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Original Research Article

Evaluation of N Terminal –Pro B Natriuretic Peptide in Patients with Renal Dysfunction

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Abstract

Natriuretic peptides and N terminal natriuretic peptide are peptide secreted from cardian atrium in response to stretch in cardiac muscle and considered marker in cardiac dysfunction , this study aiming to evaluate the level of NT-pro BNP in patients suffered from kidney failure .

This study were established on patient suffering from renal dysfunction who were attended .nephrology unit in Merjan Teaching Hospital in Babylon city .All patients were undergone complete laboratory and clinical examination to establish diagnosis of renal impairment and degree of renal dysfunction as blood urea and creatinine and estimation of hemoglobin level for diagnosis of anemia .

This study confirmed on patients with chronic renal failure and highlighted on the relationship between renal dysfunction and level of NT-proBNP. Serum NT-proBNP were analysed through ELISA technique among patients with CRF mean and standard deviation of level among patients and control groups were149 ± 36.5 **u unit/ml** ±,36± 6.5**u unit/ml** respectively and comparism mean of NT-proBNP between patients and control group was indicated that there is significant difference between two groups at p value< 0.05 as analysed by students t test .

The study reveals there is positive correlation between duration of renal dysfunction and level of NT-proBNP . The study revealed there is no effect of gender on NT-pro BNP .

Conclusion :- NT-pro BNP excretion is mainly by kidney and it is level disturbed by renal dysfunction and we considered it as marker for evaluation the relationship between renal and cardiac function and the degree of effecting of kidney on cardiac function in renal failure condition .

Key words: NT-pro BNP ,BNP ,CRF ,ELISA .

الخلاصة

يفرز الأذين نوع خاص من الببتايد هو Natriuretic peptides and N terminal natriuretic peptid استجابة للشد في عضلة القلب وتعتبر علامة من علامات عجز القلب.

اجريت هذه الدراسة على مرضى الفشل الكلوي المراجعين لوحدة الكلية الصناعية في مستشفى مرجان التعليمي في مدينة بابل حيث اجري للمرضى الفحص السريري والمختبري لتشخيص الفشل الكلوي ودرجة الفشل الكلوي حيث تم تقدير اليوريا والكرياتينين في الدم وتقدير مستوى الهيموجلوبين لتشخيص فقر الدم .

اعتمدت هذه الدراسة على تقييم مستوى NT BNPعند المرضى الذين يعانون من الفشل الكلوي ومقارنتها بمجموعة السيطرة. وأكدت هذه الدراسة على ان المرضى الذين يعانون من الفشل الكلوي المزمن لديهم ارتفاع ملحوظ في مستوى هذا الببتايد، وسلطت الدراسة الضوء على العلاقة بين الفشل الكلوي ومستوى proBNP–NT. وقد تم تحليل مصل proBNP–NT من خلال تقنية ELISA بين المرضى الذين يعانون من الفشل الكلوي وكان معدل مستوى الببتايد والانحراف المعياري بين المرضى ومجموعات السيطرة 149 ± 36.5 **u unit/ml** ±,36± 6.5**u unit/ml** على التوالي مما يدل على أن هناك فرق كبير بين المجموعتين في قيمة p <٠.٠٥ . وتكشف الدراسة أن هناك علاقة طردية بين مدة الفشل الكلوي ومستوى .NT–proBNP وكشفت الدراسة عدم وجود تأثير الجنس علىNT BNP .

Introduction

The description of chronic kidney disease in the last period had been simplified and final identification for chronic renal failure as it related with deterioration of glomerular filtration rate over a period of 3 months. Deterioration in filteration of kidney of less than 60 mL/min/1.73 m2 in adult establish the diagnosis of renal failure and for rate than 60 mL/min/1.73 m2 can considered renal failure if there are some other markers indicate renal defective as urine sediment or abnormal in x ray or renal biopsy beside other finding [1].

It had been proved that Patients suffering from deterioration in renal function mainly filteration and reabsorption ,those people are at high risk for developing cardiac problem from effect of disturbance in hemostasis and this due to cooperation between both renal and cardiovascular system [2-3].

*Brain -natriuretic peptide (BNP) and N-terminal (NT)-proBNP are type of peptides hormones which are mainly produced by heart in response to increasing stretching in the cardiac wall. These two neurochrome peptides are used as tool assessed in establishing the diagnosis of congestive heart failure (CHF) and as prognostic tool in assessed mortality in patients suffered from CHF, populations at risk of developing chronic heart failure, recent myocardial infarction, and acute coronary syndromes without myocardial necrosis ,this marker for diagnosis tension factors on heart [4-6].

Ventricular stretch causes synthesis and production of BNP which is peptide made of about 32 amino acid and NT-pro BNP is about 76 amino-acid and the latter considered precursor for natriuretic hormone which considered the biological active form , their release to blood stream with equal quantity into the circulation, but analysis the difference in secretion of these two markers and change in their levels are not easy work for analysis accurately [7-9].

BNP and NT-pro BNP like other hormones have to be excreted after end of their action but their excretion pathway are different, BNP after completion the biological action bind on its specific receptor which is distributed mainly in liver ,kidney lung and endothelium lining of vessels [10,11]. The NT-pro BNP clearance occurs only through renal system kidney. These two peptide so effected if there are disturbance in renal function because in renal dysfunction effect their clearance rate beside the effect of receptors but the kidney effect on NT-pro BNP more than BNP because the later elimination effected by other factor as receptor site in different position so if there is deterioration in renal function this will reflected on the ellemination and clearance of these peptide especially on NT-proBNP because the elimination pathway is through renal system [12].

Renal failure has many complication that lead to increase the mortality rate among these complication is cardiovascular complication accompany the patients with kidney failure .which predicted from deterioration in glomerulo filteration rate beside electrocardiography (ECG) changes [13].

Study proofed that patients with renal dysfunction has negative effect on cardiac muscle mainly left ventricle function because of increasing load on heart lead to stretching well of ventricular muscle and this considered as link between heart and kidney function and this condition can be referred as cardiorenal syndrome [14-15].

In renal failure there is increase in fluid volume and this cause effect on heart that cause stretch and increase tension on ventricular wall and sensitized the heart for secretion and release BNP paired with NT-proBNP this peptide after binding to specific receptor start their action through increasing sodium excretion from kidney and decrease renal re-absorption of sodium from renal tubules with net result is increasing in

renal out put of sodium and water and decrease retention of them to circulation and thus decrease tension and produce vasodilatation and decrease tension on heart muscle but if there is defect in function of kidney this mechanism s are not well working and this lead to increase tension on heart from that associated with impairment of kidney function [16].

BNP and NT-proBNP are both released into circulation due to cardiac overload in patients with renal failure and from study the rate of secretion of these two peptides in patients with renal failure the degree of deterioration in kidney function can be evaluated .

NP as marker to determining the deterioration in heart function from the effect of renal system till now this subject remain not clear and the mechanism for evaluation this relationship are not well established. BNP which is considered the biologically active portion of NT-proBNP is clearance mainly achieved through the process of endocytosis and lysosomal degradation after binding to characteristic NP clearance receptor type C and secondarily via proteolysis by neutral endopeptidase [17].

. Peripheral receptors for NT-proBNP are not clear but the last evidence proof that it is clearance mainly by renal system[18]. There is a study indicated that NT-pro BNP is more susceptible than BNP by changes and defective in renal function [19]. There is a study indicated that there are some degree of connection and relationship between the degree of changes in GFR and NT-proBNP but not BNP in asymptomatic stage III and IV in chronic kidney disease (CKD). Out patients in whom there is cardiac risk linked with renal failure and this related to coordination between cardiovascular and renal system to control hemostasis [20, 21].

The patients with (CKD) had been developing changes in in left ventricular (LV) structure and function [22, 23]. Both left ventricular systolic and diastolic dysfunction are commonly observed in end-stage renal disease (ESRD), may be associated with subsequent development of cardiac failure and mortality [24, 25].**)**

Material and Methods

Selection groups

Group1: patients with chronic renal failure attended Merjan Teaching Hospital

Group 2: Healthy persons act as control groups

NT-proBNP level estemsted by ELISA technique and the standared curve for estimation of NT-proBNP were represented in figure 1.

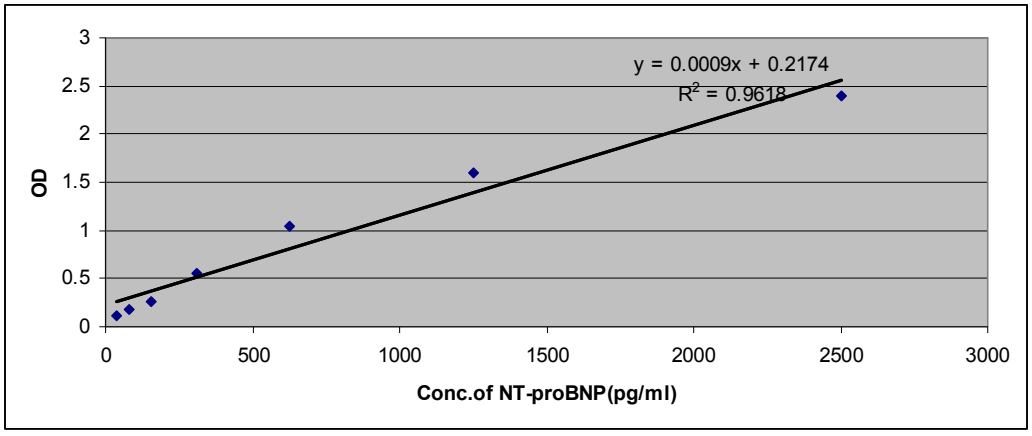

Figure 1 : Standard curve of NT-pro BNP

Hemoglobin level was estimated for patients with chronic renal failure and diagnosis of anaemia were established according to WHO criteria for diagnosis of anaemia [26], and this classification are representing in figure 2.

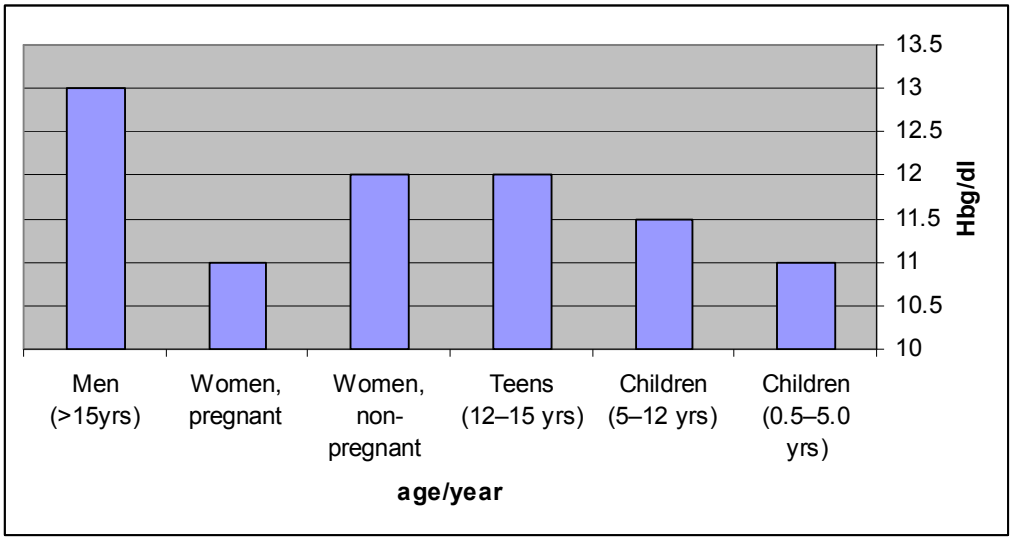

Figure 2 : Hemoglobin thresholds for diagnosis of anemia

Results

Analysis of data for the mean of Human NT-pro BNP level by students t-test was revealed that there are significant difference in estimated level Human NT-pro BNP between patients and control and the result was represented in table 1.

Table 1 : HumanNT-pro BNP mean difference between patients and control

	Groups	Mean ± SD u unit/ml	P value
Human NT-pro BNP	**Patients CRF**	149 ± 36.5	**0.001***
	Healthy control	36± 6.5	

*p value<0.05 considered significant

Hemoglobin (HB) estimated for CRF patients and patients classified according to severity of anaemia , the patients with severe anaemia in which Hb<8 g/dl were 55% and patients with moderate anamia in which Hb between 8-11 gldl were 55% and the result was representing in figure 2 .

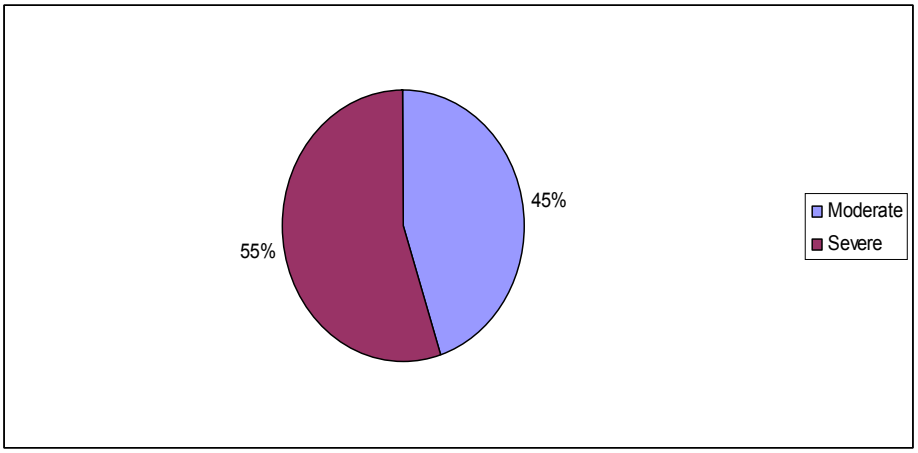

Figure 3 : Hemoglobin level among renal disorder patients

Positive correlation between Human NT pro BNP level and duration of disease in patients with chronic renal failure were representing in figure 4.

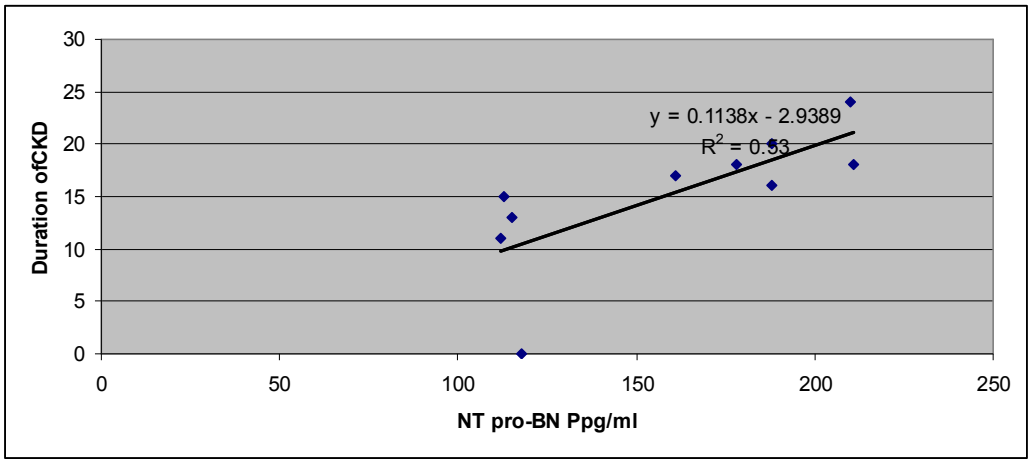

Figure 4 :Correlation between Human NT pro BNP and duration of renal dysfunction

Gender effect on NT-proBNP

By study the effect of gender one value of NT-pro BNP between males and females the results show no difference in estimated level according to gender at p value <0.05

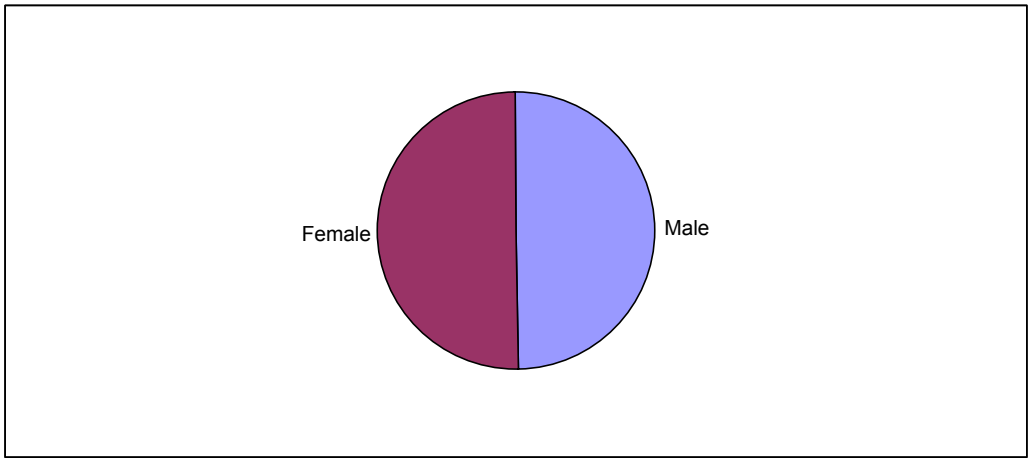

Figure 5 : Gender effect on NT-pro BNP

Discussion

Natriuretic peptide were used as diagnostic tool for heart failure [27].The normal hemostasis balance in circulation mainly through sodium reabsorption and excretion through kidney and this balance were achieved through cooperation between renal and cardiovascular system and this balance required for intact renal function so any deviation in work of renal tubules lead to distortion of this hemostasis which reflect on heart function.

For reach to cause of disturbance in BNP and NT-proBNP we need to study all the factors influence on the level of these two peptide as cardiac and non cardiac causes .these two peptide when secreted from heart cause natriuresis and duiresis so increase renal excretion of sodium with water to decrease the fluid over load on heart and this mechanism considered counteracting process for action of aldosterone hormone which secreted from adrenal gland through stimulation from activation of renin-angiotensin-aldosterone system by sympathetic nervous system, this system through aldosterone action which cause renal tubule reabsorption of sodium while natriuretic peptide cause counteract against this mechanism by increasing the sodium and water excretion through renal system through increasing filtration rate of glomeruli [28].

Heart failure causes disturbance in hemostasis that increase fluid over load on heart which cause stretching on heart wall and increase the secretion of these two peptide ,and because their action on kidney they required for intact renal function beside their clearance are mainly through kidney and NT-proBNPare exretion only through kidney so any disturbance in function of kidney will effect on level of these two peptide mainly NT-proBNP because it is exclusively excreted clearance take place through kidney, so if there are impairment in kidney function causes disturbance in their level which is correlated with deterioration in in filteration capacity of kidney and this can be considered as link between kidney and renal system [29].

In this work which was done on chronic renal failure patients evaluation of level of NT-proBNP in patients groups revealed significant increase in the level of this peptide compared with control as statistical analysed by students t test .this result was agreed with result of Rajat Tagore et al. and Pornpen Srisawasdi et.al [30,31].

Most patient in this study with renal disease has anaemia as representing in figure no. 2 and this anaemia is renal related cause because in renal dysfunction lead to defective kidney function as endocrine by defective in erythropoiten hormone or defective in its receptor which accompany patients with renal function impairment and worse the condition of anaemia accompany renal failure [32]. and cause negative effect on heart that

stimulate release of NT-pro BNP and BNP and the NT-pro BNP is mainly clearance by renal so evaluation of this peptide is useful in study the relation ship between the effect of renal disorder and cardiac function .

We can concluded from this study that patients with renal dysfunction has negative effect on cardiac function .this result may be due to fluid disturbance in patient with renal disease which has negative effect on heart via rennin angiotensin system and beside decrease renal clearance in renal impairment patients contributed to elevation in NT-proBNP level [33] .

Deterioration in renal filtration rate in renal failure patients will have effect on the level of NT-proBNP concentrations through influence of renal function on the clearance of this peptide that cause increase in the level of this peptide and the relation between GFR and change in level of NT-proBNP establishing with the study performed by Vickery et al(28). that showed that NT-proBNP was affected with progression of CKD andthis study also agree with studies of Leo H et al which reach to same result [34].

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