

## **The Relationship Between Hyperglycemia and the Rheumatoid Factor in the Serum of Diabetic Patients**

*Ali M. Al-Gharawi\**

Date of acceptance 9/9/2008

### **Abstract:**

This study was conducted to determine the relationship between two most common diseases in Iraqis patients , which are Diabetic mellitus (DM) and Rheumatoid Arthritis (RA); seeking rheumatoid factor in hyperglycemic sera.

The results revealed that ; 62.5% of hyperglycemic (HG) patients had positive rheumatoid factor (RF) . No difference in number between both gender of HG patients (20 males and 20 females ) , RF reaction was nearly similar in males and females of HG patients ( 12 &13 respectively ) . Only 40% out of patient controls had positive RF . None of the apparently healthy subjects had positive RF .

**Key Words:** DM & RF; hyperglycemia & rheumatoid.

### **Introduction:**

Diabetes is a condition in which a person's body is not able to make enough insulin or use insulin for production of energy from blood glucose [1].

Diabetes mellitus (DM) is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin. According to WHO standard the patient is proved to be DM when checked twice to have either one of the following results:

F.B.G $\geq$  140 mg/dl or R.B.G $\geq$  200 mg/dl [2]

Diabetes is the most common metabolic disorder all over the world . The incidence of diabetes is showing an alarming rise in developing countries [3] . It is ranked seventh among the leading causes of death , and third when all its fatal complications are taken into account [4].

Rheumatoid arthritis (RA) is a chronic systemic inflammation

involving primarily the synovial membranes and the articular structures of multiple joints . The disease is often progressive and result in pain , stiffness and swelling of joints . In late stages deformity and ankylosis development [5].

Raised levels of systemic inflammation have also been shown to predispose in developing both insulin resistance [6 & 7] , and type 2 diabetes mellitus ( DM) (8-10).

This study intends to clarify whether there is a relationship between DM and rheumatoid arthritis by performing rheumatoid factor in hyperglycemic patient sera.

### **Patients and Methods:**

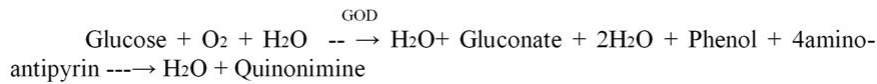
Serum samples from sixty subjects were selected to perform this project. Forty diabetic patients ( according to WHO standard , 140 mg/dl or more as fasting blood glucose (FBG). Serum samples from ten patients having different diseases used as patients control. And serum samples from ten apparently healthy , subjects used as healthy controls.

\* College of Health and Medical Technology.

The first two groups ( patients groups) were chosen from the Teaching Laboratories, Medical City/ Baghdad . The last healthy group were our colleagues in the college . Blood samples were centrifuged within 30 minutes from blood collection , 5 min. centrifugation at 3000 rpm. sera on same day were tested for blood

glucose , and freezed until time of processing (within 30 days) RF-Latex test.

Enzymatic colorimetric methods ( GOD,POD) (11) were performed . Glucose is oxidized by glucose – oxidase to gluconate and hydrogen peroxide according to the following equation:



**Reagents:**

Reagent 1	Tris-buffer PH 7 ( 100 mmol/L)
Buffer Solution	Phenol (0.3 mmol/L)
Reagent 2	Glucose Oxidase ( 10.000 U/L)
	Peroxidase (1000 U/L)
	4-amino-antipyrine ( 2.6 mmol/L)
Reagent 3	Standard Glucose ( 100 mg/dL)
	(5.56 mmol/L)

**Procedure:**

Steps	Sample	Standard	Blank
Serum	10 µL		
Standard		10 µL	
Reagent	1.0 ml	1.0 ml	1.0ml

The reagents were mixed and let to stand for 15 min. at 37°C water bath or 30 min. at 18 – 20 °C on bench . The absorbance ( A ) was then measured for sample and standard at 500 nm against reagent blank.

**Calculation:**

$$\text{Glucose concentration} = \frac{A \text{ sample}}{A \text{ standard}} \times \text{standard concentration}$$

Normal Fasting range ( Enzymatic Method):

- 65 – 110 mg/dL
- 3.6 – 6.1 mmol/L ( SIU)

The RF – Latex was performed as a slide agglutination test for the qualitative and semi quantitative detection. Latex particles coated with

human gammaglobulin are agglutinated when mixed with samples containing RF .

**Reagents:**

Latex--- Latex particles coated with human gamma-globulin, pH 8.2 sodium azide 0.95g/L

Control (+)---Human serum with a RF concentration >30 IU/ml, sodium azide 0.95g/L

Control (-) --- Animal serum , sodium azide 0.95g/L

**Procedure:**

- 1- Allow the reagents and samples to reach room temperature . The sensitivity of the test may be reduced at low temperature.
- 2- Place 50  $\mu$ L of the sample and one drop of each positive and negative control into separate circles on the slide test.
- 3- Swirl the RF latex reagent gently before using and add one drop ( 50  $\mu$ L ) next to the sample to be tested.
- 4- Mix the drops by a stirrer, spreading over the surface of the circle . Different stirrers for each sample have been used.

Note: Spin react kit from Spain has been used in this research , and kit procedure was followed.

**Result and discussion:**

This research was carried out in the Teaching Laboratories , Medical City , Baghdad . Sixty subjects were chosen ; 40 hyperglycemic patients , 10 having different diseases used as patient control group , and 10 apparently healthy subjects used as healthy control group.

Pradhan and colleagues reported that the development of type 2 DM in women was predicted by elevated levels of C-reactive protein (CRP) and interleukin 6 , both markers of systemic inflammation [8].

The authors of two further longitudinal cohort studies found that markers of inflammation such as CRP , raised white cell count , and low serum albumin were associated with development of diabetes over prolonged periods [9 & 10].

The results of this study show that half of the 60 subjects were positive and half were negative RF ( 29 and 31 respectively ) . But when each group is observed alone : none of the healthy control had positive RF; while a respectable number of patients from both groups showed positive RF ( 29 out of 50 ) , as shown in table & figure (1).

Table (1) Summarized the results of rheumatoid factor (RF) for all the studied groups (Hyperglycemic HG patients , patient control or patients having other diseases and apparently healthy controls )

RF reaction	HG patients	Patient control	Healthy control	Total
+ve	25	4	0	29
-ve	15	6	10	31
Total	40	10	10	60

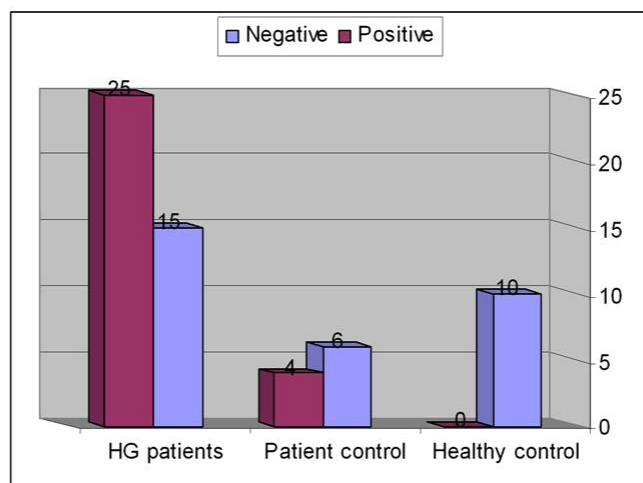


Figure (1) : Rheumatoid factor results for all the studied groups, as in table 1.

When hyperglycemic (HG) patients seen in detail ( Table and Figure 2 ) ; 62.5% of them observed to be positive RF and only 37.5% were negative ( 25 and 15 respectively ). Mean while , no

difference in gender among HG patients whether they were positive ( 12 M and 13 F ) or were negative ( 8 M and 7 F ).

Table (2) : Distribution of subjects having hyperglycemic serum samples among rheumatoid factor (RF).

RF	+ve			-ve			Total
	♂	♀	Total	♂	♀	Total	
Number	12	13	25	8	7	15	40
Percent	30%	32.5%	62.5%	20%	17.5%	37.5%	100%

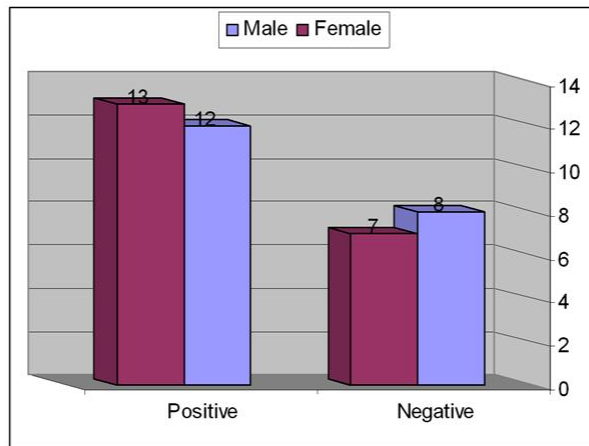
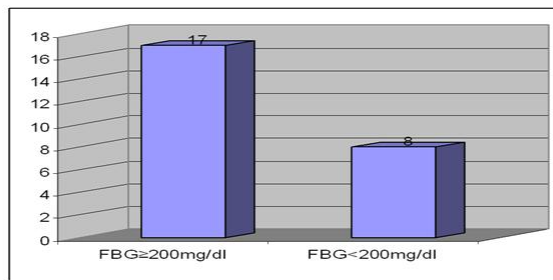


Figure (2) : Distribution of subjects having hyperglycemia among RF .

Finally , table (3) shows the distribution of HG patients having positive RF according to fasting blood glucose (FBG) levels .The group which has FBG less than 200 mg/dl were (32 % ) , while were (68%) with FBG more than or equal to 200 mg/dl.

Table (3) : Distribution of Hyperglcemic (HG) +ve RF patient according to FBG levels.

HG	FBG<200mg/dl	FBG≥200g/dl	Total
Number	8	17	25
Percent	32%	68%	100%



Figure(3): Distribution of HG +ve RF patient according to FBG levels.

Our results are in agreement with other studies [12&13] and in reverse to others [14 & 15]. It could be explained that Simard and Mittleman [14] did not specify whether they included both types 1 and 2 DM, but given that all patients were included in the study and were over 60 years of age ; it is likely that the majority of patients included in this study had type 2 DM . While Hakala *et al.* [15] reported that all patients included in the study were type 1 DM.

The potential role of resistance as a cardiovascular risk factor in patients with inflammatory arthritis has been examined by Srenson, *et al.* ,who reported an impaired glucose handling in a sample of RA patients compared to controls [16]. These investigators also found evidence of an inverse relationship between insulin sensitivity and acute phase markers in RA. More recently , Dessein, *et al.* reported a significantly higher levels of insulin resistance in patients with inflammatory arthritis compared with control , and an association between high CRP concentration and insulin resistance [17] .

In conclusion , there is a relationship between hyperglycemia and rheumatoid factor in the serum of diabetic patients. Ideally , large – scale ,prospective studies are needed to gain a clearer picture of the reality of this hypothesis.

#### References:

1. American Diabetes Association. Standard of medical care for patients with diabetes mellitus [position statement] . Diabetes care 1999;22(suppl.1):S32-S41.
2. Christopher Haslett, Edwin R. Chilver, John AA., and Nicholas A .; Davidsons principle and practice of medicine, 18<sup>th</sup>.ed. London : Churchill Livingstone, 1999, 272-280.
3. Jonathan E. , David Mc C. Paul Z. and Maximillan De Courtan. Type 2 diabetes world wide according to new classification and criterion ; Diabetes care , vol.23, 2000, suppl 2.
4. Min H.K. Department of internal Medicine, Seoul National University Hospital, Korea. Non insulin dependent diabetes mellitus (NIDDM) in Korea Diabetes Med. 1996; ( 9 Suppl 6 ) : S13 -5.
5. Krishna, V. DNB : Text book of pathology , 2006, pp: 987-989.
6. Xu, H., Barnes, G T., Yang, Q., *et al.* Chronic inflammation in fat , plays a crucial role in the development of obesity- related insulin resistance. J Clin. Invest. 2003;112:1821-30.
7. Festa , A. , DAgostino , R. Jr, Howard, G. *et al.*, Chronic subclinical inflammation as part of the insulin resistance syndrome : the Insulin Resistance Atherosclerosis Study (IRAS) . Circulation 2000;102:42-7.
8. Pradhan, AD, Manson, JE, Rifai, N., *et al.* C- reactive protein , interleukin-6, and risk of developing Type 2 Diabetes mellitus . JAMA 2001;286:327-34.
9. Schmidt , MI, Duncan, BB, Sharrett, AR, *et al.* Markers of inflammation and prediction of Diabetes mellitus in adults ( Atherosclerosis Risk in Communities study ) : a cohort study . Lancet : 1999; 535: 1649-52.
10. Barzilay JI., Abraham, L., Heckbert, SR. *et al.* The relation of markers of inflammation to the development of glucose disorders in the elderly . Diabetes ,2001;50:2384-9.
11. Digeion B. Blood Glucose Determination . Ann. Biol. Clin. 1975, 33:3.

12. Kaipianen – Seppanen , D. , Aho.K., Isomaki, H. and Lagkaso, M. Incidence of rheumatoid arthritis in Finland during 1980-1990. Ann Rhum. Dis. 1996;55:608-11.
13. Doran, M. F., Pond GR, Crouson, *et al.* , Trends in incidence and mortality in rheumatoid arthritis in Rochester , Minnesota over 40-year period. Arthritis Rheum. 2002; 46: 625-31.
14. Simard JF , Mittleman MA., Prevalent rheumatoid arthritis and diabetes among NH ANES III participants aged 60 and older . J Rheumatol 2007; 34:469-73.
15. Hakala M., Vahlberg T., Niemi PM *et al.* No association between rheumatoid arthritis and insulin dependent diabetes mellitus : an epidemiologic and immunogenetic study . J Rheumatol . 1992; 19 : 856-8.
16. Svenson KL, Pollare T, Lithell H. & Hallgren R. Impaired glucose handling in active rheumatoid arthritis : relationship to peripheral insulin resistance . Metabolism , 1988; 37: 125-30.
17. Dessein PH , Joffe BI , Stanwix AE , *et al.* The acute phase response does not fully predict the presence of insulin resistance and dyslipidemia in inflammatory arthritis . J Rheumatol, 2002; 29:462-6.

### العلاقة بين ارتفاع السكر والعامل الرثوي في مصلى مرضى السكري

علي محمد الغروي\*

\*كلية التقنيات الصحية والطبية/ باب المعظم

#### الخلاصة:

يعد مرض السكري من أمراض العصر المزمنة والمقيبة , ومن مسببات الالتهابات. لذا تمت دراسة علاقة هذا المرض بداء التهاب المفاصل الرثوي (Rheumatoid Arthritis RA) من خلال دراسة عامل الالتهاب (rheumatoid factor RF) في مصلى مرتفعي السكر (hyperglycemia). تم انتقاء (40) مريضاً يعاني ارتفاع السكر على أساس الفحص السريري والمختبري وعشرة أشخاص يعانون أمراضاً مختلفة غير السكري كمجموعة سيطرة وعشرة متبرعين من السويين ظاهرياً ولأعمار مضاهية للمرضى . تم الفحص السريري في العيادة الخارجية لمدينة الطب / بغداد . اجري العمل في المختبرات التعليمية لمدينة الطب . ومن هذا العمل المحدود لوحظ ما يلي : اظهر 62.5% من المرضى مرتفعي السكر (hyperglycemic HG) قيمة موجبة للعامل (RF) بينما اظهر فقط 40% من مجموعة السيطرة القيمة الموجبة للعامل ولم تظهر في نفس الوقت أي قيمة موجبة للعامل (RF) لمجموعة المتبرعين من السويين ظاهرياً.

كان عدد الرجال والنساء من مرضى مرتفعي السكر متساوياً ( 20 : 20 ) . وقد اظهر الجنسين تفاعلاً ايجابياً +ve للعامل الرثوي (RF) متقارباً ( 12 رجلاً : 13 امرأة ) .