# Treatment manners, glycemic control, and c-reactive protein in patients receiving antidiabetic or antidiabetic with antihypertensive drugs in basra

**Article** *in* Asian Journal of Pharmaceutical and Clinical Research · November 2018

DOI: 10.22159/ajpcr.2018.v11i11.29588

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Vol 11, Issue 11, 2018

Online - 2455-3891
Print - 0974-2441

Research Article

# TREATMENT MANNERS, GLYCEMIC CONTROL, AND C - REACTIVE PROTEIN IN PATIENTS RECEIVING ANTIDIABETIC OR ANTIDIABETIC WITH ANTIHYPERTENSIVE DRUGS IN BASRA

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***Received: 10 September 2018, Revised and Accepted: 16 October 2018***

**ABSTRACT**

**Objective:** This study aimed at investigating the relationship between treatment manners, glycemic control, and C-reactive protein (CRP) serum level in patients receiving antidiabetic drugs (ADM) alone or ADM with antihypertensive (AHT) drugs in Basra.

**Methods:** Patients receiving ADM or ADM with AHT drugs, not suffering from complications, were recruited from Al-Mawanee General Hospital in Basra. Socioeconomic characteristics, blood pressure (BP), and treatment plans were recorded. Blood samples were obtained to measure glycated haemoglobin (HbA1c), lipids profile, and high sensitive (hs-CRP).

**Results:** A total of 26 men and 50 women were involved. Lower mean HbA1c was found in patients receiving ADM with AHT drugs compared with those on ADM drugs only (p=0.0013). Lower mean systolic BP (p<0.0001) and diastolic BP (p=0.0078) were found in patients receiving ADM drugs only compared with those receiving ADM with AHT drugs. Lower mean hs-CRP was found in women receiving ADM with AHT drugs compared with those on ADM drugs only. Treatment manners had no effect on mean hs-CRP in men and women receiving ADM with AHT drugs; however, there was a significant direct correlation of hs-CRP with HbA1c (p=0.002) and triglycerides (p=0.009), but inversely with high-density lipoprotein cholesterol (p=0.011) in women receiving ADM drugs only.

**Conclusion:** High levels of hs-CRP are associated with poor glycemic control and dyslipidemia, therefore, consequently increased cardiovascular risk. Due to its value as a risk predictor, hs-CRP should be included in routine monitoring of Type-2 diabetic patients.

**Keywords:** Antidiabetic drugs, Antihypertensive drugs, C-reactive protein.

 DOI: http://dx.doi.org/10.22159/ajpcr.2018.v11i11.29588

## INTRODUCTION

In Iraq, the high rate of incidence of diabetes and hypertension has been documented. Diabetes and hypertension are the two main risk factors in the development of ischemic heart disease, cardiac hypertrophy, and cardiac failure. Cardiovascular diseases are the most common causes of mortality over the world. Previous studies have demonstrated that individuals with diabetes [1] and hypertension [2,3] have higher levels of C-reactive protein (CRP) compared with individuals without these conditions in the general population. Increased risk of cardiovascular disease has also been associated with increased levels of CRP [4,5]. CRP synthesis and secretion are mainly in hepatic cells [6]. It is regulated by the action of many activated cytokines such as interleukin-6 (IL-6), IL-1, and tumor necrosis factor-alpha [7]. CRP is a sign of systemic inflammation in blood [8]. The normal plasma level of CRP in a healthy population without evidence of acute inflammation is 2 mg/L or less [9]. There is a rapid rise in the circulating CRP by as much as 3000-fold in response to inflammation, infection or acute tissue injuries, which drop rapidly when inflammation or injury is resolved [10]. Many studies are focused on the association of chronic elevation of CRP with an increased risk of cardiovascular disease and atherosclerosis [11-14]. If CRP is concerned in the pathophysiology of cardiovascular disease, it could be accepted that lowering CRP levels would reduce the progress of the disease and its complications. CRP causes atherosclerosis by various mechanisms, such as the release of reactive oxygen species (ROS), CRP increases the generation of ROS by monocytes and neutrophils [15,16] directly. ROS have been concerned in the beginning and continuation of atherosclerosis [17]. Furthermore, CRP increases the expression of adhesion molecules [18]. Furthermore, CRP has been concerned in the destabilization of atherosclerotic plaques [19]. Moreover, CRP can mediate the uptake of LDL into macrophages to form foam cells [20].

The aim of this study was to investigate the association between drug treatments, glycemic control, and serum level of CRP in Iraqi patients receiving antidiabetic drugs (ADM) drugs or ADM with antihypertensive (AHT) drugs.

## METHODS

This study was conducted during the period from February to May, 2018, and the patients were selected during their visit to Diabetes Endocrine and Metabolism Centre in Al-Mawanee General Hospital in Basra. Institutional Ethical Committee approved the study, and informed consent was obtained from the subjects. Patients receiving ADM drugs or ADM with AHT drugs, not suffering from complications, were recruited. A total of 76 diabetic patients aged between 42 and 67 years were included in this study 50 patients were females and 26 were males. 42 patients using ADM with AHT drugs, from which 30 were females and 12 were males. The other 34 patients were using ADM drugs only. Patients were excluded from the study if they were Type1 diabetic patients or if they have any cognitive problems. Socioeconomic characteristics, blood pressure (BP), and treatment plans were recorded. Fasting blood samples were obtained to measure glycated hemoglobin (HbA1c), lipids profile, and high sensitive (hs-CRP). HbA1c up to 7% reflected adequate glycemic control, while HbA1c >7% reflected poor glycemic control, as recommended by the American Diabetic Association guidelines [21]. Hypertension was defined as a systolic BP >140 mmHg or diastolic BP >90 mmHg, or current use of AHT drug treatment [22].

### Laboratory investigations

HbA1C was measured by D-10 Dual Program Bio-Rad Laboratories, Inc., Hercules, CA 94547, 220-020, California, USA. D-10 Dual Program is

based on chromatographic separation of the analytes by ion-exchange (high-performance liquid chromatography). Hs-CRP was measured by Cobas Integra 400. Serum lipids (cholesterol, triglycerides, and high-density lipoprotein cholesterol (HDL-C)) were assayed using automated enzymatic methods (Dimension Vista 1500T Intelligent Lab System from Siemens Company-Germany) at the biochemistry laboratory.

**Statistical analysis**

Statistical analysis was performed using GraphPad Prism software (version 7.0, GraphPad Software, Inc., San Diego, CA). Descriptive statistics, such as mean ± standard deviation, were calculated for all estimated parameters. Comparison between two means was performed using unpaired Student t-test for normally distributed parameters. Associations between variables were examined using Pearson's correlation coefficients. All p values that were <0.05 were considered significantly different.

## RESULTS

A total of 26 men and 50 women were recruited. Lower mean HbA1c was found in patients receiving ADM with AHT drugs compared with those on ADM drugs only (p=0.0013). Lower mean systolic BP (p<0.0001) and diastolic BP (p=0.0078) were found in patients receiving ADM drugs only compared with patients receiving ADM with AHT drugs. Lower mean hs-CRP was found in women receiving ADM with AHT drugs compared with those on ADM drugs only (Table 1). Furthermore, the main AHT drugs used by the patients involved in this study were angiotensin receptor blockers (losartan and candesartan), angiotensin-converting enzyme inhibitors (captopril and enalapril), calcium channel blockers (CCBs) (amlodipine and diltiazem), and β-blocker drug carvedilol. Furthermore, the main ADM drugs used by the patients involved in this study were glibenclamide, glimepiride, metformin, and insulin.

**Table 1: Measured hs-CRP, HbA1c, and BP according to treatment manner (Mean±STDEV) of Type-2 diabetic patients or Type-2 diabetes with hypertension patients**

| Variables | Mean±STDEV users of ADM only[A] | Mean±STDEV users of ADM and AHT[B] | p value |
|---|---|---|---|
| Age (years) | 54.1±6.3 | 56.6±5.7 | 0.0738 |
| HbA1C (%) | 10.36±2.3 | 8.86±1.6 | 0.0013 |
| Systolic BP (mmHg) | 122.7±6.7 | 149.5±18.8 | < 0.0001 |
| Diastolic BP (mmHg) | 80.59±7.3 | 85.2±7.3 | 0.0078 |
| hs-CRP (mg/L) | | | |
| Male | 2.00±0.9 | 1.8±0.8 | 0.3089 |
| Female | 6.7±4.5 | 2.6±1.4 | <0.0001 |

[A]Total number=34, men (14), women (20). [B]Total number=42, men (12), women (30). ADM: Antidiabetic, AHT: Antihypertensive; STDEV: Standard deviation, HbA1c: Glycated hemoglobin, hs-CRP: Highly sensitive, CRP: Statistically significant values are shown in bold font (significance *P*<0.05), BP: Blood pressure

Treatment manner had no effect on mean hs-CRP in men; however, there was a significant direct correlation of hs-CRP with HbA1c (p=0.002) and triglycerides (p=0.009), but inversely with HDL-C (p=0.011) in women receiving ADM drugs only. Furthermore, the treatment manner had no effect on mean hs-CRP in men and women receiving ADM with AHT drugs (Table 2).

## DISCUSSION

This study was designed to investigate the association between drug treatments, glycemic control, and serum level of CRP in Iraqi patients receiving ADM drugs or ADM with AHT drugs.

Diabetes mellitus is associated with numerous complications. Hyperglycemia increased BP, dyslipidemia, oxidative stress, and inflammation are all characteristics of type 2 diabetes mellitus and are concerned in the development of vascular complications [23,24] so that control of diabetes leads to decreased risk of these complications. Most of the diabetic patients involved in our study were uncontrolled regardless of which ADM drug treatment was used. This study revealed that the lower mean of HbA1c found in patients receiving ADM with AHT drugs compared with those on ADM drugs only. Few studies are found concerned in the combined effects of ADM with AHT drugs on the HbA1c level.

The previous study revealed that the adverse effect of some AHT drugs on blood glucose homeostasis may influence their cardiovascular protection role. Different classes of AHT drugs have different effects on blood glucose homeostasis. Some of the AHT drugs such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, some of the CCBs such as azelnidipine and manidipine and some of the β-blockers such as carvedilol and nebivolol revealed to have advantageous effects on glucose metabolism. Conversely, diuretics and other β-blockers have an unfavorable effect on glucose metabolism [25].

Lower mean hs-CRP was found in women receiving ADM with AHT drugs compared with those on ADM drugs only. Treatment manners had no effect on mean hs-CRP in men; however, there was a significant direct correlation of hs-CRP with HbA1c and triglycerides, but inversely with HDL-C in women receiving ADM drugs only. Furthermore, the treatment manners had no effect on mean hs-CRP in men and women receiving ADM with AHT drugs.

## CONCLUSION

These results indicated that high levels of hs-CRP are associated with poor glycemic control and dyslipidemia, therefore, consequently increased cardiovascular risk.

Due to the valuable effect of hs-CRP as a cardiovascular risk predictor, it should be included in routine monitoring of Type-2 diabetic patients.

## AUTHOR'S CONTRIBUTION

None.

**Table 2: Correlations between hs-CRP with HbA1c, lipid profile, and BP in men and women of type -2 diabetic patients or type-2 diabetes with hypertension patients**

| hs-CRP | HbA1c | Cholesterol | TG | HDL-C | SBP | DBP |
|---|---|---|---|---|---|---|
| hs-CRP | r=−0.328 | r=−0.043 | r=−0.052 | r=0.01 | r=−0.045 | r=0.142 |
| (DM group) male (n=14) | p=0.147 | p=0.852 | p=0.823 | p=0.965 | p=0.845 | p=0.538 |
| Female | r=0.537 | r=0.329 | r=0.466 | r=−0.455 | r=−0.104 | r=−0.132 |
| (n=20) | p=0.002 | p=0.147 | p=0.009 | p=0.011 | p=0.584 | p=0.487 |
| hs-CRP | r=0.314 | r=−0.310 | r=0.150 | r=−0.370 | r=0.023 | r=0.002 |
| (DM+HT group) male (n=12) | p=0.320 | p=0.326 | p=0.643 | p=0.236 | p=0.943 | p=0.994 |
| Female | r=0.043 | r=0.215 | r=−0.044 | r=0.357 | r=−0.078 | r=−0.043 |
| (n=30) | p=0.822 | p=0.254 | p=0.818 | p=0.053 | p=0.682 | p=0.821 |

DM: Diabetes mellitus, HT: Hypertension, HbA1c: Glycated hemoglobin, TG: Triglyceride, HDL-C: High-density lipoprotein cholesterol, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, hs-CRP: Highly sensitive, CRP: Statistically significant values are shown in bold font (significance P<0.05)

**CONFLICTS OF INTEREST**

The authors declare that they have no conflicts of interest.

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