

Clinical Study of Chronic Fatigue Syndrome among Iraqi Patients

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Abstract

Fifty-three CFS patients were enrolled in this study to clarify the main clinical features which shed light on this syndrome and how to discriminate between it and other disorders. Several parameters had been investigated and the results were compared with 35 apparently healthy control volunteers group. The current results revealed that there was highly significant difference between CFS in comparison with control group in main clinical symptoms particularly impaired concentration or temporary loss of memory, headache & generalized fatigue of new types in addition to, unrefreshing sleep and muscle pain ($P = <0.001$). The present results showed that CFS incidence was higher among females than males who are at age group (20-40) years. Furthermore, majority of CFS patients were over-weight (i.e. BMI =25.9 Kg/m²). Women showed higher severity of symptoms than men, particularly obese ones. Finally, it could be concluded that the neuropathy (i.e. cognition) is the main distinct symptom beside unrefreshing sleep made the stock of parameters that differentiate CFS from healthy individuals.

Keywords: CFS; BHI; Cognition

دراسة سريرية لمتلازمة التعب المزمن بين المرضى العراقيين

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المخلص

أدرج 53 مريض اسمائهم في هذه الدراسة الذين يعانون من تزامن اعراض التعب المزمن لغرض توضيح الملامح او ان اعراض السريرية الرئيسية التي تلقي الضوء على تزامن الاعراض وكيفية الترميز مابين مرضى التزامن والاعتلالات الجسدية الاخرى . وتم بحث (ستقصاء) عدة معايير ومقارنة النتائج مع مجموعة مؤلفة من 35 متطوعاً كان من الواضح عليهم انهم يتمتعون بصحة جيدة. وأظهرت النتائج الحالية أن هناك فرق ذو أهمية كبيرة بين الذين يعانون من اعراض التعب المزمن بين مجموعة التحقق من صحة نتائج الاختبارات الاخرى في الاعراض السريرية الرئيسية خصوصاً التركيز الضعيف أو فقدان مؤقت للذاكرة وصداع وتعب استقراءي لانواع جديدة فضلاً عن النوم الذي لايجدد القوة وآلام في العضلات ($p=0.001$).

وأوضحت النتائج الحالية بأن تزامن اعراض التعب المزمن كان اعلى في الاناث مما عليها الحال في الرجال الذين هم في المجموعة العمرية ما بين (20 – 40) سنة. فضلاً عن ذلك فإن معظم مرضى التعب المزمن في اوزان اكثر من المطلوب (بعبارة اخرى $BMI=25.9 \text{ Kg/m}^2$) وكان هناك درجة عالية في الاعراض بين النساء أكثر مما هو عليه الحال في الرجال خصوصاً البدنيات منهن . واخيراً فإنه يمكن الاستنتاج بأن العصابة (المرض العصبي) بعبارة أخرى المعرفة الادراك هي الأعراض الرئيسية الواضحة المعالم فضلاً عن النوم الذي لايجدد القوة والذي جعل مجموعة المعايير ترسم الفرق ما بين الاشخاص الذين يعانون من تزامن اعراض التعب المزمن والاشخاص الأصحاء .

1. Introduction

Chronic fatigue syndrome (CFS) is a multisystem condition of unknown cause that affects mostly young adults, with ages ranging between 20 and 40 years. It was reported that the male to female ratio is 1:4 in some series [1, 2]. The estimated prevalence was to be between 0.2% and 2.6% of the general population [3, 4]. Chronic fatigue syndrome should be suspected in patients with signs and symptoms of an unexplained fatigue that have persisted for at least 6 months and did not improve with rest. It was noticed that the fatigue should be accompanied by 4 or more of the following symptoms: impaired short-term memory and concentration, odynophagia, tender cervical or axillary lymph nodes, muscle pain, arthralgia with no signs of inflammation, headache of a new kind, with different characteristics or severity, unrefreshing sleep, and exhaustion lasting more than 24h after exercise. All these symptoms should be indicative of a serious functional disorder, as proposed by the international diagnostic criteria established by the Centers for Disease Control (CDC) in Atlanta, Georgia, in 1994 [5]. In 2003, a new case definition for CFS was proposed with the intention of excluding psychiatric cases, as was put forward in the Canadian consensus document on CFS [6]. The Canadian criteria are useful and complementary to the CDC criteria, and enable us to study the symptoms in clusters (neurological, muscle, cognitive, neuro-vegetative and immunological).

In 2011, these criteria were updated, and post exertional exhaustion was proposed as a hallmark of the disease [7]. Chronic fatigue syndrome is associated with different comorbid phenomena [8, 9], that are obviously noticed among CFS patients than non-CFS individuals [10]. Studies referred to predominant of CFS females rather than males. Hence there are few studies on the profile of men with CFS. The differences between men and women in terms of health are partly determined by biological differences that, in addition to reproductive functions, involve genetic, hormonal and neurometabolic factors. The objective of this study was to evaluate the clinical characteristics of CFS patients with different BMI and compare them healthy volunteers in order to determine whether there is an effects of gender differences, BMI on the clinical symptoms

among patients with CFS and, thus, to establish a differential clinical profile, with implications involving the prognosis and therapeutic management.

2. Materials & Methods

During the period between June / 2016-September/2016; 53 CFS cases were diagnosed according to the criteria of the Centers for Disease Control and Prevention (CDC) CFS criteria. Those cases for patients who attending the Medical City teaching Hospitals. All the patients underwent many investigations and their results were compared with those for 35 apparently healthy control groups. Those investigations included liver function tests, Thyroid function tests, kidney function test & lipid profile investigations. Furthermore, a questionnaire was applied for each subject enrolled in the study, which included patients' names, gender, medical history, clinical features, body weight, and his (her) length and other parameters.

3. Results

3.1. Demographical picture of the studied subjects

Table 4. 1 revealed the demographic picture of the studied subjects. This table represented that there was no significant difference between the mean of age for studying subjects [45.63 ± 2.071 & 40.96 ± 1.875 years for healthy control (HC), and chronic Fatigue Syndrome (CFS) groups, respectively] (P value = 0.184), as well as the ratio of females to males among those groups [1.92 , 2.2 and 1.28 for healthy control, RA and CFS respectively] ($P = 0.911$). However, there was a significant difference in the mean age of disease onset [35.05 ± 1.859 , 40.10 ± 0.875 years for RA and CFS respectively] ($P < 0.05$).

Table 1: Demographical picture of the studied groups

Parameters	The studied Groups		P values
	HC	CFS	
Gender No. (%) :			
Male	12 (34.3)	19(35.8)	Chi-Square P= 0.0911 (NS) (P>0.05)
Female	23 (65.7)	34(64.2)	
Total	35 (100)	53 (100)	
Female /Male Ratio	1.92	1.79	
Mean of Age (years) \pm SE	45.63 ± 2.071	40.96 ± 1.875	ANOVA & LSD P=0.184 (NS)

Mean of Age Onset (years) \pm SE	-	40.10 \pm 0.875	Chi Square P=0.001 (HS)
Family History No. (%)	-	4 (7.55)	Chi-square P =0.001 (HS)
BMI (Kg/ m ²) [Mean \pm SD]	26.539 \pm 2.025	25.957 \pm 4.798	ANOVA P=0.067 (NS)
Total No.	35	53	

3.2. Effect of age on the incidence of CFS

In Table 2 the distribution of the studied groups according to the age groups. It seems that there is no significant difference in the frequency of individuals among each age group (P value =0.518). In spite of that, it's clear from this table that the high frequencies were observed among the age group of 20-40 years [46.9% of CFS] in comparison with (37.1) % of the healthy control group. About half the CFS patients were in the age group 20-40 years, which was the highest in comparison with the same patients of the other age groups.

Table2: Distribution of the studied groups according to the age groups.

Age groups / Year		Studied groups		Pearson Chi-Square (P-value)
		Healthy Control	Patients (CFS)	
20 – 40	N	13	26	P=0.518 Non sign. (P>0.05)
	%	37.1%	49.1%	
41 – 60	N	18	21	
	%	51.4%	39.6%	
> 60	N	4	6	
	%	11.4%	11.3%	
Total	N	35	53	
	%	100.0%	100.0%	

3.3. Frequencies of different clinical features among CFS cases

Studying the incidence of the main clinical features, among CFS patients reveal that headache, temporary loss of memory and generalized fatigue were manifested in 100% of CFS patients while unrefreshing sleeping and muscle pain were observed in 98.1% of patients. However, tender lymph nodes were recorded in lower frequency (84.9%)

Table 3: Distribution of the studied groups according to the Clinical feature

	Clinical features	HC	CFS	P value
1.	Unrefreshing Sleep	-	52 (98.1)%	< 0.01 HS
2.	Muscle pain	1	44 (83.1)%	< 0.01 HS
3.	Sore throat	1	40 (75.5%)	< 0.01 HS
4.	Pain in the joints without swelling or redness	2	39 (73.6%)	< 0.01 HS
5.	Headache	3	53 (100%)	< 0.01 HS
6.	Tender lymph node	-	30 (56.6%)	< 0.01 HS
7.	Impaired concentration or temporary loss of memory	-	53 (100%)	< 0.01 HS
8.	Generalized fatigue	-	53 (100%)	< 0.01 HS

3.4. Correlation between clinical features and gender

Considering the effect of gender on the development of the clinical feature, Table 4 revealed that the severity of clinical features were more prominent among females rather than males such as unrefreshing sleep, sore throat, joint pain, headache temporary loss of memory and generalized fatigue which appeared in 100.0% of females while only headache, impaired concentration and generalized fatigue were seem to be all males suffering from (i.e. 100.0%). Obviously, from this table there were highly significant differences in the frequencies of muscle pain, sore throat, and joint pain between females and males [97.1 %, 100.0% and 100.0% Vs. 57.9%, 31.6 and 26.3% for those symptoms respectively].

Table 4: Distribution of the clinical features according to the gender

	Clinical features	Males	Females	P value
1.	Unrefreshing Sleep	18 (94.7%)	34 (100.0)%	>0.05NS
1.	Muscle pain	11(57.9%)	33 (97.1)%	< 0.03 HS
2.	Sore throat	6 (31.6%)	34 (100.0%)	< 0.01 HS
3.	Pain in the joints without swelling or redness	5 (26.3%)	34 (100.0%)	< 0.01 HS
4.	Headache	19 (100.0%)	34 (100%)	>0.05 NS
5.	Tender lymph node	11(57.9%)	19 (55.9%)	>0.05 NS
6.	Impaired concentration or temporary loss of memory	19 (100.0%)	34 (100%)	>0.05 NS
7.	Generalized fatigue	19 (100.0%)	34 (100%)	>0.05 NS

3.5. Relationship between Clinical Features and BMI

Effect of BMI on the development of CFS and progression of its clinical features were shown in Table 5. This table revealed that most obese and over weighed CFS patients were suffering from unrefreshing crush sleeping, joint pain, headache, impaired concentration and generalized fatigue (100% for each). Meanwhile, the lean or normal body weighed patients were less complaining from these symptoms (95.2%, 66.7%, 33.3% for unrefreshing sleeping, muscle

pain and joint pain respectively. However, the other clinical features were occurred in similar percentage (i.e. 100.0% for headache, impaired concentration and generalized fatigue).

Table 5: Distribution of the clinical features among different BMI groups

Clinical features	BMI (Kg/ m ²)		
	Normal (18 - 24.9)	Over-weight (25 - 29.9)	Obese (> 30)
1) Unrefresh Sleep	20 (95.2%)	23 (100.0%)	9 (100%)
2) Muscle pain	14(66.7%)	23 (100.0%)	7(77.8%)
3) Sore throat	13 (61.9%)	22 (95.7%)	5 (55.6%)
4) Pain in the joints without swelling or redness	7 (33.3%)	23 (100.0%)	9 (100%)
5) Headache	21 (100.0%)	23 (100%)	9 (100%)
6) Tender lymph node	4 (19.1%)	19 (82.6%)	7(77.8%)
7) Impaired concentration or temporary loss of memory	21 (100.0%)	23(100%)	9 (100%)
8) Generalized fatigue	21 (100.0%)	23 (100%)	9 (100%)
Total	21(100.0%)	23(100.0%)	9(100.0%)

3. Discussion

The current results indicated to spread of CFS among many Iraqi population's samples. Obviously, the incidence with CFS was more than what estimated in this study. Researchers have declared to the role of pathogenic agent as a causative etiological agent for CFS. However, the recent studies reckoned genetic factors, perhaps, may play a crucial role in CFS development. The results of the present study reckoned 40.10 years as a mean of age of patients. Institute of Medicine of the National Academy reported that the average age of onset is 33, although ME/CFS has been reported in patients younger than age 10 and older than age 70 [11] According to Ashley Welch (2015) report which reviewed by Robert Jasmer, that the average of age for CFS patients is 33 years [12]. While, Jason *et al.* (2009) in their review pointed to the age over 38 years as a predictive age for CFS [13]. Although, older age (< 65 years) is a greater risk than the younger for disease development [13, 12]. The present findings were in concomitant with those above observations.

Moreover, an investigation [14] referred to two age peaks in the incidence of CFS/ME that was noticed among the Norwegian population; often at 10-19 years and 30-39 years. Nevertheless, these data were previously reported [15]. The current findings revealed a higher mean of age of disease onset 40.10 ± 0.875 which may be agreed with that fact that there are two peaks in age of disease onset results in raising the mean of CFS patients' ages of onset and subsequently the mean of their ages. On the other hand, this mean is lower than that of another study which revealed that the mean age is 46.4 years. This fact is in harmony with the findings of many autoimmune diseases in which the average of Iraqi patients age is lower than that for abroad. Now days, it is well accepted and became well known that the environmental conditions in Iraq play a significant role in the initiation and early development of autoimmune diseases

Regarding the gender, the results of this study revealed that most CFS patients were females (64.2%) as well as a disease control group (RA) with no significant difference between them. These findings were pointed to by many researches which related to the hormonal differences between males and females, which enhance the activation of T_H2 cells that participate in the development of the disease [16]. The strong female preponderance and the two age peaks suggest that sex- and age-specific factors may modulate the risk of CFS/ME. Yet, the current female to male ration was lower than that estimated by the others [17, 18]. The explanation for this variation may be attributed to the low sample size of the present investigation with long duration of the previous study (between 2008 up to 2012). There are clinical phenomena in CFS that are also observed in other immune inflammatory diseases that are more prevalent in women (systemic lupus erythematosus, multiple sclerosis, rheumatoid arthritis, Sjögren's syndrome and irritable bowel syndrome) [19], with improvement in the symptoms during pregnancy and worsening during menstruation and childbirth. For all the above, it is logical to hypothesize that CFS will affect more women than men, although, at the present time, the clinical phenotype that differentiates men from women has not been defined.

Obesity may stand behind developing many diseases and the possibility of its role in CFS development was considered. The effect of obesity on the clinical symptoms was examined in the current study.

On the contrary, Schur *et al.* (2006) and then in (2011) [19, 20] declared that: "In CFS patients, the prevalence of obesity was low despite risk factors for weight gain. Fatigue severity and BMI were unrelated in women with CFS, but this relationship may differ for men". This latter evidence may interpret the low variations between the studied groups besides the low frequency of obese individuals.

The demographic picture of the studied patients revealed that the majority of CFS patients were either over-weight or obese. Studies have denoted that obesity enhances the development of many diseases. However; other studies stated that there were no significant differences in mean of BMI between CFS and control group [21, 22]. The description of CFS among children was studied too [23]. At the present time, the most widely accepted hypothesis for the pathogenesis of CFS characterizes it as a genetic-based process, with different triggering factors and subsequent neuroimmunological and immunoinflammatory dysfunction, which would produce the different symptoms observed in patients [24, 27]. Till now there is no single or specific test for diagnosis of CFS and the previous attempts were to identify the criteria for its diagnosis which based on a physical picture of CFS.

From clinical view the unrefreshing sleep, headache, temporary loss of memory, and generalized fatigue were the main clinical symptoms that showed by Iraqi CFS patients with female predominance particularly obese ones. These finding in agreement with the results of the previous mentioned studies [28, 30]. Yet, it is still the need for a system of database for analysis of these findings or CFS subtyping in order to be able to give a right decision about this disease since many scientists tried and continue to draw a real picture about the final identification of this disease [28,33].

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