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Increased Serum Cytokines Levels in Type 2 Diabetes Mellitus Associated with Arterial Hypertension: A Link to Cardio-Metabolic Risk Factors

Arteryel Hipertansiyonla İlişkili Tip 2 Diabetes Mellitusta Yüksek Serum Sitokin Düzeyleri: Kardiyometabolik Risk Faktörleri ile Bir Bağlantı

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Abstract

Purpose: Serum levels of cytokines as well as the inflammatory markers are increased in type 2 diabetes (T2D) patients. Few studies mention the association of hypertension with proinflammatory and inflammatory biomarkers in T2D patients. This study aimed to test the hypothesis that there is alteration in serum levels of cytokines in T2D patients with hypertension compared with normotensive T2D patients taking into consideration the cardio-metabolic risk factors, such as obesity and dyslipidemia.

Material and Method: A cross-sectional study was carried out in the Center of Diabetes Mellitus in Erbil in cooperation with College of Pharmacy-Hawler Medical University and College of Medicine, Al-Mustansiriya University in Iraq. A total of 180 patients with T2D were classified as normotensive (group 1) and hypertensive (group 2). Cardio-metabolic risk factors were evaluated via measuring body weight, body mass index, waist circumference, blood pressure, fasting serum glucose and lipid profile, glycosylated hemoglobin A1c and high-sensitivity C-reactive protein. Serum interleukin- (IL)-1β, IL-17, and tumor necrosis factor-alpha (TNF-α) were measured using the enzyme-linked immunosorbent assay method.

Results: The measurements of cardio-metabolic risk factors in group 2 were significantly higher than in group 1. Significant high serum levels of IL-1β, IL-17, TNF-α and high-sensitivity C-reactive protein were observed among group 2 patients. Fasting serum triglyceride levels significantly correlated with IL-17 and TNF-α among groups 1 and 2 patients whereas significantly correlated with IL-1β among group 2 patients only.

Discussion: Proinflammatory and inflammatory markers are significantly high among patients with T2D with hypertension. There is an inverse relationship between the components of metabolic syndrome and the cytokines levels in group 2 patients.

Keywords: Type 2 diabetes, hypertension, cytokines

Öz

Amaç: Tip 2 diyabet (T2D) hastalarında enflamatuvar göstergelerin yanı sıra serum sitokinleri de artmıştır. Az sayıda çalışmada pro-enflamatuvar ve enflamatuvar göstergelerin hipertansif T2D hastalarda arttığı ele alınmıştır. Bu çalışmada obezite ve dislipidemi gibi kardiyo-metabolik risk faktörleri de dikkate alınarak T2D'li hipertansif hastalarla normotansif T2D hastalar serum sitokin düzeylerinin farklı olduğu hipotezi bakımından karşılaştırıldı.

Gereç ve Yöntem: Erbil Diyabet Merkezi ile birlikte Hawler Üniversitesi Farmakoloji Fakültesi ve Irak Al-Mustansiriya Üniversitesi Tıp Fakültesi işbirliğinde kesitsel bir çalışma yürütülmüştür. Toplamda 180 hasta normotansif (grup 1) ve hipertansif (grup 2) olarak araştırmaya dahil edildi. Kardiyo-metabolik risk faktörleri vücut ağırlığı, vücut kitle indeksi, bel çevresi, kan basıncı, açlık serum glukozu, lipid profili, glikozile hemoglobin ve yüksek duyarlılıkta C-reaktif protein ölçülerek değerlendirildi. Serum interlökin (İL)-1β, İL-17, tümör nekrozis factor-alfa (TNF-α) enzime bağlı immün assay tekniği ile ölçüldü.

Bulgular: Kardiyo-metabolik risk faktörleri grup 2 hastalarında daha yüksekti. Grup 2'de anlamlı yüksek serum İL-1β, İL-17, TNF-α düzeyleri gözlendi. Grup 1 ve 2'de hastalarında açlık serum trigliserid düzeyleri ve İL-17, TNF-α düzeyleri arasında anlamlı korelasyon varken İL-1β için yalnızca grup 2 hastalarında anlamlı korelasyon vardı.

Tartışma: Pro-enflamatuvar ve enflamatuvar göstergeler hipertansif T2D hastalarda belirgin yüksek değerlerde saptandı. Hipertansif T2D hastalarda kardiyo-metabolik sendromun ciddiyeti arttıkça sitokin düzeyleri azalma eğilimindeydi.

Anahtar kelimeler: Tip 2 diyabet, hipertansiyon, sitokinler

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Introduction

Interleukin (IL) 17 and T-helper 17 (Th17) cells play a role in the pathogenesis of different autoimmune diseases, such as systemic psoriasis, rheumatoid arthritis, inflammatory bowel disease, lupus erythematosus, and multiple sclerosis (1) as well as in type 1 diabetes (T1D) pathogenesis (2). In T1D, the immune cells and their cytokines inflammatory mediators are involved in the destruction of pancreatic beta cells (3). Therefore, this type of diabetes mellitus (DM) is characterized by alterations in IL-1 beta (IL-1β), IL-6, tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) levels (4,5,6). In type 2 DM (T2D), IL-1β is also increased and the IL-6 is involved in the development of insulin resistance (7). In T2D complicated with retinopathy, serum levels of IL-6, IL-17, interferon-γ, TNF-α, IL-2 and IL-10 are increased (8). Experimental and human studies explored the role of IL-1β in the production of IL-17 by human adipose tissue CD4+ T cells that are involved in obesity-associated T2D (9). Patients with T2D and arterial hypertension have an increased secretion of TNF-α, IL-6, IL-17 and reduced secretion of IL-10 in comparison with healthy individuals (10). In their study, Mahmoud and Al-Ozairi (11) reported the following findings: T cells were responsible for the development of cardiovascular complications; there was a significant increase in expression of CD4+TNF-α, CD4+IL-1β+, and IL-17+T and a significant correlation between low density lipoprotein and CD4+IL-1β. Another study reported a significant negative correlation between high density lipoprotein and CD4+IL-17 in T2D patients with metabolic disorder (12). In a study by Sumarac-Dumanovic et al. (13), it was found that in newly diagnosed T2D, the serum level of IL-17 was increased but it did not show significant correlation with the insulin resistance index while the serum IL-17 was significantly reduced after therapeutic glucose regulation. The rational of this study is based upon the experimental and clinical studies that on the pathogenesis of hypertension and T2D. There is no doubt that low-grade inflammation playe a role in the pathogenesis of essential hypertension and DM. Accordingly, we can expect to have abnormal levels of proinflammatory markers in the atherosclerotic plaques in hypertension or in the circulating biological fluids. Therefore, the aim of the study was to test the hypothesis that there is alteration in serum levels of cytokines in T2D patients with hypertension compared with normotensive T2D patients taking in consideration the cardio-metabolic risk factors; obesity and dyslipidemia.

Materials and Methods

A cross sectional study was carried out in the Center of Diabetes Mellitus in Erbil in cooperation with College of Pharmacy-Hawler Medical University and College of Medicine, Al-Mustansiriya University in Iraq. The study was conducted according to the principles of the Declaration of Helsinki and with the approval of the local ethics review board. Written informed consent was obtained from each patient before enrollment into the study. The inclusion criteria were T2D without or with hypertension treated with oral hypoglycemic agents alone and/or once- or twice-daily insulin according to the clinical status of the patient. Hypertensive patients were treated with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and/or calcium channel blockers. The present study excluded patients with a history of rheumatoid arthritis, hematological, neoplastic, renal, liver or thyroid diseases, as well as those receiving treatment with anti-inflammatory drugs. Patients with acute or chronic infections and autoimmune diseases (e.g. systemic lupus erythematous) were also excluded from the study. The patients were divided into two groups:

Group 1 (n=90): Normotensive T2D patients.

Group 2 (n=90): Hypertensive T2D patients.

Data on demographical characteristics, medical history and treatment were collected in the center. Modifiable risk factors, events or complications, and current therapy were recorded. A person who reported smoking on admission was defined as current smoker. Height, weight, waist circumference, and hip circumference were measured, and body mass index (BMI) was calculated using Quetlete's equation.

BMI (kg/m^2) = weight (kg)/height2 (m)

Blood pressure was measured in the sitting position and the mean of three readings was taken. The mean arterial blood pressure was determined using the following equation: diastolic blood pressure + (1/3 x pulse pressure).

Pulse pressure is equal to systolic-diastolic blood pressure.

Peripheral venous blood was drawn into tubes immediately after admission, then, the samples were centrifuged at 2500 rpm for 10 min, and the sera were separated for determination of fasting serum glucose, glycosylated hemoglobin (HbA_{1c}) (%) and lipid profile. The determinants of lipid profile included fasting serum cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein and very low-density lipoprotein. The principle of measurement of the fasting serum glucose and lipid profile was an enzymatic-based reaction. The absorbance of serum reagent reaction was detected by visible spectrophotometry at specific wavelength for each test according to the instruction of the manufacturers. Quantitative determination of serum high-sensitivity (hs) CRP, IL-17, IL-1β, and TNF-α was carried out using the enzyme-linked immunosorbent assay (ELISA) method. The principle of the ELISA technique is that the wells of each kit are pre-coated with antibody of each inflammatory and proinflammatory markers and an antigen (the proinflammatory marker in the circulating biological fluid) -antibody reactions occur to give a colored solution after adding the stop-reaction solution and then the absorbance is measured at 450 nm. A standard curve for each biological fluid is constructed and the concentration of each marker is calculated from the linear regression equation of the standard curve.

Statistical Analysis

Data were expressed as number, percent, and means ± standard deviation. Unpaired student's t-test, was used to evaluate the differences between the two groups and a simple (Pearson's) correlation test was used to detect the correlations between the inflammatory markers and cardio-metabolic risk factors. For all tests, a two-tailed $p \leq 0.05$ was considered statistically significant. All calculations were made using Excel 2003 program for Windows.

Results

A total of 180 patients were enrolled in this study. The mean age of group 1 patients was significantly higher than that of group 2 patients (Table 1). Current smoking was found in 55.6% and 61.1% of group 1 and group 2 patients, respectively. The mean duration of DM was significantly short in group 2 patients compared with group 1 (10.2 versus 11.04). There were no significant differences (p>0.05) in anthropometric measurements between men in groups 1 and 2 (Table 1). The mean value of body weight and BMI in group 2 women was significantly higher than in women of group 1 (p<0.001) (Table 1). Table 2 shows that four determinants of blood pressure were significantly (p<0.001) higher in group 2 patients compared with group 1 patients. There were no significant differences in the blood pressure determinants between men and women in each group (p>0.05). Table 3 shows that the fasting serum lipid profile and glycemic status values were significantly higher in both genders of group 2 compared that in group 1 (p<0.001). The mean high-density lipoprotein level in both genders of group 2 was significantly less than those in group 1. Further analysis revealed that the mean level of high-density lipoprotein in women was significantly higher than men in each group and the HbA_{1c} percent among women was significantly lower than men in group 2 (Table 3). Table 4 shows that the proinflammatory cytokines were significantly increased in group 2 patients than in patients of group 1 (p<0.001). Serum levels of IL-17, IL-1β and TNF-α were increased by >2.2, 1.3 and 1.9 folds of that in group 1 patients respectively. The serum levels of IL-1β were significantly higher among men than among women in group 2 (p=0.04). The levels of serum hs-CRP were significantly increased among group 2 patients and amounted 1.2 folds of that among group 1 patients (p<0.001). Table 5 shows that the only significant correlation between cardio-metabolic risk factors and inflammatory markers in normotensive diabetic patients were observed between IL-17 and serum triglycerides (r=+0.219, p=0.02), TNF-α and mean arterial pressure (r=-0.340, p=0.001), and with serum triglycerides level (r=+0.330, p=0.002). In hypertensive diabetic patients (group 2), significant inverse correlations were observed between the pro-inflammatory cytokines and serum triglycerides levels (Table 6).

Discussion

The results of this study show that serum levels of pro-inflammatory and inflammatory markers are significantly higher among diabetic-hypertensive patients compared with diabetic-normotensive patients. These markers show a significant correlation with serum triglycerides levels. High BMI values observed in both groups, but they were significantly higher among group 2 patients and, therefore, it is an associated risk factor for

Table 1. Characteristics of the study

	Group 1 (n=90)	Group 2 (n=90)
Gender Men:Women	46:44	49:41
Age (year)	66.0±5.0	63.1±4.8*
Smoking current	50 (55.6)	55 (61.1)
Duration of disease (year)	10.2±1.90	11.04±2.36**
Men		
Weight (kg)	100.2±4.4	101.5±5.9
Height (m)	1.72±0.03	1.72±0.04
Body mass index (kg/m^2)	33.7±1.3	34.4±2.2
Women		
Weight (kg)	90.1±4.1	95.7±5.9*
Height (m)	1.69±0.02	1.69±0.04
Body mass index (kg/m^2)	31.6±1.2	33.6±2.0*

The results are expressed as number (%) and mean ± standard deviation. *p<0.001, **p=0.01 compared with corresponding values in group 1

Table 2. Blood pressure measurements

Blood pressure (mmHg)	Group 1		Group 2	
	Men (n=49)	Women (n=41)	Men (n=46)	Women (n=44)
Systolic	123.5±4.3	123.3±5.7	150.6±5.6*	150.5±5.6*
Diastolic	77.4±4.5	78.7±3.7	90.8±3.6*	90.7±3.3*
Pulse BP	46.1±5.7	44.6±6.8	59.8±5.4*	59.8±5.4*
Mean arterial	92.8±3.6	93.5±3.1	110.6±3.4*	110.6±3.4*

The results are expressed as mean ± standard deviation. *p<0.001 compared with corresponding values in group 1. BP: Blood pressure

Table 3. Fasting lipid profile and glucose determinants

Measurements	Group 1		Group 2	
	Men (n=49)	Women (n=51)	Men (n=46)	Women (n=54)
Total cholesterol (mg/dL)	236.6±12.8	235.4±15.7	290.2±20.1*	291.7±19.8*
Total triglycerides (mg/dL)	195.9±11.1	195.3±11.8	277.5±34.6*	266.8±35.0*
Low density lipoprotein (mg/dL)	154.6±13.7	150.4±15.8	198.5±20.5*	196.5±20.5*
Very low density lipoprotein (mg/dL)	39.2±2.2	39.1±2.4	55.5±6.9*	53.5±7.0*
High density lipoprotein (mg/dL)	42.8±3.3	45.9±3.2†	36.2±3.0*	41.9±4.0*†
Glucose (mg/dL)	249.6±41.3	253.3±34.3	274.4±35.1*	282.7±35.6*
Glycosylated hemoglobin (%)	7.93±0.57	7.90±0.46	9.0±1.0*	8.5±0.9*††

The results are expressed as mean ± standard deviation. *p<0.001 compared with corresponding values in group 1, †p<0.001, ††p=0.02 compared with men gender in each group

high blood pressure. There is evidence that the severity of obesity is significantly correlated with blood pressure levels even in healthy subjects (14). The significant longer duration of DM among group 2 patients explained the association of hypertension as one of the outcomes of long-standing T2D is macrovascular complication (15). The pattern of lipid profile was atherogenic in both groups and in both genders. This pattern accelerates the development of hypertension among group 2 patients as dyslipiemia is a common event in T2D and play a role in the development of atherosclerosis, besides, it is one pillar of cardio-metabolic risk factors. A recent study demonstrated that there was a significant linear correlation between blood pressure and lipid profiles and serum cholesterol levels showed the strongest association with blood pressure in T2D (16). The significant high levels of fasting serum glucose and HbA_{1c} among group 2 patients was not a dependent factor responsible for high blood pressure. Chew et al. (17) found that the determinants of uncontrolled hypertension included ethnicity, older age, recent diagnosis of DM and overweight. Co-morbidity of T2D and hypertension may be related to significant high levels of proinflammatory and inflammatory biomarkers among group 2 patients in this study. Recently, Kologrivova et al. (10) found significant high levels of IL-17 and TNF-α among patients with T2D complicated with arterial hypertension. The significant high levels of serum IL-1β and hs-CRP among group 2 patients indicate that low-grade inflammation existed and shared in the pathogenesis of hypertension as a complication of T2D. Mahmoud and Al-Ozairi (11) suggested that T cells are involved in the development of T2D and its complications as the authors found a significant expression of IL-1β, IL-17 and TNF-α in T2D and they were significantly correlated with hyperglycemia and dyslipidemia. The results of this study add a new information that the proinflammatory cytokines (IL-17 and TNF-α) significantly correlated with fasting serum triglycerides in normotensive T2D patients while the significant inverse correlations of IL-1β, IL-17 and TNF-α with serum levels of triglycerides were observed among group 2 patients (18). This finding has been reported for the first time and it indicates that the cytokines levels tended to be decreased as the severity of cardio-metabolic risk factors increased. A previous study found a significant positive independent correlation between serum triglycerides and TNF-α or other inflammatory markers

Table 4. Proinflammatory cytokines and inflammatory marker levels

Measurements	Group 1		Group 2	
	Men (n=49)	Women (n=41)	Men (n=46)	Women (n=44)
Interleukin 17	29.8±5.9	29.1±5.7	63.3±7.5*	63.1±8.5*
Interleukin 1β	43.1±7.5	41.4±7.2	55.6±13.0*	54.7±13.0*†
Tumor necrosis factor-α	20.4±4.1	20.3±3.7	39.2±8.1*	39.2±7.6*
High sensitivity C-reactive protein (µg/mL)	8.3±1.2	8.4±1.2	9.8±1.5*	9.7±1.5*

The results are expressed as mean ± standard deviation. *p<0.001 compared with corresponding values in group 1, †p=0.04 compared with men gender in group 2

Table 5. Correlations between cardio-metabolic risk factors and inflammatory markers in normotensive diabetic patients (group 1)

	Body mass index (kg/m²)	Mean arterial blood pressure (mmHg)	Serum triglycerides level (mg/dL)	Serum high density lipoprotein level (mg/dL)	Glycosylated hemoglobin (%)
Interleukin 17	0.109	-0.2	0.219*	-0.126	-0.128
Interleukin 1β	0.062	0.033	-0.048	-0.003	-0.201
Tumor necrosis factor-α	0.008	-0.340***	0.330**	-0.103	-0.126
High sensitivity C-reactive protein (µg/mL)	0.046	-0.046	-0.037	0.086	0.166

The results are expressed as correlation factors, *p=0.02; **p=0.002; ***p=0.001.

Table 6. Correlations between cardio-metabolic risk factors and inflammatory markers in hypertensive diabetic patients (group 2)

	Body mass index (kg/m²)	Mean arterial blood pressure (mmHg)	Serum triglycerides level (mg/dL)	Serum high density lipoprotein level (mg/dL)	Glycosylated hemoglobin (%)
Interleukin 17	-0.142	-0.044	-0.305*	0.048	-0.014
Interleukin 1β	-0.104	0.033	-0.385**	0.065	-0.138
Tumor necrosis factor-α	-0.207	0.077	-0.504***	0.038	-0.188
High sensitivity C-reactive protein (µg/mL)	-0.018	-0.049	-0.04	-0.016	0.035

The results are expressed as correlation factors, *p=0.005, **p=0.001, ***p<0.001

in autoimmune diseases that express a profound inflammatory process (19). Therefore, the possibility of considering the serum triglyceride levels as an inflammatory marker is arisen. Surendar et al. (20) reported an association between IL-17 and blood pressure, with an increase in the number of metabolic risk factors, the IL-17 levels showed a decline.

Conclusion

We conclude that proinflammatory and inflammatory markers, including IL-1β, IL-17, and TNF-α, are available in significant high concentrations in T2D patients with hypertension. Serum triglycerides levels show the strongest positive correlation with the cytokines (IL-17, TNF-α) among T2D-normotensive patients and such correlation followed an inverse pattern among T2D-hypertensive patients suggesting the severity of cardio-metabolic risk factors.

Ethics

Ethics Committee Approval: The study was conducted according to the principles of the Declaration of Helsinki and with the approval of the local ethics review board, Informed Consent: All the participants were informed and signed the consent form.
Peer-review: Externally and Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Zhian Dezayee and Marwan Al-Nimer, Concept: Marwan Al-Nimer, Design: Marwan Al-Nimer, Data Collection or Processing: Zhian Dezayee, Analysis or Interpretation: Marwan Al-Nimer, Literature Search: Zhian Dezayee, Marwan Al-Nimer, Writing: Marwan Al-Nimer.
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References

1. Maddur MS, Miossec P, Kaveri SV, Bayry J. Th17 cells: biology, pathogenesis of autoimmune and inflammatory diseases, and therapeutic strategies. Am J Pathol. 2012;181:8-18.
2. Emamaullee JA, Davis J, Merani S, Toso C, Elliott JF, Thiesen A, Shapiro AM. Inhibition of Th17 cells regulates autoimmune diabetes in NOD mice. Diabetes. 2009;58:1302-1311.
3. Rowe PA, Campbell-Thompson ML, Schatz DA, Atkinson MA. The pancreas in human type 1 diabetes. Semin Immunopathol. 2011;33:29-43.
4. Lechleitner M, Koch T, Herold M, Dzien A, Hoppichler F. Tumour necrosis factor-alpha plasma level in patients with type 1 diabetes mellitus and its association with glycaemic control and cardiovascular risk factors. J Intern Med. 2000;248:67-76.
5. Chase HP, Cooper S, Osberg I, Stene LC, Barriga K, Norris J, Eisenbarth GS, Rewers M. Elevated C-reactive protein levels in the development of type 1 diabetes. Diabetes. 2004;53:2569-2573.
6. Dogan Y, Akarsu S, Ustundag B, Yilmaz E, Gurgoze MK. Serum IL-1beta, IL-2, and IL-6 in insulin-dependent diabetic children. Mediators Inflamm. 2006;2006:59206.
7. Feve B, Bastard JP. The role of interleukins in insulin resistance and type 2 diabetes mellitus. Nat Rev Endocrinol. 2009;5:305-311.
8. Zhang C, Xiao C, Wang P, Xu W, Zhang A, Li Q, Xu X. The alteration of Th1/Th2/Th17/Treg paradigm in patients with type 2 diabetes mellitus: Relationship with diabetic nephropathy. Hum Immunol. 2014;75:289-296.
9. Dalmas E, Venteclef N, Caer C, Poitou C, Cremer I, Aron-Wisnewsky J, Lacroix-Desmazes S, Bayry J, Kaveri SV, Clement K, Andre S, Guerre-Millo M. T cell-derived IL-22 amplifies IL-1beta-driven inflammation in human adipose tissue: relevance to obesity and type 2 diabetes. Diabetes. 2014;63:1966-1977.
10. Kologrivova IV, Suslova TE, Koshel'skaya OA, Vinnitskaya IV, Trubacheva OA. System of matrix metalloproteinases and cytokine secretion in type 2 diabetes mellitus and impaired carbohydrate tolerance associated with arterial hypertension. Bull Exp Biol Med. 2014;156:635-638.
11. Mahmoud F, Al-Ozairi E. Inflammatory cytokines and the risk of cardiovascular complications in type 2 diabetes. Dis Markers. 2013;35:235-241.
12. Zeng C, Shi X, Zhang B, Liu H, Zhang L, Ding W, Zhao Y. The imbalance of Th17/Th1/Tregs in patients with type 2 diabetes: relationship with metabolic factors and complications. J Mol Med (Berl). 2012;90:175-186.
13. Sumarac-Dumanovic M, Jeremic D, Pantovic A, Janjetovic K, Stamenkovic-Pejkovic D, Cvijovic G, Stevanovic D, Micic D, Trajkovic V. Therapeutic improvement of glucoregulation in newly diagnosed type 2 diabetes patients is associated with a reduction of IL-17 levels. Immunobiology. 2013;218:1113-1118.
14. Okafor C, Anyaehie U, Ofoegbu E. The magnitude of obesity and its relationship to blood pressure among the residents of enugu metropolis in South East Nigeria. Ann Med Health Sci Res. 2014;4:624-629.
15. Picard F, dos Santos P, Catargi B. [Diabetes, obesity and heart complications]. Rev Prat. 2013;63:759-764.
16. Nasri H, Behradmanesh S, Ahmadi A, Baradaran A, Nasri P, Rafieian-Kopaei M. Association of serum lipids with level of blood pressure in type 2 diabetic patients. J Renal Inj Prev. 2014;3:43-46.
17. Chew BH, Mastura I, Shariff-Ghazali S, Lee PY, Cheong AT, Ahmad Z, Taher SW, Haniff J, Mustapha FI, Bujang MA. Determinants of uncontrolled hypertension in adult type 2 diabetes mellitus: an analysis of the Malaysian diabetes registry 2009. Cardiovasc Diabetol. 2012;11:54.
18. Esser N, Legrand-Poels S, Piette J, Scheen AJ, Paquot N. Inflammation as a link between obesity, metabolic syndrome and type 2 diabetes. Diabetes Res Clin Pract. 2014;105:141-150.
19. Svenungsson E, Gunnarsson I, Fei GZ, Lundberg IE, Klareskog L, Frostegard J. Elevated triglycerides and low levels of high-density lipoprotein as markers of disease activity in association with up-regulation of the tumor necrosis factor alpha/tumor necrosis factor receptor system in systemic lupus erythematosus. Arthritis Rheum. 2003;48:2533-2540.
20. Surendar J, Aravindhan V, Rao MM, Ganesan A, Mohan V. Decreased serum interleukin-17 and increased transforming growth factor-beta levels in subjects with metabolic syndrome (Chennai Urban Rural Epidemiology Study-95). Metabolism. 2011;60:586-590.