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Association of IL6,IL18 and FH-125 in treatment resistant among patients with schizophrenia

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Abstract

Background:

Schizophrenia is mental illness described by atypical behavior and a reduced ability to understanding truth. Symptom include false beliefs, confused thinking unclear or, hearing voice and other People do not, reduced emotional expression, social engagement and lack of motivation. Schizophrenia patient often have other mental health problems like depressive, anxiety, or substance-use disorders.

Methods:

During the period from January 2019 to May 2019, a total of 37 patients with TRS and 37 control without autoimmune disease non-pregnant were included in this study. All these parsons were attending the AL Hakeem General hospital, their ages grouped from (18-70) years. Male to Female ratio 1/1. Erythrocyte Sedimentation Rate (ESR), White Blood Cell Count to prove all participants in this study free from infectious disease for exclusion criteria. IL6, IL18 and FH-125 in serum samples were measured by (ELISA).

Results:

The result obtained from the study groups recorded people: 44(59.46%) female and 30 (40.54%) male, the ratio of male to female was 1:1 their age ranged from (15-50) years and mean age (33.15) years indicated that there were no significant differences $p > 0.05$ (0.95) in patients with TRS compared with control group according to age. demonstrated the level of IL6 in TRS and control group. There was significant deference ($P<0.05$) in serum levels of Interlaken 6 in patients with TRS compared with control group

Conclusion:

1- There was a statically significant correlation between IL-6 and TRS.
2- Elevated serum levels of IL-18 in serum of patients with TRS ware compared with control.
3- Complement F-H125 elevated in serum of patient with TRS was compared with controls.
4- No significant correlation between biomarkers in TRS patient and socio-demographic profile such as (gender, age, residence, occupation, Weight).

Keyword: *IL6, IL18 , FH-125, treatment resistant, schizophrenia*

Introduction:

The treatment-resistant Schizophrenia indicates Schizophrenia patient, who although at least 2 acceptable trials of classical medications, has insistence severe to moderate positive symptoms, or negative symptoms or disorganization, jointly with labor function over a prolonged phase of period and poor social. This definition

reflectes the point of view of people with disease, their mental health care supporters and family members [1].

TRS is the purpose of strong interest for the reason of modern progresses in its etiology and treatment. The definition of TRS is, though, still contentious. It should reproduce varied needs and the legitimate and viewpoints of Schizophrenia peoples; mental health care givers, their family members, public health officials, mental health managers, and those who supply the indirect and direct prices of treatment Schizophrenia [2]

Through the primary period after the identification of schizophrenia has been made, physician should be especially ready in diagnosis the patient as TRS in order to weaken the acute social suicidality and disability which might result if it is no recognized and acceptably treated. presently, TRS is frequently stable. Conversely, some TRS patients may return to develop reactivation to drug or undergo natural decrease of positive symptom in future life [3]

The association between TRS and treatment responsive Schizophrenia is not accurately white and black. No specific psychological path of Schizophrenia specially proposes TRS [3]

Projected that TRS is considered at last spectrum of antipsychotic medication response relatively than being visibly distinguished from TRS. Though, patients with TRS do head to get prominent cognitive symptoms and negative and severe pathology than patients whose illness responds to antipsychotic medications [4]

Schizophrenia is the chronic sickness that developed to numerous levels of clinical worsening lacking persistent reduction or healing. In difference with TRS, chronicity is linked with a promising reaction to drug, in which features of schizophrenic are mostly under control for six months or lengthier or there is limited healing to the premorbid prior to function [5]

Interleukin-18 (IL-18) is a pro inflammatory mediate which acted as essential role in Th1 responses. IL-18 is created by macrophage, and unsuitable IL-18 creation has been known to be complicated in immunological disturbances. Schizophrenia is a communal illness whose etiological is still indistinct, though, a triggering of the inflammation response including the (Th1) cytokine response, may be linked to the physiopathology of schizophrenia [6]

The role of the complement system in Schizophrenia has not yet been widely explored. The multicomponent composition of complement makes it complex and expensive to examine the roles of individual components, and so more general assays that measure the overall activity of, for example, a whole pathway (total hemolytic activity) has been used. These are likely to be less informative than single component assays. Largely, involvement of the immune system has been a relatively low priority for Schizophrenia research, because the evidence of classic inflammatory pathology has been consistently lacking, although several scientists since 1937 have been pointing to the possible role of autoimmune and infectious processes in the etiology of Schizophrenia [7]

The importance of the study was to examine the role of using complement-related proteins (complement complex Factor-H), Interleukin-6 (IL6) and Interleukin-18 (IL18)) as serum biomarkers. However, the biomarkers could help explain the pathogenesis of the disease and the present biomarkers for TRS which would be

supportive for diagnosis and might help know the molecular basis for these conditions, in the outlook studies, to be directly concerned in causing the disease symptoms, they would be very important targets for prevention efforts and rational treatment.

Hypothesis

Association of IL6, IL18 and FH-125 in treatment resistant among patients with Schizophrenia.

Aim and objectives

Investigate the IL18, IL6, FH-125 biomarker in the serum of patient treatment resistant Schizophrenia and to find out the correlation with different sociodemographic profile.

Materials and Methods

Case control study was carried out from January, 2019 to may, 2019. The sample size collected from 37 cases, there were 22 females and 15 males, and the patients age was 18-70 years

A total number of 37 patients (15 males / 22 females) is included in this study. Age range is (18-70) years old attended AL Hakeem General hospital, Psychiatric Department for medical care cheek up and examination. The diagnosis was based on the clinical examination under supervision of psychiatric physicians

All patients were asked special questionnaire regarding age , sex , occupation , residence, socio economic state, family history, the duration of disease, the treatment or any therapy had been received during previons months.

People included in this study were (22 males –15 females). Age range is (18-70) Years old. Specimens were collected from Schizophrenia patients if they did not receive any medications.

study as well as pregnant women.

Specimen Collection

The specimens were collected from all people in this study groups. These specimens are immediately processed and investigated as shown in Figure (1).

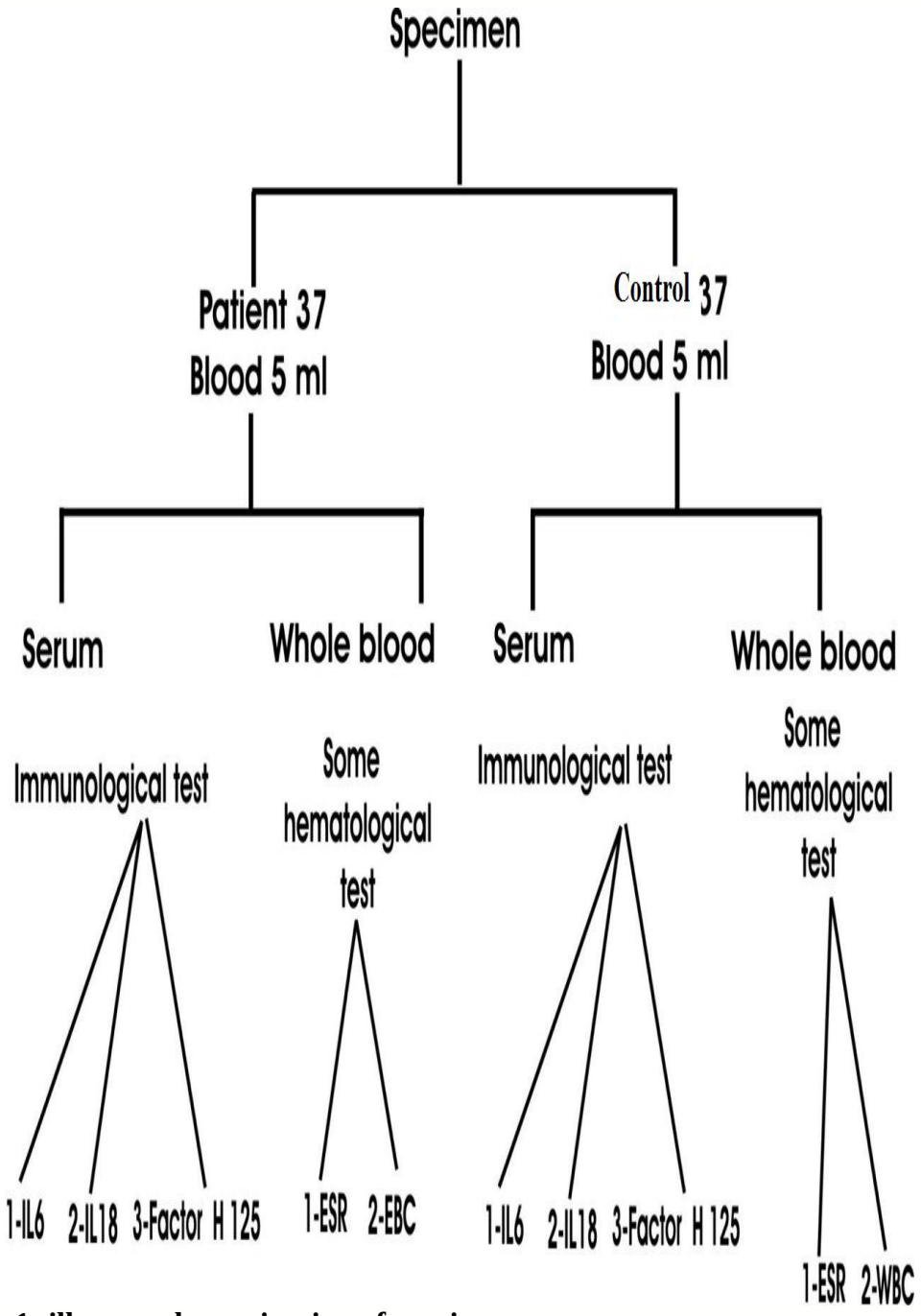

Figure 1: illustrated examination of specimen

Five ml of the blood was obtained by venipuncture from all cases and controls but, before drawing the blood, the skin had to be cleaned with 70 % alcohol, then the blood samples were distributed into 2ml of blood to EDTA tube for some hematological (ESR and WBC) and 3ml of blood collected in plain tube for immunological tests, the sample is allowable to clot at 37 C, then centrifuged for 15 minutes at 2000-3000 rpm. The serum obtained was separated into several aliquots and stored in deep freeze until needed for investigation.

Methods

:Hematological Tests Erythrocyte Sedimentation Rate (ESR)

White Blood Cell Count

Immunological Test.

A: Human Complement Factor H ELISA (Bioassay Technology Laboratory)

B: Human Interleukin 6 ELISA Kit Cat.No E0143Hu (Bioassay Technology Laboratory)

C: Human Interleukin 18 ELISA Kit (Bioassay Technology Laboratory)

Statistical Analysis:

Data of case control study were translated into codes and then converted into a computerized data base. Statistical analysis was done using spss version 7.5 computer software.

The statistical significance of the two groups was analyzed by chi seq and T- test.

P.value less than 0.05 level of significance was considered statistically significant.

Results

Study Subjects:

Gender Distribution

The results of table (4-1) presented the gender distribution between male and female.

The result obtained from the study groups recorded people: 44(59.46%) female and 30 (40.54%) male, the ratio of male to female was 1:1 .

Table (1-1): Differences in gender distribution among cases with Treatment Resistant Schizophrenia and controls.

Gender	Controls		Case with TRS		Total
	N	%	N	%	
Females	22	59.46 %	22	59.46%	44
Male	15	40.54 %	15	40.54 %	30
Total	37	100%	37	100%	74

* P-value =1, chi square test

Age Distribution

The data in this study were shown in Table (1-1-2), their age ranged from (15-50) years and mean age (33.15) years indicated that there were no significant differences p > 0.05 (0.95) in patients with TRS compared with control group according to age.

Table (1-1-2): Differences in mean age between case with Treatment Resistant Schizophrenia and controls

Age (year)	Controls	Case with TRS
Range	(15-50)y	(15-50)y
Mean	33.15	33.15
SD	13.08	8.23
SE	2.92	1.84
N	37	37

P value= 0.95 /T test

1-3: Distribution of Interlaken 6 in the Studied Groups.

Table (1-3) and Figure (1-1) demonstrated the level of IL6 in TRS and control group. There was significant deference (P<0.05) in serum levels of Interlaken 6 in patients with TRS compared with control group.

Table (1-3) A difference mean serum concentration of IL6 in studied groups

Interlaken 6	Controls	Case with TRS	P value
Mean	88.53125	288.65115	0.000254
SE	8.56	35.1	
SD	38.28287	157.36499	
N	37	37	

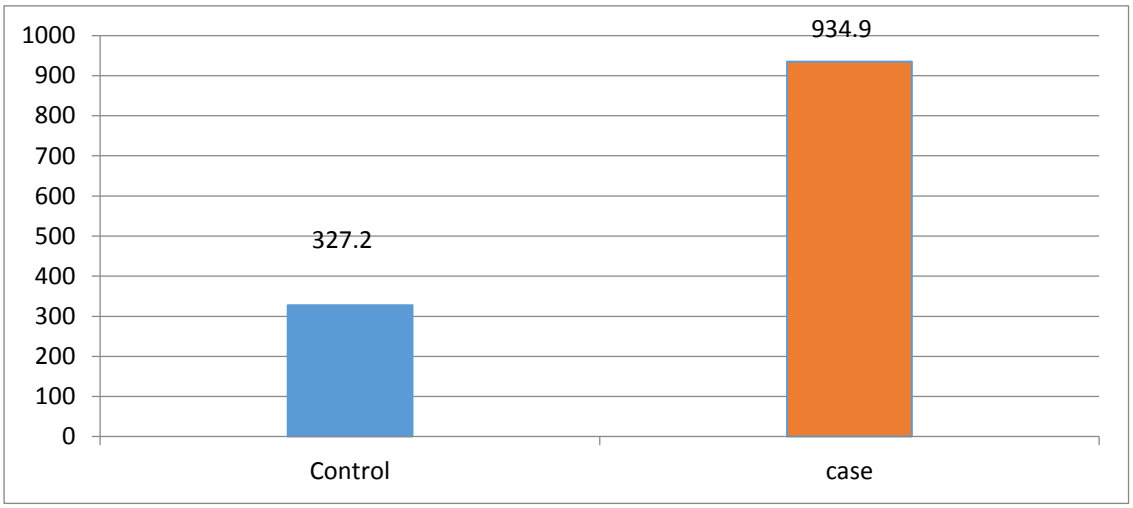

Figure (1-1): Distribution of serum level concentration of Interlaken6 between TRS patients and control.

1-4: Distribution of serum concentration of Interlaken 18 in the studied groups.

The result of Table (1-4) and Figure (1-2) showed that there was a significant important difference (P<0.05) in mean of serum levels concentration Interlaken 18 in patients with TRS compared with control group.

Table (1-4): the differences in mean of serum concentration IL-18 between cases and controls.

IL18	Controls	Case	P value
Mean	10.599	37.185	0.000107
SE	1.16	3.1	
SD	5.204	13.877	
N	37	37	

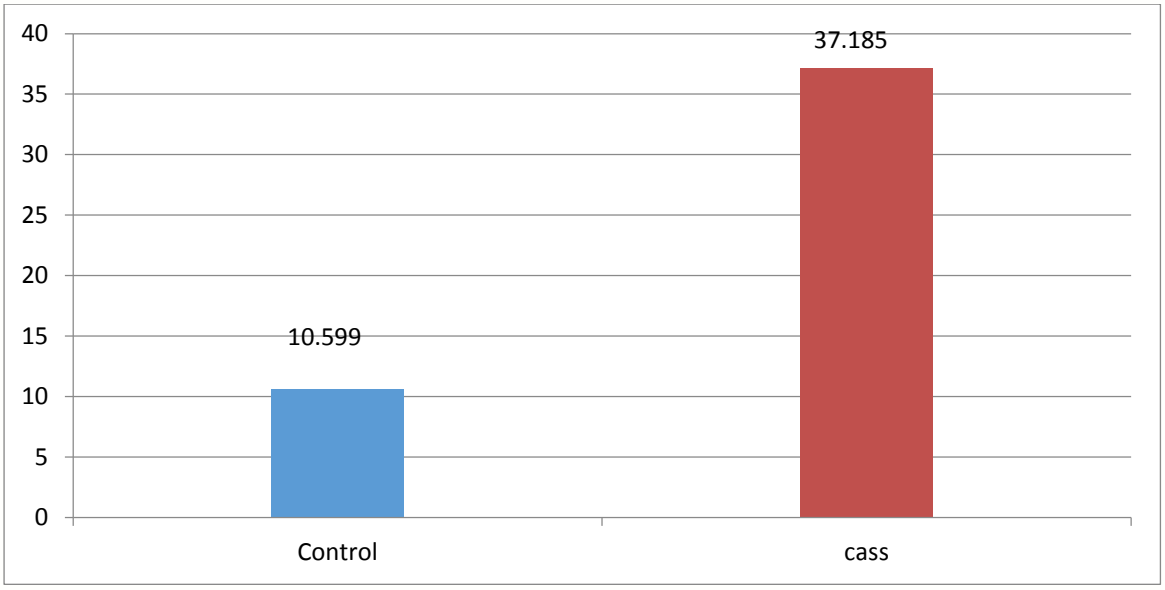

Figure (1-2) comparison between serum level concentration of IL18 in Treatment Resistant Schizophrenia patients and control

1-5: Distribution of Serum Complement-Factor H 125 in the Studied Groups

The results of Table (1-5) and Figure (1-3) demonstrated significant differences P<0.05 (0.00538) in serum levels of Complement –Factor H125 in patients with TRS compared with control group.

Table (1-5) Difference in mean level of complement factor H125 between cases and control.

C-FH	Controls	Case	P value
Mean	327.2	934.9	0.000538
SE	31.66	74.68	
SD	141.6	334.1	
N	37	37	

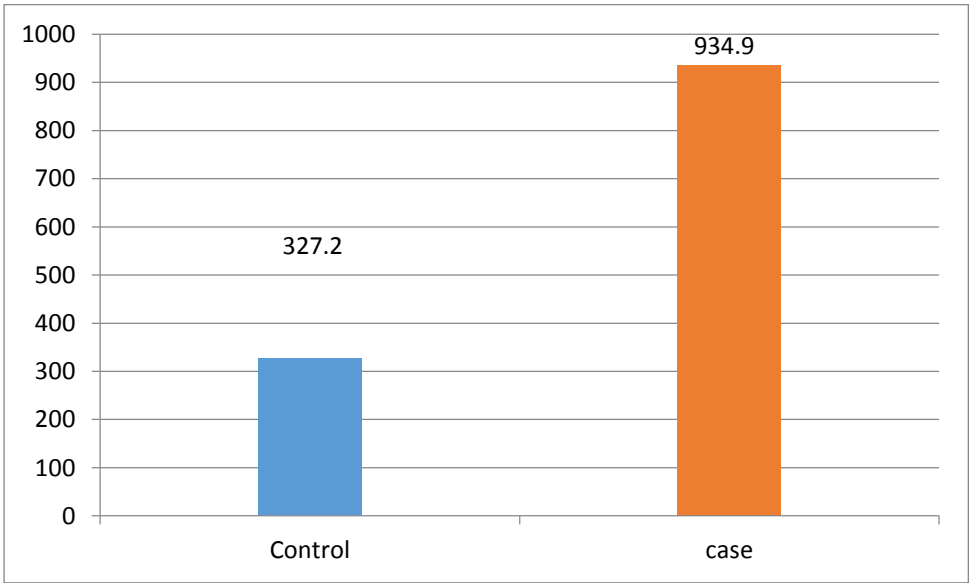

Figure (1-3) compare of serum level concentration Complement –Factor H 125 between TRS patients and control

1-6: comparison of serum biomarkers levels according to gender in patients.

The result of Table (4-6) indicated that there were no significant differences ($p>0.05$) in serum bio markers levels according to gender in TRS .

Table (1-6) bio markers levels according to gender in TRS .

Markers	Mean± S.E.		p-value
	Male N=15	Female N=22	
IL -6	314.93±36.25	254.59±30.6	0.21 T/ test
IL-18	41.9±3.39	37.17±2.94	0.30 T/ test
C.FH	906.07±66.11	972.088±81.22	0.56 T/ test

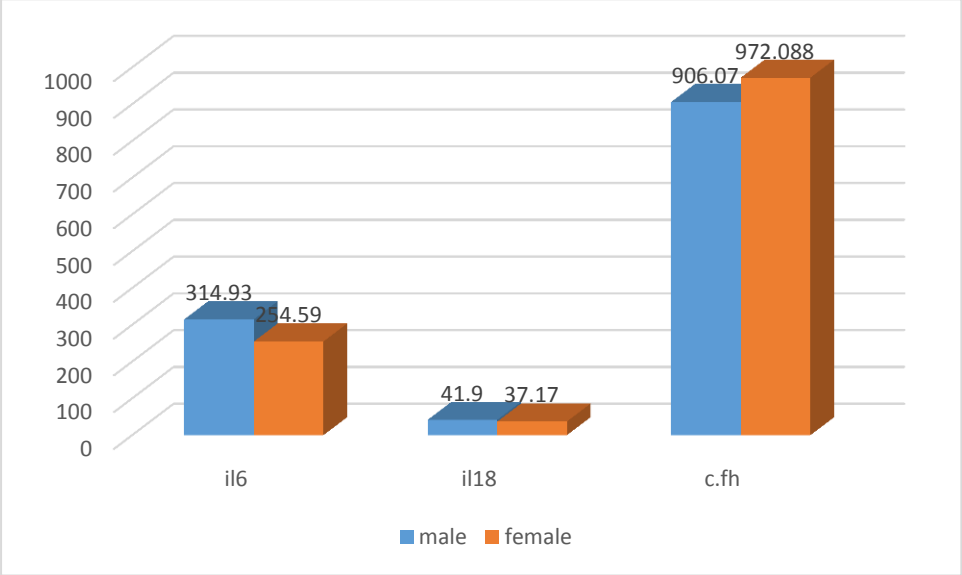

Figure (1-4) Biomarkers levels according to gender in TRS.

1-7: comparison of serum biomarkers concentration according to Age in patient with TRS.

The results of Table (1.7) indicated that there were no significant differences ($p > 0.05$) in the serum biomarkers levels in patients with TRS according to age group.

Table (1-7) Biomarkers levels according to age in TRS

Markers	Mean± S.E.		p-value
	(15-29) N=12	(30-55) N= 25	
IL -6	324.84±37.31	248.98±28.1	0.1182 T/ test
IL-18	43.26±3.8	35.494±2.36	0.09 T/ test
C.FH	699.76±46.3	1,054.7±67.7	0.001 T/ test

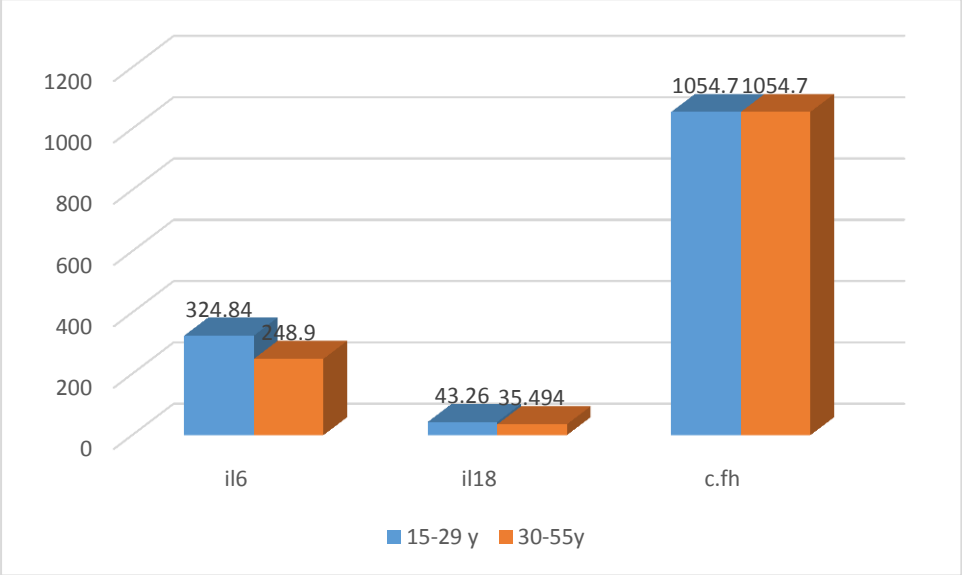

Figure (1-5) Biomarkers levels according to age in TRS.

1-8: comparison of serum biomarkers levels according to occupation in patients with TRS.

The results of Table (1.8) indicated that there were no significant differences ($p > 0.05$) serum biomarkers levels in patients with TRS according to occupation group.

Table (1-8) Biomarkers levels according to occupation in TRS

Markers			p-value
Makers	Employed N=11	Un employed N= 26	
IL -6	312.8±34	280.06±20.7	0.56 T/ test
IL-18	29.3±2.1	41.6±2.5	0.05 T/ test
C.FH	1,.52.5±93.4	900.4±68.2	0.21

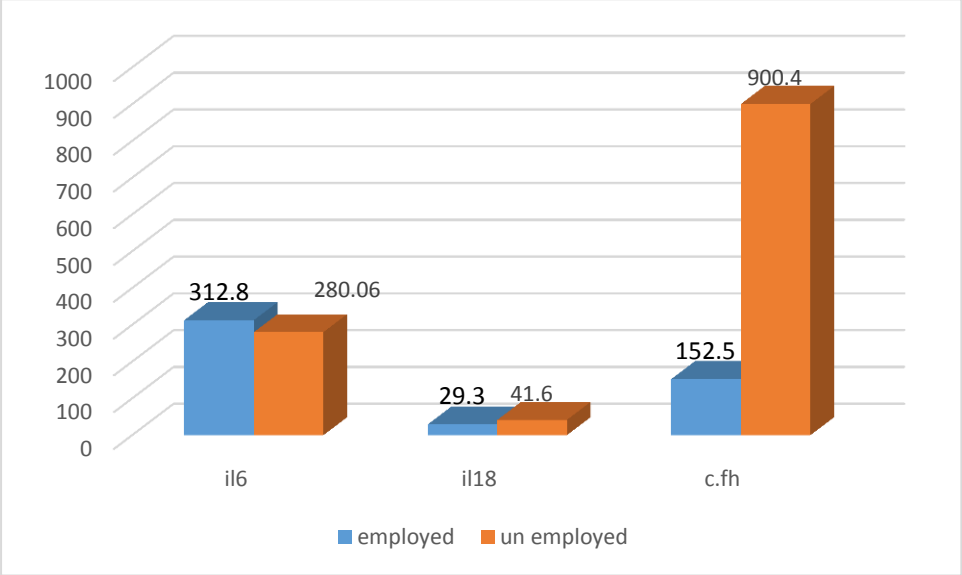

Figure (1-5) Biomarkers levels according to occupation in TRS.

1-9: comparison serum biomarkers levels according to resident in patients with TRS.

The results of Table (1.9) indicated there were no significant differences ($p > 0.05$) of serum biomarkers levels (IL-6,IL-18 and CHF-125in patients with TRS according to residence group**.**

Table (1-9) Biomarkers levels according to residence in TRS

Markers	Mean± S.E.		
	Urban	Rural	p-value
IL -6	321.51777±34.01	214.896±20.7	0.57 / T-test
IL-18	40.2±2.7	36.07±4.1	0.41 T-test
C.FH-125	950.91±470.4	931.2±71.2	0.87 T-test

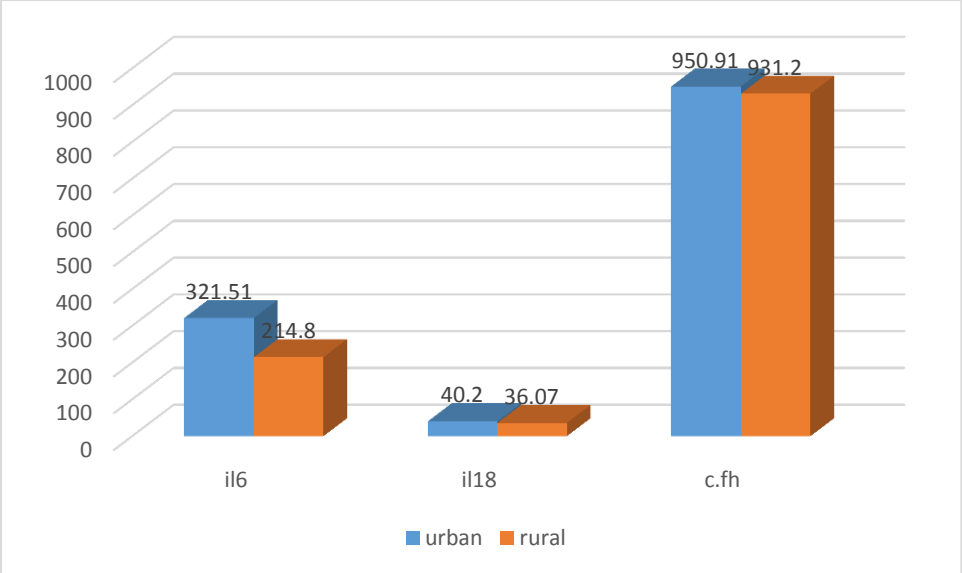

Figure (1-6) Biomarkers levels according to residence in TRS

1-10: comparison serum biomarkers levels according to weight in patients.

The results of Table (4.10) indicated there were no significant differences ($p > 0.05$) serum biomarkers levels in patients with TRS according to weight group.

Table (1-10) Biomarkers levels according to weight in TRS

Markers	Mean± S.E.		p-value
	(50-79) N=10	(80-110) N= 27	
IL -6	328.1±38.2	254.7±28	0.15
IL-18	7.88±2.4	37.57±2.7	0.34
C.FH	1,031.6±183.8	838.9±46.7	1.44

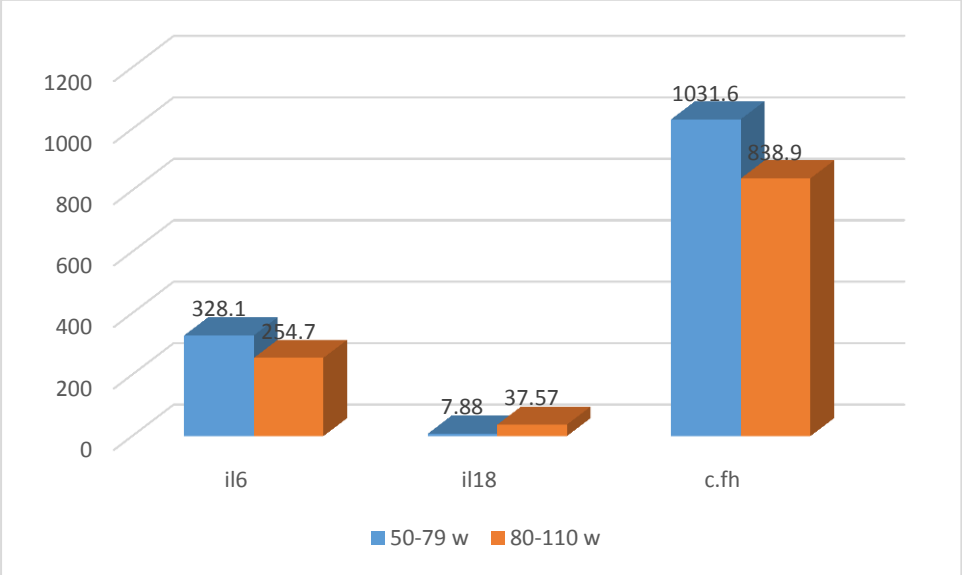

Figure (1-7) Biomarkers levels according to weight in TRS.

Conclusion

5- There was a statically significant correlation between IL-6 and TRS.
6- Elevated serum levels of IL-18 in serum of patients with TRS ware compared with control.
7- Complement F-H125 elevated in serum of patient with TRS was compared with controls.
8- No significant correlation between biomarkers in TRS patient and socio-demographic profile such as (gender, age, residence, occupation, Weight).

References

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