

Study of The relationship between uric acid level and some lipid profile for heart disease patients in Alnasseriya city

Wesam Rissan Naif*

الخلاصة

أجريت هذه الدراسة لتقييم العلاقة بين مستوى حمض اليوريك و بعض الدهون في الدم لمرضى القلب في مدينة الناصرية حيث تم أخذ عينات الأمصال لـ (75) مريض، بالإضافة إلى مجموعة السيطرة التي تشمل (45) من الأشخاص الأصحاء وشملت الدراسة الحالية متغيرات العمر والوزن وقياس تراكيز كل من الكوليسترول ، البروتين الدهني العالي الكثافة HDL، البروتين الدهني الواطئ الكثافة LDL ، الدهون الثلاثية ، و حمض اليوريك . وأوضحت الدراسة عدم وجود فروق ذات دلالة إحصائية ($P>0.05$) في متوسط العمر للمرضى بالمقارنة مع الأشخاص الأصحاء مع وجود فرق كبير لارتفاع متوسط الوزن للمرضى مقارنة مع الأشخاص الأصحاء ($P<0.01$). المستويات المعنوية العالية ($P< 0.01$) في متوسط تراكيز كل من الكوليسترول ، LDL والدهون الثلاثية في المرضى مقارنة مع الأشخاص الأصحاء ، ولا يوجد فرق معنوي ($P>0.05$) في متوسط تركيز HDL في كلا المجموعتين. كما أظهرت درجة عالية من الزيادة المعنوية ($P< 0.01$) في متوسط تركيز حمض اليوريك في المرضى الذين يعانون أمراض القلب عند مقارنة النتائج مع متوسط تركيز حمض اليوريك في الأشخاص الأصحاء . في هذه الدراسة أظهرت أن هناك علاقة ارتباط عالية ذات دلالة إحصائية بين حمض اليوريك وكل من الكوليسترول، LDL ($P< 0.01$) وهناك علاقة ارتباط مع حمض اليوريك والدهون الثلاثية ($P< 0.05$) ولكن لا توجد علاقة ارتباط بين حمض اليوريك و HDL ($P>0.05$)...

Abstract

The present study was carried out to evaluate the relationship between uric acid level and some lipid profile for heart disease patients in Alnasseriya city in the sera samples of (75) patients, in addition to control group involving (45) apparently healthy.

The current study included age ,weight , cholesterol, HDL , LDL, triglyceride ,and uric acid concentration. The study clarified no significant differences ($p>0.05$) in mean age of patients when compared with healthy control and high significant difference of mean weight between two groups ($p<0.01$). A highly significant elevated ($P< 0.01$) in the mean concentration of cholesterol, LDL and triglyceride in patients when compared with healthy control ,no significant ($P> 0.05$) in the mean concentration of HDL in both two groups .It also showed a highly significant increased ($P<0.01$) in the mean concentration of uric acid in heart disease patients when the results compared with the mean concentration of uric acid in healthy control . In the present study showed there was high significant correlation between uric acid and cholesterol, LDL ($P<0.01$) and significant correlation with triglyceride ($P<0.05$) but no significant correlation between uric acid and HDL ($P>0.05$).

*Community Health Dept. Technical Institute Al-Nassiria

Introduction

Heart disease is an umbrella term for a variety of different diseases affecting the heart [1,2] or is any disorder that affects the heart's ability to function normally [1,3]

Types of heart disease

A. Coronary heart disease B. Cardiomyopathy C. Cardiovascular disease
D. Heart failure E. Hypertensive heart disease F. Inflammatory heart disease
G. Valvular heart disease [4].

Cholesterol is classified as a sterol (a contraction of steroid and alcohol) found in the cell membranes and transported in the blood plasma of all animals. It is an essential component of mammalian cell membranes where it is required to establish proper membrane permeability and fluidity. Although cholesterol is essential for life, high levels in circulation are associated with atherosclerosis. [5]

According to the lipid hypothesis, abnormally high cholesterol levels (hypercholesterolemia), or, more correctly, higher concentrations of LDL (Low density lipoprotein cholesterol) and lower concentrations of functional HDL (High density lipoprotein cholesterol) are strongly associated with cardiovascular disease because these promote atheroma development in arteries (atherosclerosis). This disease process leads to myocardial infarction (heart attack), stroke and peripheral vascular disease. Since higher blood LDL, especially higher LDL particle concentrations and smaller LDL particle size, contribute to this process more than the cholesterol content of the LDL particles, LDL particles are often termed "bad cholesterol" because they have been linked to atheroma formation. On the other hand, high concentrations of functional HDL, which can remove cholesterol from cells and atheroma, offer protection and are sometimes referred to colloquially as "good cholesterol". These balances are mostly genetically determined but can be changed by body build, medications, food choices and other factors [6,7].

Triglyceride an unsaturated fat. It is the main constituent of vegetable oil and animal fats. They play an important role in metabolism as energy sources and transporters of dietary fat. Triglycerides cannot pass through cell membranes freely. In the human body, high levels of triglycerides in the bloodstream have been linked to atherosclerosis, and, by extension, the risk of heart disease and stroke. The risk can be partly accounted for by a strong inverse relationship between triglyceride level and HDL-cholesterol level [8].

Uric acid is the final oxidation (breakdown) product of purine metabolism and is excreted in urine. However, the independent role of serum uric acid as a risk factor has been undergoing debate for years. In fact, mild hyperuricemia is often a concomitant finding of obesity, lipid abnormalities, and insulin resistance, all of which are components of the metabolic syndrome [10,11]. The association between serum uric acid and early hypertensive and

atherosclerotic organ damage is intriguing and suggests that mild hyperuricemia might be a marker of incipient cardiovascular involvement. Several pathophysiological mechanisms linking SUA to cardiovascular damage at the cellular and tissue level have been proposed, including proliferation of vascular smooth muscle cells, stimulation of the inflammatory pathway [16]. In addition, uric acid has proved to be an excellent marker for tissue ischemia and endothelial dysfunction [18] and it has been shown to play a role in the development of atherosclerotic lesions [19].

Materials and Methods

A total of 75 patients with heart diseases (35 women,40 men) were entered present study ,the median age of patients was 64 years (range 47-75) .They were admitted to the coronary care units of AL-Hussain education hospital. 45 healthy non smoking (20 women,25 men) median age 61 years old (range 48-73) were normal healthy control ,sinus to period from (May. 2010 to the end of Jul. 2011).

Total serum cholesterol is determined by enzymatic hydrolysis and oxidation [20], the high density lipoprotein-cholesterol (HDL-C) was determined by the precipitant method [21] , triglyceride (TG) were estimated by the enzymatic colorimetric method [22].

The determined of low density lipoprotein-cholesterol (LDL-C) can be calculated mathematically [23] :
$$\text{LDL-C} = \text{Cholesterol} - (\text{TG}/2.2) - \text{HDL-C}$$

serum uric acid was measured with use of an enzymatic colorimetric method [24].

Statistical Analysis:

The suitable statistical methods were used in order to analyze and assess the results, they include the followings:

1- Descriptive statistics:

Summary statistic of the readings distribution [mean, SD, T-Test , Pearson Correlation (r)]

2- Graphical presentation by (Bar & scatter –chart)

Results& Discussions

Table (1) :Mean distribution of age and weight body in studied groups (Healthy control and Patient)

Characteristic Mean ± SD	Healthy control (H)			Patients (P)			T-Test	P-value	
	Female (F1) N=20	Male (M1) N=25	Total N=45	Female (F2) N=35	Male (M2) N=40	Total N=75			
Age/year	60.2±7.2	61.5±6.7	60.9±6.9	61.8±7.0	63.9±6.4	62.9±6.7	0.170	0.790	NS
Body weight\Kg	70.6±4.9	74.9±4.8	73.0±5.3	79.3±4.1	80.9±7.4	80.1±6.1	5.425	0.000	HS

HS: High significance when P<0.01
P>0.05

NS: No significance

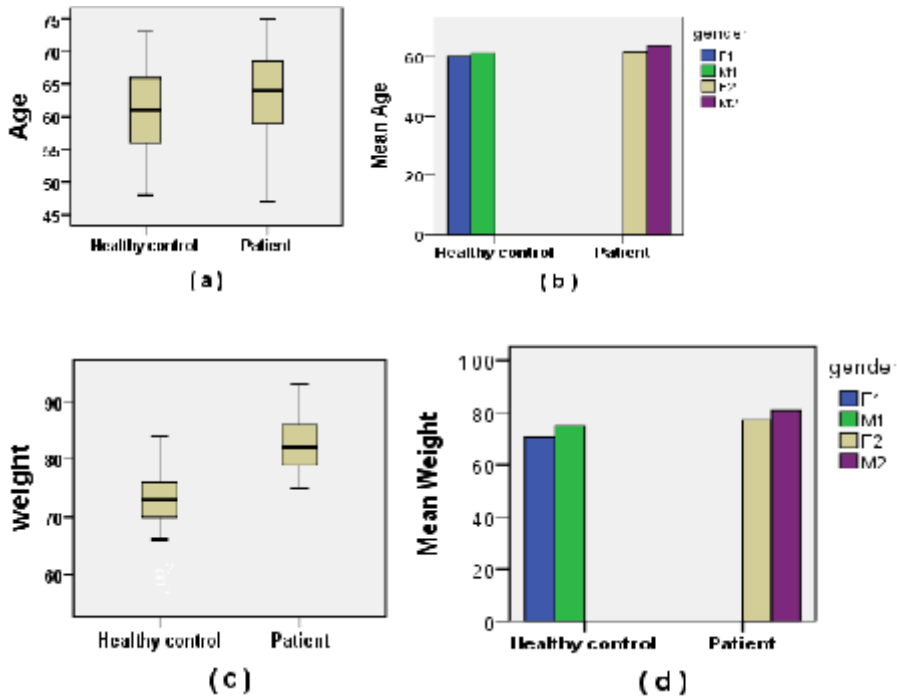


Figure (1- a,b)(1-c,d):Distribution of studied groups according to age and weight body

Table(1) and figure (1-a,b) showed that no statistically differences in age were observed between patient groups and healthy control groups ($p>0.05$), Heart diseases occur in middle age because they have stress due to many responsibilities with their families and works and because of the occurrence of other risk factors like diabetes mellitus and hypertension in this age which independent to sex, the majority of the sample are male and the level of education [25]. The same table (1) and figure (1-c,d) there was a statistically high significant difference of mean weight between two groups ($p<0.01$). Epidemiological evidence showed clearly that elevated in weight of person lead to many diseases such as heart diseases , hypertension and diabetes mellitus results from altered lipoprotein metabolism due to increased production (hyperlipidemias) [26].

Table (2): Mean distribution for (Cholesterol , HDL , LDL ,Triglyceride and Uric acid) concentration in studied groups (Healthy control and Patients

Characteristic (mg\dl)	Healthy control (n =45) (mean \pm SD)	Patients (n =75) (mean \pm SD)	T-Test	P - value	
Cholesterol	201.04 \pm 25.94	301.17 \pm 40.33	-14.89	.000	HS
HDL	52.20 \pm 5.24	50.11 \pm 9.06	1.413	.160	NS
LDL	29.89 \pm 9.10	58.57 \pm 7.12	-19.20	.000	HS
Triglyceride	90.07 \pm 28.50	141.71 \pm 40.31	-7.53	.000	HS
Uric acid	5.66 \pm 1.66	9.53 \pm 1.58	-8.19	.000	HS

HS: High significance when $P<0.01$

NS: No significance $P>0.05$

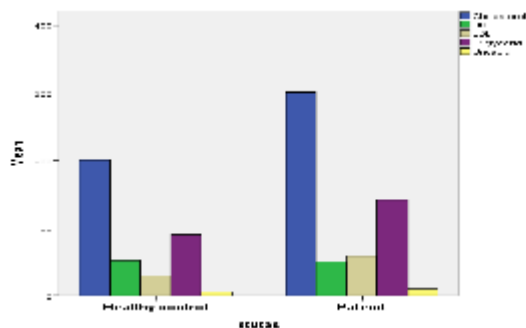


Figure (2): Mean distribution for (Cholesterol , HDL , LDL , Triglyceride and Uric acid) concentration in studied groups (Healthy control and Patients)

Data illustrated by table and figure (2) clearly showed a highly significant increased ($P<0.01$) between the mean of cholesterol , LDL and triglyceride in patients (301.1 ± 40.3) (58.5 ± 7.1) (141.7 ± 40.3) respectively when compared with the mean of in healthy control (201.0 ± 25.9)(29.8 ± 9.1)(90.0 ± 28.5) respectively .

The concentration of cholesterol and triglyceride was highly elevated in heart diseases patients compared with the healthy control groups ,the findings are in good agreement with other studies [27,28], who found that effects of increased cholesterol deposition in the arterial wall ,promotion of smooth -muscle –cell proliferation ,and induction of monocyte chemo tactic activity in endothelial cells [28] .The determination of serum cholesterol is one of the important tools in the diagnosis an classification of lipemia, high blood cholesterol is one of the major risk factors for heart diseases [29,30]. In healthy individuals, about thirty percent of blood cholesterol is carried by HDL ,data from the landmark Framingham heart study showed that for a given level of LDL ,the risk of heart diseases increase 10-fold as the HDL varies from high to low .Conversely, for a fixed level of HDL, the risk increase 3-fold as LDL varies from low to high[31].

The most common lipid alterations were elevation of serum triglycerides (TG) and cholesterol [32],while elevated triglycerides (hypertriglyceridemia) are linked with raised concentrations of fibrinogen and coagulation factors VII and XII, and with impaired fibrinolysis as determined by enhanced gene expression and concentrations of plasminogen activator inhibitor-1 [33].Triglyceride-rich lipoproteins may also be directly atherogenic [34].

It was clear from the above table and figure that a highly significant increased ($P<0.01$) in the mean of uric acid in heart disease patients (9.53 ± 1.5) when the results compared with healthy control (5.66 ± 1.66).

The above results agreed with the results obtained by Skinner et al. who observed that serum uric acid has antioxidant properties and contributes to free radical scavenging activity in human serum. When uric acid interacts with peroxynitrite to form a stable nitric oxide donor, vasodilatation increases and the potential for peroxynitrite-induced oxidative damage decreases [35]. Thus, uric acid can be protective against oxidative stresses, but it can also lead directly or indirectly to vascular injury[36] .Others has been reported that uric acid promotes vascular smooth muscle proliferation and up regulates the expression of platelet-derived growth factor and monocyte chemo attractant protein-1 .Hypoxanthine is converted to uric acid via xanthine, this reaction can be catalyzed by xanthine hydrogenase and xanthine oxidase, the latter of which produces uric acid and superoxide. Thus, it is possible that, in certain diseased conditions, hyperuricemia is accompanied by the increased production of reactive oxygen species, which may result in the modulation of

vascular contractility [37]. Another possible explanation is that hyperuricemia may induce endothelial dysfunction by decreasing the production of nitric oxide in the vascular endothelial cells. Adenosine synthesized locally by vascular smooth muscle in cardiac tissue is rapidly degraded by the endothelium to uric acid, which undergoes rapid efflux to the vascular lumen due to low intracellular pH and negative membrane potential [38]. Uric acid synthesis is increased in vivo under ischemic conditions, and therefore elevated serum uric acid may act as a marker of underlying tissue ischemia. In human coronary circulation, hypoxia, caused by transient coronary artery occlusion, leads to an increase in the local circulating concentration of uric acid [39]. In conclusion, elevated serum uric acid may be a marker of local and systemic tissue ischemia and provides one possible explanation for a non-causal associative link between hyperuricemia and cardiovascular disease.

Table (3) :The correlation between uric acid and lipid profile

Correlations		Cholesterol	HDL	LDL	Triglyceride	
Spearman's rho	Uric acid	Correlation Coefficient	.791**	-	.757**	.532*
		Sig. (2-tailed)	.000	.578	.000	.00
		P- Value	HS	NS	HS	S

* = S : Correlation is significant at the 0.05 level (2-tailed).

** = HS : Correlation is high significant at the 0.01 level (2-tailed).

In the present study showed there was high significant correlation between uric acid and cholesterol, LDL ($P < 0.01$) and significant correlation with triglyceride ($P < 0.05$) but no significant correlation between uric acid and HDL ($P > 0.05$)... Table (3),this results indicate that the Lipid profile is often as a medical routine screening to evaluate risk of heart diseases in healthy adults ,and many but not all epidemiological studies have suggested that high serum uric acid is a risk factor for Cardiovascular disease (CVD) [40] and warranted to evaluate its prognostic implications and potential utility in the monitoring of therapy [41,42]. This raised level of serum uric acid parallel to an increased risk of CVD could be either primary or secondary to underlying causes of CVD [43]. Furthermore, in nondiabetic subjects an elevated level of uric acid has been shown to be an independent predictor of coronary heart disease (CHD) and total mortality [44]. However, the specific role of serum uric acid in this constellation remains uncertain although may be involved in platelet adhesiveness, aggregation or inflammation and may be implicated in the genesis of hypertension [45].

References

- 1- Criqui MH. Epidemiology of cardiovascular disease. In: Goldman L, Ausiello D, eds. *Cecil Medicine*. 23rd ed. Philadelphia, Pa: Saunders Elsevier; chap 49, 2007.
- 2- Arialdi M, Miniño, M.P.H., Melonie P. Heron, Ph.D., Sherry L. Murphy, B.S., Kenneth D. Kochanek, M.A. "Deaths: Final data for 2004" *National Vital Statistics Reports*, Vol.55, No.19, 2007.
- 3- Hitti, Miranda. "Heart Disease Kills Every 34 Seconds in U.S.". Fox News . Retrieved on 2007.
- 4- American Heart Association :And if they didn't smoke that number would be way way way down!?! Heart Disease and Stroke Statistics-2008 Update. AHA, Dallas, Texas, 2008.
- 5- Christie, William. " Lipid analysis: isolation, separation, identification, and structural analysis of lipids" *Ayr, Scotland: Oily Press*,2003.
- 6- Durrington P . "Dyslipidaemia" *Lancet*, Vol. 362, No.9385, PP. 717–31, 2003.
- 7- Brunzell JD, Davidson M, Furberg CD, Goldberg RB, Howard BV, Stein JH, Witztum JL . "Lipoprotein management in patients with cardiometabolic risk: consensus statement from the American Diabetes Association and the American College of Cardiology Foundation" *Diabetes Care*, Vol. 31, No.4, PP. 811–22, 2008.
- 8- Kwiterovich PO. "The Metabolic Pathways of High-Density Lipoprotein, Low-Density Lipoprotein, and Triglycerides: A Current Review" *Am J Cardiol*, Vol.86, No.5, 2000.
- 9- Culleton BF, Larson MG, Kannel WB, Levy D. "Serum uric acid and risk for cardiovascular disease and death: the Framingham Heart Study" *Ann Intern Med*, Vol.131, PP.7–13, 1999.
- 10- Wang JG, Staessen JA, Fagard RH, Birkenhager WH, Gong L, Liu L. " Prognostic significance of serum creatinine and uric acid in older Chinese patients with isolated systolic hypertension" *Hypertension*, Vol.37, PP.1069–1074, 2001.
- 11- Mazzali M, Kanellis J, Han L, Feng L, Xia YY, Chen Q, Kang DH, Gordon KL, Watanabe S, Nakagawa T, Lan HY, Johnson RJ. "Hyperuricemia induces a primary renal arteriopathy in rats by a blood pressure-independent mechanism". *Am J Physiol Renal Physiol*, Vol.282, PP.991–997, 2002.
- 12- Langlois M, De Bacquer D, Duprez D, De Buyzere M, Delanghe J, Blaton V. "Serum uric acid in hypertensive patients with and without peripheral arterial disease" *Atherosclerosis*, Vol.168, PP.163–168, 2003.
- 13- Patetsios P, Song M, Shutze WP, Pappas C, Rodino W, Ramirez JA, Panetta TF. "Identification of uric acid and xanthine oxidase in atherosclerotic plaque" *Am J Cardiol*, Vol.88, PP.188–191, 2001.

- 14- Meattini F. et al. "The 4-hydroxybenzoate/4-aminophenazone chromogenic system" *Clin Chem*, Vol.24, No.12, PP.2161-2165, 1978.
- 15- Burnstein M. et al. *Journal of lipid research*, Vol.11, PP.583-595, 1970.
- 16- Fossati P et al. Triglycerides. *Clin Chem*, Vol.28, No.10, PP.2077-2080, 1982.
- 17- Friedwald W.T., Levy R.I. and Friedricksson D.S. "Estimation of the concentration of low density lipoprotein cholesterol in plasma without use of ultracentrifuge" *Clin. Chem*, Vol.18, PP.499-520, 1972.
- 18- Fossati P et al. *Clin Chem*. No.26, PP.227-231, 1980.
- 19- Good, W and Bonita, A "Home cardiac rehabilitation for congestive heart failure. A nurse case management approach" *Rehabilitation Nursing*, Vol.24, No.4, PP.143-145, 1999.
- 20- Betteridge, D.J. "Diabetes, Lipoprotein metabolism and atherosclerosis" *Br. Md. Bull*, Vol.45, PP.285-311, 1989.
- 21- Rath M, Niendorf A, Reblin T, Dietel M, Krebber HJ, "Detection and quantification of lipoprotein(a) in the arterial wall of 107 coronary bypass patients." *Arteriosclerosis*, Vol.9, PP.579-92, 1989.
- 22- Grainger DJ, Kirschenlohr M, Metcalfe JC, Weissberg PL, Wade OP, "Proliferation of human smooth muscle cells promoted by lipoprotein(a)" *Science*, Vol.260, PP.1655-1658, 1993.
- 23- Burtis A et al. *Tietz Textbook of Clinical Chemistry*, 3rd ed AACC 1999.
- 24- Tietz NW et al. *Clinical Guide to laboratory Tests*, 3rd ed AACC 1995.
- 25- Philip Barter, M.D. "HDL Cholesterol, LDL Cholesterol, and Cardiovascular Events" *NEJM*, Vol.27, 2007.
- 26- Khawaldeh, A. and Ajlouni, Y. "Hyperlipidemia in non-insulin dependent diabetes mellitus" *Bahrain Med. Bull*, Vol.21, No.4, PP.138-142, 1999.
- 27- M. John, Henry N. and Pierre A "Triglyceride-rich lipoproteins and high-density lipoprotein cholesterol in patients at high risk of cardiovascular disease: evidence and guidance for management" *J European Society of Cardiology*, 2011.
- 28- Grundy SM, Vega GL. "Two different views of the relationship of hypertriglyceridemia to coronary heart disease. Implications for treatment" *Arch Intern Med*, Vol.152, PP.28-34, 1992.
- 29- Skinner KA, White CR, Patel R et al. "Nitrosation of uric acid by peroxynitrite. Formation of a vasoactive nitric oxide donor" *J Biol Chem*, Vol.273, PP.2491-2447, 1998.
- 30- Ishizaka N, Ishizaka Y, Toda EI et al. "Higher serum uric acid is associated with increased arterial stiffness in Japanese individuals" *Atherosclerosis*, 2006.

- 31- White CR, Brock TA, Chang LY et al. “Superoxide and peroxynitrite in atherosclerosis” *Proc Natl Acad Sci USA*, Vol.91,PP. 1044–1048, 1994.
- 32- Kroll K, Bukowski TR, Schwartz LM, Knoepfler D. “Capillary endothelial transport of uric acid in guinea pig heart” *Am J Physiol*, Vol.262, (2 Part 2),PP.420–431, 1992.
- 33- De Scheerder IK, van de Kraay AM, Lamers JM et al.“Myocardial malondialdehyde and uric acid release after short-lasting coronary occlusions during coronary angioplasty: potential mechanisms for free radical generation” *Am J Cardiol*,Vol.68,PP.392–395, 1991.
- 34- Culleton BF, Larson MG, Kannel WB, Levy D. “Serum uric acid and risk for cardiovascular disease and death” *Ann Intern Med*,Vol.25,No.131,PP 7-13,1999.
- 35- Ioachimescu AG, Brennan DM, Hoar BM, Hazen SL, Hoogwerf BJ. “Serum uric acid is an independent predictor of all-cause mortality in patients at high risk of cardiovascular disease: a preventive cardiology information system (PreCIS)database cohort study” *Arthritis Rheum*,Vol.29,No.58,PP 623-630,2008.
- 36- Whitelaw DC, O’Kane M, Wales JK, Barth JH. “Risk factors for coronary heart disease in obese non-diabetic subjects” *Int J Obes Relat Metab Disord* ,Vol.30,No.25,PP.1042–1046,2001.
- 37- Ruggiero C, Cherubini A, Ble A, Bos AJ, Maggio M, Dixit VD, et al. “Uric acid and inflammatory markers” *Eur Heart J*,Vol.34,No. 27,PP 1174 – 1181,2006.
- 38- Brand FN,McGee,DL,Kannel WB,Stockes J,Castelli WB.”Hyperuricaemia as a risk factor of coronary heart disease:the Framingham study “*Am J Epidemiol*,No.121,PP.11-18,1985.
- 39- Selby JV, Friedman GD, Quesenberry CP Jr. “Precursors of essential hypertension” *Am J Epidemiol*,Vol.39,No.131,PP.1017-1027,1990.