

**C-REACTIVE PROTIEN IN ST ELEVATION
MYOCARDIAL INFARCTION IN DIABETIC AND
NON-DIABETIC PATIENTS**

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Abstract

Aims of study:

Determining the role of C-reactive protein in patients with acute myocardial infarction and comparing its value diabetic and non-diabetic patients and study its prognostic significant .

Methods:

A group of 219 patients who had acute ST elevation myocardial infarction were studied for period from December 2008 to December 2009 . , 59 were females and 160 were males

CRP were measured in all patients on admission with semi quantitative CRP latex test kit produced by plasmatic Laboratory Product Ltd (UK).

Results:

Out of 219 patients 76 (34.7%) patients had inferior Myocardial infarction and 143(65.3%) patients had anterior Myocardial infarction The mean level of C-reactive protein was higher in diabetic patients (51.5±49.6 mg/l) than non-diabetic patients (28.98±41.01 mg/l) , this was statistically significant (p=0.002).

The mean CRP level was higher in diabetic with acute anterior MI (53.9 ±42.43mg/l)than non-diabetic was (30.9±40.63 mg/l) this was statistical significant difference (P=0.01).Also this is statistical significant difference(P= 0.005) among patients presented with acute inferior MI (43.4±39.54) mg/l Vs (26.2±35.98)mg/l in diabetic and nondiabetic respectively .

Hospital mortality was 43 (19.6%) patients . mean level of C-reactive protein in patients who died in the hospital was significantly higher in diabetic than non-diabetic patients (61.92±47.2 mg/l) Vs.(48.66±32.7 mg/l) respectively.

conclusions:

diabetic patients with acute MI had higher level of C-reactive protein than non-diabetic

CRP on admission is a strong predictor for hospital mortality in both diabetic and non-diabetic with acute MI

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INTRODUCTION

C-reactive protein (CRP) is an acute-phase protein ⁽¹⁾ . CRP is exclusively made in the liver in response to factors released by adipocytes and is secreted in increased amounts within 6 hours of an acute inflammatory stimulus ⁽²⁾ .

inflammatory processes widely assumed to play role in Atherosclerosis , and the evolution of plaque instability underlying atherothrombotic events ⁽³⁾

CRP could promote complement activation and thus inflammation in the plaques , and there is experimental evidence supporting a possible role of complement in atherogenesis ^(4,5) .

CRP has also been reported to stimulate tissue factor production by peripheral blood monocytes in vitro and could thereby have important procoagulant effects ⁽⁶⁾ .

. Addition of CRP to LDL in cell culture systems has been reported to stimulate formation of foam cells ,which are a typical feature of atherosclerotic plaques ⁽⁶⁾.

HMG CoA-reductase inhibitors(statins), reproducibly reduce CRP values, independently of their effects on lipid profiles ⁽¹⁹⁾. It is not known whether this reflects direct effects on hepatocytes, anti-inflammatory effects within atherosclerotic plaques , and / or anti-inflammatory effects elsewhere. However , recent studies suggest that statins reduce the risk of future cardiovascular events to the same extent in patients with raised LDL cholesterol values and in those with normal LDL but with base-line CRP concentrations above the median ⁽⁷⁾.

Peak plasma CRP levels correlated positively with LV volume indices at almost 6 months; that is , the higher the rise in circulating CRP, the more advanced the LV remodeling will be and the more it will lead to congestive heart failure and cardiac death⁽⁸⁾. So Plasma CRP levels may be potent predictors of late LV function and remodelling after a first MI ⁽⁹⁾.

Measuring CRP levels in the peripheral blood could provide valuable information for short and long-term risk stratification after Acute myocardial infarction .

Aims of study:

Determining the role of C-reactive protein in patients with acute myocardial infarction and comparing its level in diabetic and non-diabetic patients and study its prognostic significant .

Patients and Methods:

A total of 219 patients, 59 (26.9%) females whose age ranged between 40-86 years, mean age (67.7±10.3) years, 160 (73.1%) males whose age ranged between 22-93 years, with mean age of (60.4±8.6) years were included in this study from December 2008 to December 2009 in Al-Basrah, Al-Sadir and Al-faihaa general hospitals in Basrah city south of Iraq.

Inclusion criteria :

Patients included in this study those who were admitted to CCU and diagnosed and treated as ST Elevation Myocardial Infarction (STEMI) according to the recommendations of European society of cardiology and American college of cardiology⁽¹⁰⁾.

Diabetic was diagnosed according to WHO criteria⁽¹¹⁾:

CRP Measurement: A sample of a blood was drawn from every patient included in the study on admission for measurement of CRP using CRP latex test kit produced by Plasmatec Laboratory Product Ltd (UK)(picture 1) which is qualitative and semi-quantitative estimation of CRP in human serum sample.

Principle : the assay is performed by testing a suspension of latex particles coated with anti-human CRP antibodies against unknown serum. the presence of visible agglutination indicates an increase in levels of CRP to a clinically significant level.

Procedure :

Qualitative method: a drop of undiluted serum was placed using the sample pipettes provided 50ul onto a circle of a test slide (picture 2) then one drop of the latex reagent was added (picture 3) next to the drop of serum then spread the mixture on the entire area of the test circle and gently shake the slide for 2 minutes. presence of agglutination indicates a level of CRP equal or $>6\text{mg/l}$ while the lack of agglutination indicates a CRP $<6\text{mg/l}$ in the sample.

Semi-quantitative method: was performed in the same way as the qualitative test using dilutions of the serum in saline, phosphate buffered saline or glycine saline provided as in table (1)

The titer is expressed as the reciprocal of the highest dilution showing macroscopic agglutination.

Performance characteristics :

Diagnostic sensitivity 95.6% . diagnostic specificity 96.2% .

Statistics:

The study is a case control study . SPSS 15 software program was used for estimation of the; odd ratio for evaluation of associations between variables , chi-square and P value for estimation of significance of the results which was obtained in the study; P value less than 0.05 was considered significant statistically .

Results:

Two hundred nineteen patients were studied; 59 (26.9%) were females and 160 (73.1%) were males , 77(35.1%) of the patients had diabetes ;45 (20.5 %) were males and 32 (14.6 %) were females ;while non-diabetic were 142 (64.9%) patients ;115 (52.5%) were males and 27 (12.3%) were females (Table 2).

Acute anterior MI was more frequent than inferior in studied patients , 143(65.3%) vs.76(34.7%)respectively (P=0.001) in both diabetic and non-diabetic patients ;60(27.4%) vs.17(7.8%) (P=0.003) and 83(37.9%) vs.59(26.9%) (p=0.04);respectively.(Table 3).

Table 4 demonstrates that the mean level of CRP on admission was (36.9±45.42) mg/l in studied patients , it was higher (51.5±49.6) mg/l in diabetic patient than non-diabetic patients (28.98±41.01) mg/l .This was statistically significant (P=0.002) .

The mean CRP level was higher In diabetic patients with acute anterior MI (53.9 ±42.43) mg/l than non-diabetic patients (30.9±40.63) mg/l and this was statistically significant (P=0.01).Also there was statistical significant difference(P= 0.005) among patients presented with inferior MI mean CRP level was (43.4±39.54) Vs (26.2±35.98)mg/l in diabetic and non-diabetic respectively .

The mean CRP level was not statistically significant difference (P=0.508)for patients presented with anterior Vs inferior MI (for both diabetic and non-diabetic); (40.57±47.2) mg/l and (30.07±41.29) mg/l respectively .(table 5)

The hospital mortality among studied patients was 43(19.6%) patients. Mean level of CRP in diabetic patients who died in the hospital was (61.92±47.2) mg/l and in non- diabetic was (48.66±32.7)mg/l ,which was statistically significant difference(P =0.001).

the mean level of CRPwas higher in patient who died in the entire group than those who survived (56.37±41.8) mg/l Vs (32.18±45.09) mg/l respectively. This was statistically significant (P value=0.002) (table 6)

Hospital mortality was directly proportionate with the level of CRP in both diabetic and non-diabetic patients ,and this was more significant in the diabetic(fig.1).

Discussion :

This study revealed that 64.9% of STEMI patients were non-diabetic and 35.1% were diabetic , this was consistent with the Iqbal MJ et al and Peterson et al studies^(12,13)

This study revealed that anterior MI was more frequent than inferior ,in both diabetic and non-diabetic patients .These results were consistent with Tipoo et al study ⁽¹⁴⁾ .It has been reported that diabetes exerts a potent multifactorial atherosclerotic effect, especially with increasing age⁽¹⁵⁾. Left anterior descending artery that supplies the anterior cardiac wall seems to be more susceptible to development of atherosclerosis in comparison to right coronary ⁽¹⁶⁾. Left anterior descending artery is exposed to more powerful biomechanic and hemodynamic stress resulting from the contraction of the heart, which may be related to greater endothelial and artery wall damage favoring development of atherosclerotic process. Therefore, it seems likely that more extensive

atherosclerotic lesions underlay anterior infarction, which was also observed in higher percentage of patients during present study and seems to be one of the reasons for its adverse outcome ⁽¹⁷⁾.

Non-diabetic/diabetic ratio of mean CRP level was about 1:1.8 this was consistent with Wolfgang Otter et al study ⁽¹⁸⁾. Diabetes is an independent risk factor of atherosclerosis. It is considered a state of low-grade inflammation. CRP levels have been reported to be augmented in diabetic patients ⁽¹⁹⁾.

Mean CRP level in patient with acute anterior MI had higher CRP than patients presented with inferior MI (40.5 vs. 30.07 mg/l) respectively. This is inconsistent with D.Barret et al and Tanaka A et al studies ^(20,21)

Hospital mortality was 19.6% , in Wolfgang Otter et al study it was 15.6% ⁽⁵⁷⁾ . The mean CRP in patient who died in the hospital was higher in diabetic patients than non-diabetic patients . Non-diabetic/diabetic mean CRP ratio was about 1:1.3. In Wolfgang Otter study, ratio of 1:1.4 was reported ⁽⁵⁷⁾.

In addition to the importance of diabetes in the inflammatory process and subsequent rise in CRP level ⁽²⁶⁾ , diabetic patients have more risk factors like hypertension and dyslipidemia that increase the risk of atherosclerosis and affect the plaque stability ⁽¹²⁾ .Diabetic patients are also more prone to silent ischemia due to neuropathy and their presentation with acute myocardial infarction usually later than non-diabetic patients ⁽⁵¹⁾ , and since the CRP level is time dependent , it increases with the subsequent hours after plaque rupture and occlusion of coronary artery , and it is peaked at about 48 hour after development of

myocardial infarction(35) , so delayed presentation in diabetic patients make them to have more CRP level , and more susceptible to the complication of untreated myocardial infarction and decrease their response to the treatment , like thrombolysis or primary PCI, which are more beneficial in earlier hour of myocardial infarction development .In the whole group , the mean CRP for patients who died was significantly higher than that of patients who survived with mean CRP level of died patients about twice that of survived . This result was in agreement with Wolfgang Otter et al study which found that the mean CRP level in patients who died was 2.7 that of survived patients⁽⁵⁷⁾ . The mortality was higher in diabetic group in all levels of CRP if compared to non-diabetic group , for reasons mentioned above , increasing from 16.6% to 50% in diabetic patients and from 11.1% to 33.3% in non-diabetic patients . The mortality in whole group in patients who had CRP level >6 mg/l was 16.4% which was five fold more than that of patients with CRP ≤ 6 mg/l (3.2%), Wolfgang Otter et al study revealed that the mortality in patients with CRP > 7 mg/l is seven fold that of patients with CRP level ≤ 7 mg/l⁽¹⁸⁾.This study revealed an interestingly finding that the higher CRP level the higher mortality, especially in diabetic patients.

Conclusions:

1-CRP on admission is a strong predictor for hospital mortality in both diabetic and non-diabetic for patients admitted to CCU with acute MI.

2- CRP level above the median 6 mg/l associated with increased mortality and this increased markedly with each rise in CRP level.

3- diabetic patients have higher level of CRP than non-diabetic patients and associated with poor prognosis.

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Table (1) Demonstrate sample dilution for estimation of CRP titer

Dilutions	1/2	1/4	1/8	1/16
Sample serum	100ul	-	-	-
Saline	100ul	100ul	100ul	100ul
Volume of sample	50ul	50ul	50ul	50ul
6xno. Of dilutions	6x2	6x4	6x8	6x16
Mg/l	12	24	48	96

Table (2) shows the sex distribution of diabetic and non-diabetic patients

Sex	Diabetics patients		non-diabetic patients	
	No.	percentage	No.	percentage
Male	45	20.5%	115	52.5%
Female	32	14.6%	27	12.3%
Total	77	35.1%	142	64.9%

table (3) shows the frequency of site of MI in diabetic and non-diabetic.

Site of MI	diabetic patients		non-diabetic patients	
	No.	percentage	No.	Percentage
Anterior	60	27.4%	83	37.9%
inferior	17	7.8%	59	26.9%
total	77	35.2%	142	64.8%

Table(4) shows the no. and percentage of diabetic and non diabetic patients in each CRP level.

CRP mg/l	Diabetics patients		Non-diabetic patients		Total	
	No.	Percentage ^a	No.	Percentage ^b	No.	percentage
<6	6	7.8%	27	19 %	33	15.1%
6	6	7.8%	20	14.1%	26	11.9%
12	10	13%	37	26.1%	47	21.5%
24	16	20.8%	23	16.2%	39	17.8%
48	17	22.1%	18	12.7%	35	16%
96	16	20.8%	11	7.7%	27	12.3%
>96	6	7.8%	6	4.2%	12	5.5%

a-percentage of patients within diabetic group.

b-percentage of patients within non-diabetic group

Table(5) shows the relation of site of MI in each level of CRP , in both diabetic and non-diabetic .

CRP mg/l	diabetic patients				non-diabetics patients			
	Anterior MI		Inferior MI		Anterior MI		Inferior MI	
	No.	percentage	No.	percentage	No.	Percentage	No.	percentage
<6	5	2.3%	1	0.46%	12	5.5%	15	6.8%
6	5	2.3%	1	0.46%	10	4.6%	10	4.6%
12	7	3.2%	3	1.3%	24	10.9%	13	5.9%
24	13	5.9%	3	1.3%	14	6.4%	9	4.1%
48	12	5.5%	5	2.3%	12	5.5%	6	2.7%
96	12	5.5%	4	1.8%	8	3.7%	3	1.3%
>96	6	2.7%	0	0%	3	1.3%	3	1.3%

Table (6) : shows no. and percentage of dead patients in diabetic and non diabetic in each level of CRP.

CRP mg/l	Diabetic patient who died in hospital		Non-diabetic patients who died in hospital	
	No.	percentage	No.	Percentage
<6	1	2.3%	3	6.9%
6	1	2.3%	2	4.6%
12	2	4.6%	3	6.9%
24	4	9.3%	4	9.3%
48	5	11.6%	4	9.3%
96	6	13.9%	3	6.9%
>96	3	6.9%	2	4.6%

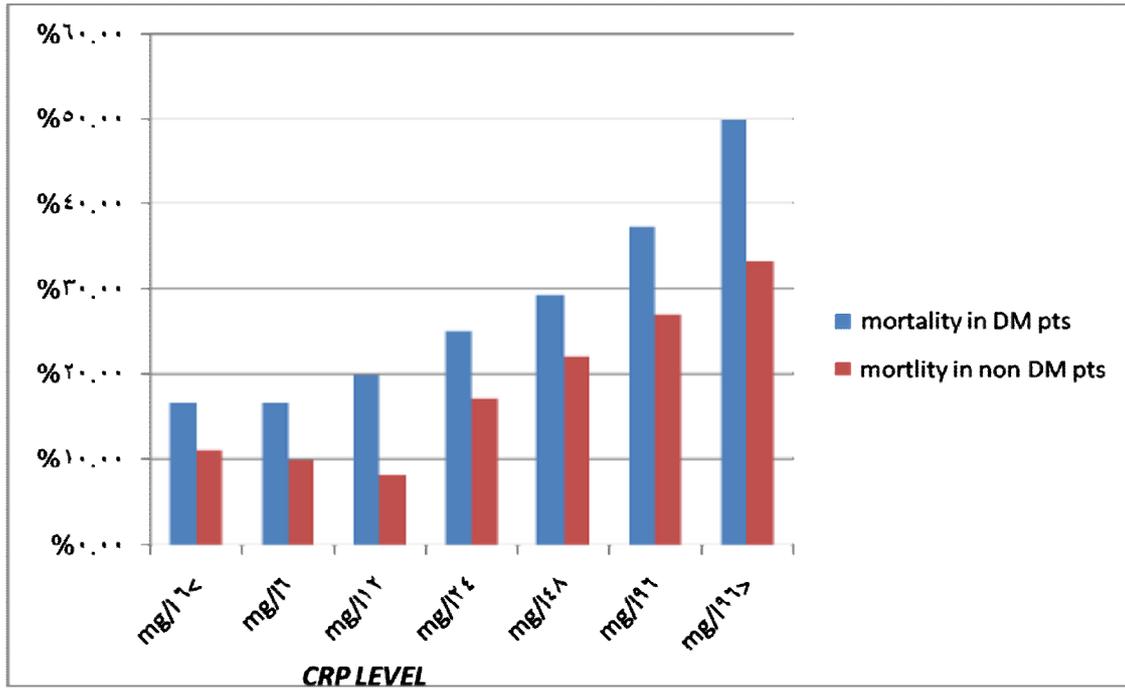


fig.(1) demonstrate the percentage of mortality in diabetic and non-diabetic patients in each CRP level.

قياس بروتين سي التفاعلي لمرضى احتشاء العضل القلبي بين المرضى المصابين والغير مصابين بالسكري

الخلاصة:

الأهداف:

- 1- تحديد تأثير بروتين سي التفاعلي في احتشاء العضل القلبي ومقارنته بين المرضى المصابين بالسكري والغير مصابين به.
- 2- قياس مستوى بروتين سي التفاعلي لمرضى كل من احتشاء العضل القلبي الأمامي والسفلي.
- 3- دراسة نسبة الوفيات الحاصلة في المستشفى لمرضى احتشاء العضل القلبي الذين وجدوا بمستويات عالية من بروتين سي التفاعلي في كل من المرضى المصابين والغير مصابين بالسكري.

الطريقة:

سجل 219 مريضا، 59 انثى و 160 ذكر ، في هذه الدراسة وتم اختيارهم من المرضى الراقدين في وحدة العناية التاجية وشخصوا وعولجوا كمرضى احتشاء العضل القلبي . اعتبر المريض مصابا بالسكري في حالة كونه مشخصا مسبقا أو يتعاطى الادوية الخاصة بالسكري . اما المرضى المكتشفون حديثا فيتم تشخيصهم على انهم مصابون بالسكري وفق معايير منظمة الصحة العالمية لتشخيص السكري . وقد تم قياس بروتين سي التفاعلي بواسطة القياس شبه الكمي (قياس بروتين سي التفاعلي بواسطة اختبار اللاتكس) المنتج بواسطة شركة بلاسماتك لابرتوري برودكت (المملكة المتحدة) .

النتائج:

من بين 219 مريضاً الذين سجلوا في الدراسة، 59 أنثى و160 ذكر، وجد أن 77 مريضاً كانوا مصابين بالسكري و 142 مريضاً غير مصاباً به . وكان 76 مريضاً شخصوا باحتشاء العضل القلبي السفلي و143 باحتشاء العضل القلبي الأمامي . وقد كان معدل مستوى بروتين سي التفاعلي في مرضى السكري 51.5 ± 49.6 ملغم/لتر و 28.98 ± 41.01 ملغم/لتر للمرضى الغير مصابين به . وجد ان معدل مستوى بروتين سي التفاعلي في مرضى السكري المصابين باحتشاء العضل القلبي الأمامي 53.9 ± 42.43 ملغم/لتر والسفلي 43.4 ± 39.54 ملغم/لتر. أما المرضى الغير مصابين بالسكري فكان معدل مستوى بروتين سي التفاعلي لمرضى احتشاء العضل القلبي الأمامي 30.9 ± 41.3 ملغم/لتر والسفلي 26.2 ± 35.9 ملغم/لتر وكما وجد أن عدد المتوفين داخل المستشفى كان 43 مريضاً وان معدل مستوى بروتين سي التفاعلي لهم كان أعلى بين مرضى السكري مقارنة بالغير مصابين بالسكري (61.9 ± 46.6 مقابل 48.6 ± 32.7 ملغم/لتر) بالتتابع.

الاستنتاجات :

- 1- بروتين سي التفاعلي عامل تنبؤ قوي للوفيات التي تحصل في المستشفى لمرضى وحدة العناية التاجية الذين يعانون من احتشاء العضل القلبي الحاد في كل من المرضى المصابين بالسكري والغير مصابين به.
- 2- مستوى بروتين سي التفاعلي أكثر من 6 ملغم/لتر يترافق مع زيادة نسبة الوفيات.
- 3- لدى مرضى السكري مستوى أعلى من بروتين سي التفاعلي مقارنة ببقية المرضى وان تزامن السكري مع الزيادة في مستوى بروتين سي التفاعلي يحمل تكهن سيء لمرضى احتشاء العضل القلبي الحاد .