II), and six IGF-binding proteins (IGFBP) [10] .These factors play critical roles in proliferation, differentiation, and function of the cells[11] .Insulin-like growth factor 1 (IGF1) is a polypeptide hormone related to insulin structurally. It is significant to the somatotropic axis, act as growth hormone (GH) downstream ,plasma levels of IGF 1 usually reveal the status of growth hormone of the individual, so it's low in GH deficiency and high in acromegaly [12] . At this time IGF1 signaling consider an essential factor for initial development of the brain [13] . IGF-1 levels is lower in ADHD Children matched with the control group[14] .The IGF axis have an significant part in the regeneration of dental tissue and most apparatuses of this axis are conveyed in dental pulp cells (DPCs) [15] .This axis also play a role in the progenitor cells differentiation into dental mineralized tissue[16],being linked with the initiation of enamel bio-mineralization[17] ,the dental pulp cells differentiation (DPCs) [18] ,and dentinogenesis reparative [19] . IGF-I and its receptors in periodontal tissues modifies the immune reaction by immunoglobulin synthesis ,inducing growth of B cell, and interleukin-6 production during inflammation [20] . The children with ADHD have a poor oral hygiene attitudes and oral health status ,and higher plaque indices than individual without ADHD[21] . the prevalence of gingivitis and caries increases in teenagers suffering from ADHD than in those without the disorder[22]. ADHD children have difficulties with over activity, staying focused communication, and impulsivity. These behaviors can make performance of oral health practices such as brushing of tooth problematic and dental examination challenging, leading to incorrect oral hygiene [23,24]. Drugs castoff in the treatment of ADHD have been described to be related with the enlargement of gingiva [25] , bruxism and xerostomia [26] . Bimstein et al. (2008) reported that Individuals with ADHD showed higher parents reporting prevalence of bruxism ,tooth pain, oral trauma , and bleeding gums [23] .

As there is no previous Iraqi study about the relation of ADHD, IGF1 and gingival health condition, so this study was conducted.

Material and Method:

This study is across sectional comparative study. It was conducted among 500 students of both gender in primary schools of AL-Shamiya sector- Al_diwania _Iraq. The practical part of the study started from mid-December2022 until the end of April 2023. The University of Baghdad, College of Dentistry ,the ethical approval committee approved this study (project no.685322). A legal permission from Al-Diwaniya Education Directorate was

obtained Prior to the data gathering, to carry out the study and to ensure cooperation of their teachers and staff. The parents of every child were informed of the design, aims, and possible benefits of the study as well as their right to quit whenever they desire, They signed an informed consent form before their contribution[27] ,in which the study sample (composed of students with ADHD aged 12 years) that was calculated according to last birthday[21]compared with group composed of students free from ADHD matching in age.

The Vanderbilt ADHD Rating Scales(NICHQ) were used to assess ADHD. which was specific scale designed to diagnostic the ADHD affected people and consisted of (18) items the first nine items (1-9) used for the inattentive symptoms of ADHD, the second nine items (10-18) used for the hyperactive symptoms while the whole 18 items used for the combined type (hyperactive, inattentive). Each item has four responses (never ,occasionally, often , very often).Questioners are given to student´s parents and asked to notice their behavior precisely before chose the score that represent the behavior of the child in each item .A group of experts (psychiatrists and psychologists) in the Department of Psychological Research at Baghdad University were responsible for the assessment of the reliability and validity. After collecting the answer from the student ,the data was analyzed and categorized into an inattentive type which consist from 6 positive response(often ,very often) into 1_9 item and hyperactive type which have 6 positive response into 10-18 and combined type is combination of both. The collection of unstimulated saliva from the primary school students was done by spiting passively to graduated collecting disposable tube until 3ml was filled. According to guidelines for saliva collection [28] , Between 11:00 AM and 1:00 PM was the time of saliva collection to reduce any circadian rhythm effects. Instruction was given to them not to drink or eat, and chewing gum at least for 1 hour before the collection [29]. They instruct to clean out their mouth by deionized or distilled water numerous time then keep quiet during saliva collection[30]. .The salivary samples were stored in a cooler box[31,32] .Then they were centrifuged for twenty minute at 1000 r.p.m.(revolution per minute), particulates were removed and samples were stored at -20℃ according to manufacture recommendation[33]. IGF1was measured by using Eliza kit (China) by using Enzyme linked-immuno-sorbent Assay.

The oral examinations were done in rooms that were available in host school ,the subjects were seated on chairs with tall back[34]. The gingival state of the children were scored according to the criteria of WHO 2013 by passing WHO CPI probe between the gingiva and the tooth to assess the bleeding reaction [35] .The sensing force was be no more than 20 gram.

The score was:
0=no bleeding
1=occurrence of the bleeding
9=tooth excluded(not recorded).
X=tooth not present.

Statistical analysis accomplished by SPSS version 26 . the descriptive analysis was used to calculate the means, standard deviations (SD) of IGF1 concentration in saliva and gingival bleeding condition. Pearson's correlation to discover the inter-relationships. $P \leq 0.05$ was considered significant.

Result:

The frequency distribution of ADHD group and control group according to gender was shown in table (1). ADHD students included 59 (71.95 %) boys and 23 (28.04%) girls, whereas, control group included 153 (42.14 %) boys and 210 (57.85%) girls .

The comparison of the mean of the CPI score between ADHD group and control group has been carried out, and the results were demonstrated in Table (2). The results clarifies that the mean of sites with bleeding were significantly more in ADHD group (9.72 ± 4.540) than control group (5.49 ± 3.788).:

Table (3) illustrate that the concentration of IGF 1 in saliva .Mean levels of IGF

were 11.67 ± 4.15 and 13.45 ± 3.10, in study and control groups respectively; the mean level was significant lower in study group in comparison with healthy control ($P< 0.05$).

The correlations between salivary IGF-1 and CPI score in study group and control group were shown in Tables (4). The present results show non-significant positive correlation in ADHD group, but in control group, the present results found non-significant negative relation.

Discussion:

This is the first Iraqi study to observe the link of salivary IGF1 with gingival health condition of ADHD children. This study illustrates that gingival index was higher in the ADHD group than control group and the result was significant, the degree of inflammation appear to be more in ADHD than non ADHD group, this may be related to many factor :

* poorer oral health status in ADHD group [36,37].

*Also have Poor oral hygiene attitudes [38] .

*Higher plaque indices [39,40] recorded in ADHD than those without ADHD

* tooth brushing is Less effective due to difficulties to stay focused and their little attention period [36] .Also they have difficulties with performing numerous motor skills [41] .The finding of this study regarding gingival inflammation agree with previous findings [42,43,44,45] but these studies investigate children that may take medication and one of medication used for treating ADHD which is amphetamine showed to raise the risk of gingival enlargement[46] . Bimstein et al. (2008) reported that Individuals with ADHD showed higher parents reporting prevalence of bleeding gums and toothache [47].

This study show that the IGF1 level was significant lower in study group in comparison with healthy control. This result was similar to previous study[48] .An earlier revision has showed that pre-pubertal children with ADHD had regular serum IGFBP-3 and IGF-I [49]. A previous cohort study showed that brain development and intelligence quotient in childhood was associated with IGF-I [50]. Wang 2022 found that that IGF-1 is not only important for muscle and bone growth, but also for the neuropsychological and neurodevelopment purpose[48].

The present results show a non-significant positive correlation between gingivitis and IGF1 in study group. This result agree with study done by (Almalki)which found that lowest IGF level was in the healthy group and highest in the group with the highest CAL[51]. Higher IGF-1 levels in acromegalic patients increase the severity of periodontal disease [52].

These results differ from other that stated the periodontitis group had the lowest levels of IGF-1 [53].

IGF-1 is reflected as a mediator key in the curing of wound and proliferation of mesenchymal cell [54]. Raja et al in (2009) stated that IGF-1 improved cell survival in PDL fibroblasts via down-regulating pro-apoptotic molecule and up-regulating anti-apoptotic molecules [55] . The local and controlled release of IGF-1 from the glucan co-gelatin microspheres can increase periodontal regeneration [56,57,58].

IGF1 has a significant role in alveolar bone remodeling[59]. The manifestation of IGF-I and its receptor in periodontal tissues helps control the immune response by prompting a development of B-cell, formation of immunoglobulin, and production of interleukin-6 during inflammation of periodontal tissues [60].

Conclusion:

This study shows that the IGF1 level is lower in study group than control group and bleeding on probing have a positive correlation with IGF1 level in saliva but the study of the relation need more interest and larger sample size.

Funding:

This research was self-funded.

Conflicts of interest:

The authors claim to have no conflicting interests.

Table (1) Demographic features of the student with ADHD and healthy control subjects:

Characteristic	Study	control
Gender		
Boy, n (%)	59 (71.95 %)	153(42.14 %)
Girl, n (%)	23 (28.04%)	210 (57.85%)

n: number of cases

Table (2) Gingival health condition among ADHD and control group

CPI Component	ADHD group	Control group	Statics	
			T test	P value
Score 0				
Mean± SD	17.95 ± 4.490	22.45 ± 3.816	1.237	0.268
Score 1				
Mean± SD	9.72 ± 4.540	5.49 ± 3.788	1.528	0.218

SD: standard deviation; *: significant at P<0.05

Table(3) salivary Insulin like growth factor1 level (mean ±SD) among study and control group:

Insulin-like growth factor-1 level(nmol/l)	ADHD group	Control group	Statics	
			T test	P value
Mean± SD	11.67 ± 4.15	13.45 ± 3.10	1.273	0.031*

SD: standard deviation; *: significant at P< 0.05

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Table (4) The relation between salivary Insulin like growth factor1 and gingival health condition in the study and control group:

CPI score	ADHD group		Control group	
	r	P	r	P
Score 1	0.177	0.267	-0.050	0.754
Score 0	-0.192	0.229	0.039	0.810

r: correlation coefficient; *: significant at P< 0.05

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