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N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE AS PREDICTOR FACTOR TO CORONARY ARTERY LESION IN KAWASAKI DISEASE

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Abstract: Background: Kawasaki disease (KD) is acute systemic vasculitis of childhood associated with the development of coronary artery lesion in 15-25% of untreated children, and in 3-5% of children treated by intravenous immunoglobulin, may lead to ischemic heart disease or sudden death. KD makes a challenge for the clinicians because the diagnosis of KD based on clinical data, not pathognamic symptoms, and no laboratory test are available to diagnose KD. **Objectives:** The present study aimed to investigate whether the serum level of N-terminal pro-brain natriuretic peptide (NT-proBNP) can be a predictive indicator not only to diagnose KD, but also used to identifying patients have character of incomplete Kawasaki disease (IKD) ,have a high risk of coronary artery lesion (CAL), and whom resistance to Intravenous Immunoglobulin (IVIG). **Methods:** The clinical data of 155 KD cases from May 2013 and June 2014 admitted to pediatric cardiology at Tongjie medical university hospital. The demographic clinical and laboratory data were retrospectively collected ,the differences in parameters were compared between three groups A)IKD, typical Kawasaki disease (TKD), and control groups, B)CAL-KD ,NCAL-KD and control groups, C)IVIG sensitive KD, IVIG non-response KD, and control groups. The statistical significance of differences among several groups was analyzed by ANOVA. When variances in groups are equal, comparisons of two groups were analyzed by using LSD test. On the contrary, when variances in groups are not equal, comparisons of two groups were analyzed by using Tamhane's T2 test, ($P<0.05$ was considered significant). **Results:** After we comparing the three groups, there were no significant difference in variables between children with IKD and TKD, as well as CAL-KD and NCAL-KD, and IVIG sensitive KD and IVIG non-response KD. These include, age, gender, day of illness, leukocytes count, serum levels of sodium, C-reactive protein, and albumin. The serum NT-proBNP level was higher in children of IKD than those TKD (1441±467.4ng/L vs. 1049.0±283.4ng/L, respectively), but not significant , higher in children with CAL than those NCAL (2608.2±745.5ng/L vs. 902.6±162.0ng/L, respectively) it is considered as significant difference , and in IVIG non- response KD than those IVIG sensitive KD (1549±1943ng/L vs. 1473±2961 ng/L, respectively), but not significant difference. **Conclusion**: The findings in this study shows the serum NT-proBNP level is high in children with KD, it is may be useful to predict who risk to coronary artery lesion in Kawasaki disease.

Keyword: Kawasaki disease, Incomplete Kawasaki disease, NT-proBNP, Coronary artery lesion, IVIG response and non response.

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1. Introduction

Kawasaki disease [KD] is idiopathic autoimmune self-limiting disease, but it is considered as parlous disease due to their complications, which mainly based on coronary artery [1]. It is idiopathic autoimmune self-limiting disease. It was discovered by Professor Tomisakan Kawasaki in Japan in 1967. It is the second wide spread vasculitis disease in pediatric. It is result from genetic and pathogenic causes by stimulation of immune system extra or over than normal response of body to bacterial or virus antigens [2]. It has replaced acute rheumatic fever as the most common cause of acquired heart disease in children in the developed world and is increasingly being recognized from several developing countries [3].

Approximately 85% of KD patients are younger than 5 years with an average of approximately 2 years. However, cases in younger and older individuals have been reported [4, 5]. Globally, KD is the most common form of childhood primary vasculitis. Delayed diagnosis and treatment results in coronary artery aneurysms in up to 25% of all affected individuals [5].

Several clinical and laboratory manifestation rise risk of coronary artery abnormality which including fever for long duration, boys, old ages, prolonged increase levels of ESR and CRP, increasing count of white blood cells, normocytic normochromic anemia, hypoalbuminemia, and thrombocytopenia. But, none of these biomarkers has reasonably high sensitivity and specificity in predicting the course of the illness [3]. Cardiac features of Kawasaki disease include heart failure, ECG abrormality, pericarditis, myocarditis, plural effusion, myocardial infarction, valvular incompetence [2].

Objectives

The present study aimed to investigate whether the serum level of N-terminal pro-brain natriuretic peptide can be a predictive indicator not only to diagnose KD, but also used to identifying patients have character of incomplete Kawasaki disease,have a high risk of coronary artery lesion, and whom resistance to Intravenous Immunoglobulin..

Subjects and Methods

2.1 Search strategy

Between May 2013 and June 2014, this retrospective study of hospital discharge records with KD cases including one hundred and fifty five patients, among them 46 were girls, and 69 boys, and the age range between 2 months - 8 years and 4 months, they were admitted at pediatric cardiology at Tongjie medical university hospital, met the diagnose as Kawasaki disease was based according to guideline of Japan research committee [6].

2.2 Inclusion criteria and exclusion criteria

These subjects defined as inclusion criteria: 1. Children fulfilled the criteria of KD. 2. Children with atypical presentation of KD.

In addition, forty patients were defined as exclusion criteria (control group) included 22 boys Moreover, 18 girls with febrile illnesses resembling picture of KD including Pneumonia 18 patients, Upper respiratory tract infection 8 patients, and Bronchitis 14 patients.

2.3 Data extraction and outcome

All eligible patients records were reviewed and data including age at presentation, sex, clinical manifestation, Laboratory data result, and also their echocardiograph result and treatment.

At onset of hospital admission the serial blood were collected at febrile acute phase before treatment, and in a febrile sub acute phase after complete treatment collected, and The biochemical, electrolytes, NT-proBNP were measured and the two dimension Echocardiograph was done before and after treatment, which help to find the coronary artery lesion to support diagnosis of KD, When they diagnosed as KD cases already they administrate the routine medical treatment. It was IVIG 2g/kg for 24 hours, plus aspirin 50 mg/kg/day. So, if the fever does not resolve after 48 hours, or recurrence of fever after a

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febrile period. Add the second dose of IVIG 2g/kg there is no response no resolves of fever, add the third dose of IVIG 2g/kg or give monoclonal antibody (Inflixmal). According to result of echocardiography, we categorized the KD patients into two groups the first group those who development of significant CAL we called it CAL-KD and the second group those who did not develop CAL we called it NCAL –KD.

In addition, make a table to compare age ranged, sex related, fever days, white blood cells count (WBCs), neutrophil (Neut. %), platelets count (PLTs), erythrocyte sedimentation ratio (ESR), albumin concentration, Alanine aminotransferase activity (ALT), Aspartate aminotransferase activity (AST, U/L), C-reactive protein (CRP), sodium ions concentration(Na^+), and N-Terminal pro-brain natriuretic peptide (NT-proBNP) between CAL-KD, NCAL-KD and the control group the response to first or single dose of IVIG, which called response, or sensitive IVIG after that classified the one hundred and fifty five patients to group again in to typical KD (TKD) and atypical or in complete KD (IKD) to compare the NCAL/CAL and IVIG NON Re/IVIG re in each group plus to same contents in other tables (sex, age, fever days, WBCs, Neut. %, PLTs, Albumin, AST, ALT, Na^+, and NT-PROBNP).

2.4 Statistical analysis

Statistical analyses were performed with SPSS for Windows version 25.0 (SPSS, Chicago, IL, USA).Measurement data are presented as means±standard deviations. Non-normal data was transformed with the natural logarithm to be normally distributed, and then processed as normally distributed data. The statistical significance of differences among several groups was analyzed by ANOVA. When variances in groups are equal; comparisons of two groups were analyzed by using LSD test. On the contrary, when variances in groups are not equal, comparisons of two groups were analyzed by using Tamhane's T2 test ($P<0.05$ was considered significant).

3. Results

Table (1) summarizes the results of both demographic data and laboratory data of KD patients, which divided in to IKD and TKD, and control patients. In the first group IKD there were 63 patients then divided into 41 boys and 22 girls, 38 of them had N-CAL and 24 case had CAL, and 8 of them IVIG NON-response and IVIG response are 56, and second group TKD there were 52 case then divided as above 28 boys and 24 girls, N-CAL are 40 and 13 CAL, IVIG NON-response 9 and IVIG response 44 and total number of control group 40 the boy: girl ratio is 22:18 this group do not have patients with N CAL/CAL and IVIG NON-re/re.

In this study we make three comparisons: 1) Comparing between IKD and the control group. 2) Comparing between TKD and the control group. 3)Comparing between IKD group and the TKD group, when we compare the age and fever days by the three comparisons there are no significant difference, in other side WBCs count, there is a significant difference between IKD and the control group($14.95\pm5.75^{*}$ $x10^3$ /μL and 11.13±9.74 $x10^3$ /μL ,respectively) also there are significant difference between TKD and control group($16.01\pm8.11^{*}$ $x10^3$ /μL and 11.13±9.74 $x10^3$ /μL, respectively), but there is no significant difference between IKD and TKD (14.95±5.75 $x10^3$ /μL and 16.01±8.11 $x10^3$ /μL, respectively) as well as （%) ,PLAT, ALT.

However, in AST there is no significant difference in the three comparisons. In addition, the CRP there is significant difference between IKD and the control group ($74.26\pm55.86^{*}$ mg/dL and 18.66±34.08 mg/dL ,respectively) also, there are significant difference between TKD and the control group($74.37\pm47.63^{*}$mg/dL and 18.66±34.08 mg/dL, respectively) but there is no significant difference between IKD and TKD (74.26±55.86 mg/dL and 74.37±47.63mg/dL,

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respectively) as well as ESR. In albumin, there is significant difference between IKD and control Group(34.96±4. 19*g/L and 41.38±2.77g/L, respectively) also, there are significant difference between TKD and the control group(34.54±4.37*g/L and 41.38±2.77g/L, respectively) but there is no significant difference between IKD and TKD (34.96±4.19g/L and 34.54±4.37g/L, respectively) otherwise in Na^+, there are no significant difference at all, in our study, we concentrate on NT-proBNP, there is difference was a significant between IKD and the control group (1441±467.4*ng/L and 119.5±115.6 ng/L,respectively) also we found a significant difference between TKD and control group (1049.0±283.4* ng/L and 119.5±115.6ng/L , respectively) but we do not found significant difference between IKD and TKD (1441±467.4 ng/L and 1049.0±283.4 ng/L ,respectively) (**Figure. 1)**.

Table 1: comparing between IKD, TKD, and control groups

Groups	Control (n=40)	IKD (n=63)	TKD (n=52)
Boy/Girl	22/18	41/22	28/24
N CAL/CAL	0	38/24	40/13
IVIG NON-re/re	0	8/56	9/44
Age (Years)	4.34±3.66	2.74±2.34	2.74±2.60
Fever days	6.46±5.93	6.15±2.29	7.16±3.89
White blood cells count (WBCs, $x10^3/\mu l$)	11.13±9.74	14.95±5.75*	16.01±8.11*
Neutrophils (Neut. %)	52.23±22.74	64.12±18.18*	62.15±17.95*
Platelets count (PLTs, $x10^3/\mu l$)	317.30±174.1	393.60±170.51*	360.41±109.08*
Alanine aminotransferase (ALT, U/L)	22.38±17.12	58.17±88.57*	55.86±68.21*
Aspartate aminotransferase (AST, U/L)	56.87±1.096	41.85±42.81	57.74±100.2
C-reactive protein (CRP, mg/dl)	18.66±34.08	74.26±55.86*	74.37±47.63*
Erythrocyte sedimentation rate (ESR, mm/hour)	16.18±13.52	50.20±29.92*	59.76±47.63*
Serum albumin (g/L)	41.38±2.77	34.96±4. 19*	34.54±4.37*
Na+ concentration (mmol/L)	137.4±2.87	135.8±3.718	135.6±4.13
N-Terminal pro-brain natriuretic peptide (NT-proBNP, ng/L)	119.5±115.6	1441±467.4*	1049.0±283.4*

The data displayed as mean±standerd deviation , *mark that mean there are significant difference (P<0.05), there no significance difference between IKD and TKD (there is no▵ mark).

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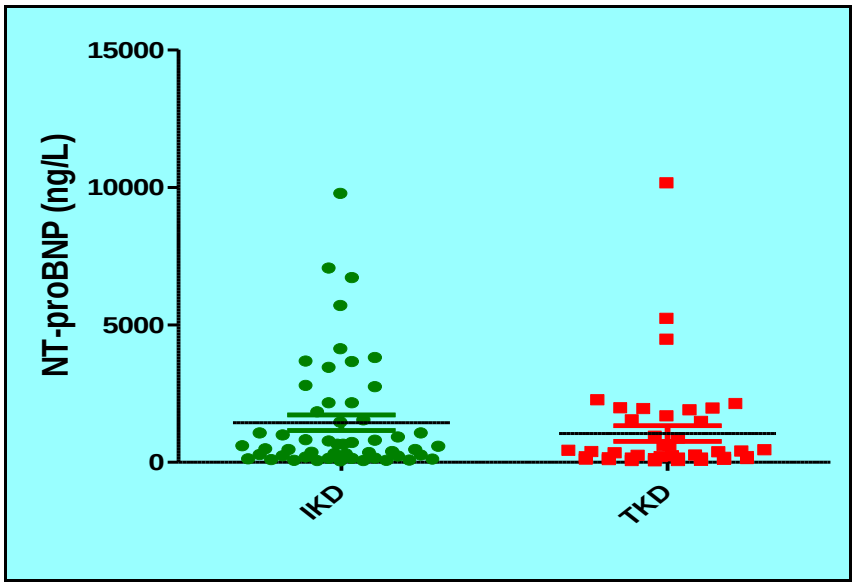

Figure 1: Comparing level of NT-proBNP between IKD and TKD groups.

Table (2) summarizes the results of both demographic data and laboratory data that have been reported as possible predictor of risk of CAL KD. Which the number of NCAL-KD group is n=79, number of CAL-KD group is n=36, and number of control group is n=40. Therefore, there was no significant difference in ratio of male to female or age between NCAL-KD, CAL-KD and control groups (M/F: 49/30 and 20/16 and 22/18; age: 2.72±2.42 and 2.78±2.55 and 4.34±3.66, respectively) also there is no significant difference was found for the days of fever. WBCs count shows a significant difference between NCAL-KD and the control group (14.88±5.70* x10 /uL and 11.13±9.74x10 /uL, respectively) also, there are significant difference between CAL-KD and control group(16.58±8.92* x10 /uL and 11.13±9.74 x10 /uL ,respectively), but there is no Significant difference between NCAL-KD and CAL-KD (14.88±5.70 x10 /uL and 16.58±8.92 x10 /uL) as well as N (percentage), PLAT, ALT. Nevertheless, in AST there is no significant difference in the three comparisons .CRP there is significant difference between NCAL-KD and control Group(71.23±48.48*mg/dL and 18.66±34.08mg/dL, respectively) also, there is significant difference between CAL-KD and control group(80.6.37±58.96* mg/dL and 18.66±34.08mg/dL, respectively) but there is no significant difference between NCAL-KD and CAL-KD (71.23±48.48 mg/dL and 80.6.37±58.96 mg/dL, respectively) as well as ESR. In albumin, there is significant difference between NCAL-KD and control Group(35.29±4.18*g/L and41.38±2.77g/L, respectively) also there are significant difference between CAL-KD and control group(33.69±4.31*g/L and 41.38±2.77g/L, respectively) but there is no significant difference between NCAL-KD and CAL-KD (35.29±4.18 g/L and 33.69±4.31g/L, respectively). Otherwise, in Na^+, there is no significant difference at all. But in NT-proBNP show result should be important in our study, so there are difference was a significant between NCAL-KD and control group (902.6±162.0*ng/L and 119.5±115.6 ng/L,respectively) In addition, we found a significant difference between CAL-KD and control group(2608.2±745.5*ng/L and 119.5±115.6ng/L, respectively)

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also, we found significant difference between CAL-KD and NCAL-KD was (2608.2±745.5ᵃng/L and 902.6±162.0 ng/L, respectively) (**Figure. 2)**.

Table 2: comparing between NCAL-KD, CAL-KD, and control groups

	Control (n=40)	NCAL-KD (n=79)	CAL-KD (n=36)
Boy/Girl	22/18	49/30	20/16
Age (Years)	4.34±3.66	2.72±2.42	2.78±2.55
Fever days	6.46±5.93	6.51±3.51	6.94±3.34
White blood cells count (WBCs, x10^3/µl)	11.13±9.74	14.88±5.70*	16.58±8.92*
Neutrophils (Neut. %)	52.23±22.74	61.74±18.09*	66.69±17.64*
Platelets count (PLTs, x10^3/µl)	317.30±174.1	389.0±134.1*	356.1±168.8*
Alanine aminotransferase (ALT, U/L)	22.38±17.12	59.34±108.22*	49.75±43.94*
Aspartate aminotransferase (AST, U/L)	56.87±1.096	50.72±87.64	39.98±29.83
C-reactive protein (CRP, mg/dl)	18.66±34.08	71.23±48.48*	80.6.37±58.96*
Erythrocyte sedimentation rate (ESR, mm/hour)	16.18±13.52	56.41±32.11*	50.63±29.99*
Serum albumin (g/L)	41.38±2.77	35.29±4. 18*	33.69±4.31*
Na+ concentration (mmol/L)	137.4±2.87	136.4±3.32	134.3±4.66
N-Terminal pro-brain natriuretic peptide (NT-proBNP, ng/L)	119.5±115.6	902.6±162.0*	2608.2±745.5*ᵃ

The data displayed as mean±standerd deviation , *mark that mean there are significant difference (P<0.05),there is ᵃ mark that mean there are significant difference when compared CAL-KD with NCAL-KD(*P*<0.05)

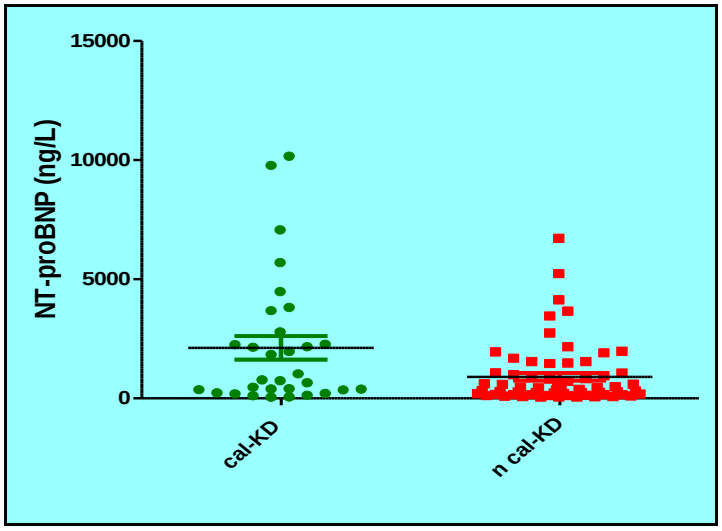

Figure 2: Comparing level of NT-PROBNP between NCALKD and CAL-KD groups

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Table (3) shows analysis of demographic data and laboratory data of IVIG non-re-KD ,IVIG sensitive group and the control group. IVIG non-re-KD group n=17, number of IVIG sensitive group is n=98,and control group n=40. So, there were no significant difference in age between IVIG non-re-KD, IVIG sensitive groups, and the control group (age:2.58±2.29 and 2.77±2.488 and 4.34±3.66, respectively) the days of fever there is no significant difference was founded. WBCs level in the IVIG non-re-KD group show significant difference when compared with control group, also can we found significant difference between IVIG sensitive group and control group, but there are no significant difference between IVIG non-re-KD and IVIG sensitive groups, as well as N(%) , ALT, but the PLTs count show significant difference when compared IVIG non-re-KD and IVIG sensitive groups with control group ,in addition shows significant difference between IVIG non-re-KD and IVIG sensitive groups(408.8.±127.5$^{\Delta}$ x10^3/µl and 373.5±149.1 x10^3/µl, respectively).

There is no significant difference at all. In AST, CRP, and ESR had a significant difference between IVIG non-re-KD and IVIG sensitive groups with the control group, and no significant difference between IVIG non-re-KD and IVIG sensitive groups. When, we see albumin, we found there significant difference between IVIG non-re-KD and control groups (33.96±3.10*g/L and 41.38±2.77g/L, respectively), also there are significant difference between IVIG sensitive group and the control group (34.70±4.41* g/L and 41.38±2.77 g/L, respectively). In addition, there is also significant difference between IVIG non-re-KD and IVIG sensitive groups (33.96±3.10$^{\Delta}$ g/L and 34.70±4.41 g/L, respectively). But in Na^+, there are no significant difference between IVIG non-re-KD and IVIG sensitive groups with control group. But, there are a significant difference between IVIG non-re-KD and IVIG sensitive groups(133.4±3.59$^{\Delta}$ mmol/L and 136.3±3.86 mmol/L, respectively). But when you see NT-PRO-BNP measurement there are a significant difference between IVIG non-re-KD group and control group (1549±1943* ng/L and 119.5±115.6 ng/L, respectively). Also there are significant between IVIG sensitive group and control group (1473±2961* ng/L and 119.5±115.6 ng/L, respectively) but no different was significant when we do comparing between IVIG non-re-KD and IVIG sensitive groups (**Figure. 3)**.

Table 3: comparing between IVIG non-re-KD, IVIG sensitive and control groups

Groups	Control (n=40)	IVIG non-re-KD (n=17)	IVIG sensitive group (n=98)
Boy/Girl	22/18	-	57/41
Age (Years)	4.34±3.66	2.58±2.29	2.77±2.488
Fever days	6.46±5.93	6.44±3.05	6.50±3.29
White blood cells count (WBCs, x10^3/µl)	11.13±9.74	13.98±7.22*	15.68±6.86*
Neutrophils (Neut. %)	52.23±22.74	59.94±19.29*	63.89±17.83*
Platelets count (PLTs, x10^3/µl)	317.30±174.1	408.8.±127.5$^{*\Delta}$	373.5±149.1*
Alanine aminotransferase (ALT, U/L)	22.38±17.12	66.62±68.69*	54.42.±96.34*
Aspartate aminotransferase (AST, U/L)	56.87±1.096	55.76±41.48	45.71±78.73
C-reactive protein (CRP, mg/dl)	18.66±34.08	74.08±57.06*	74.30±51.49*

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Erythrocyte sedimentation rate (ESR, mm/hour)	16.18±13.52	63.73±31.01*	52.68±31.24*
Serum albumin (g/L)	41.38±2.77	33.96±3.10*▵	34.70±4.41*
Na+ concentration (mmol/L)	137.4±2.87	133.4±3.59▵	136.3±3.86
N-Terminal pro-brain natriuretic peptide (NT-proBNP, ng/L)	119.5±115.6	1549±1943*	1473±2961*

The data displayed as mean±standerd deviation , *mark that mean there are significant difference (P<0.05),there is ▵ mark that mean there are significant difference when compared IVIG non-re-KD with IVIG sensitive(*P*<0.05)

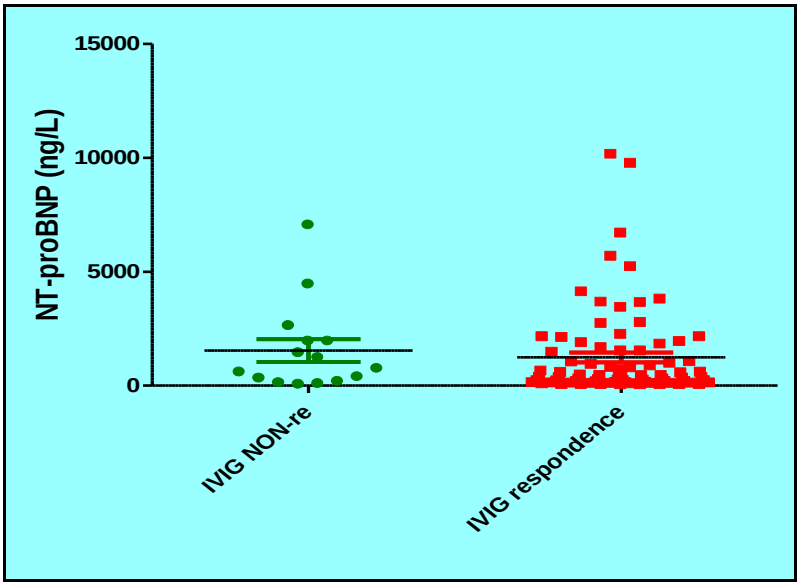

Figure 3: comparing level of NT-PROBNP between IVIG non-re-KD and IVIG sensitive groups

The data in Table 4 show the correlation between NT-proBNP and other index. This correlation was appeared between fever days. white blood cells, neutrophils (%), platelets count, C-reactive protein, serum albumin, and Na+ concentration, on the other hand, no correlation between NT-proBNP and Erythrocyte sedimentation rate, alanine aminotransferase, aspartate aminotransferase activities.

Table 4: The correlation between NT-proBNP and other index

	NT-proBNP	
	r	P Value
Fever days	-0.23	0.03▵
White blood cells count	0.344	0.001▵▵
Neutrophils (%)	0.409	<0.001▵▵
Platelets count	-0.375	<0.001▵▵
Alanine aminotransferase	-0.016	0.879
Aspartate aminotransferase	-0.044	0.674

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C-reactive protein	0.374	<0.001ᐞᐞ
Erythrocyte sedimentation rate	0.16	0.191
Serum albumin	-0.373	<0.001ᐞᐞ
Na+ concentration	-0.294	0.004ᐞᐞ

ᐞ mark that mean there are a significant difference (P<0.05), ᐞᐞ mark that mean there are a significant difference (P<0.01)

4. Discussion

The most serious complication of KD is coronary artery lesion, which develop frequency in sub acute phase, also can be seen in acute phase especially in the first 3 days of KD disease [7] appear of new aneurysm more than 6 weeks after the onset of disease is uncommon. The Japanese ministry of health classified the CAL [8] as:

1) If internal lumen diameter more than 3mm in child < 5 years or more than 4mm in Child > 5 years.

2) If internal diameter of segment equal or more than 1.5 times that of adjacent segment.

3) If the coronary lumen was irregular

CAL can be a diffuse dilation called ectasia or localized aneurysm formation [9-13]. The aneurysm had a types according the size classified in to small (when the internal diameter less than 5 ml), medium (internal diameter 5-8ml), and large or giant (internal diameter larger than 8ml) [14]. Aneurysm bigger than 8mm (giant) rare to regress [9-11], so patient who do not have complete resolution of aneurysm may go on develop coronary stenosis leading to coronary artery obstruction, and myocardial infarction later, due to premature atherosclerosis [9-11]. Cause of death in KD+CAL due to blood clot formation in aneurysm cavity leading to myocardial infarction or rupture of large aneurysm [15].

Cardiovascular systems one of serious manifestation of KD, so must be diagnose as soon as possible and exclude other inflammatory disease which had the same clinical presentation by using NT-proBNP .Normally the NT-proBNP is very high soon in neonate and then gradually decrease significantly over the age [16]. The left ventricle myocytes secrete cardiac hormones (BNP and NT-PROBNP terminal Fragment) which raise in amount proportionally to degree of ventricle dysfunction, such as congenital heart failure, myocardial infarction, even ischemia [17-20]. The regulation of these hormones by left ventricular wall tension [21]. When the cardiac myocytes undergoing to stress that leading to secrete of 134 amino acids, which considered as precursor of BNP and NT-proBNP. when these fragments come out to circulation, the first pass was liver, which cleaved it in to a single peptide and proBNP. The proBNP cleaved by endoprotease enzyme into: 1) active BNP which cleared from plasma and metabolized by kidney and vascular system. 2) Inactive NT-proBNP fragment [22], then cleared by renal exertion [23]. The reason lead to raise level of BNP not clear, but there are two possibilities [20], the first one when the cardiac muscles undergo inflammation or ischemia that is result to increase level of it, other possible due to acute phase of KD leads to resent of cytokines (such as TNF (tumor necrotic factor), Interleukin (IL1-α), (IL1-β), and Interferon Gama (γ)). These released substance play role in endothelial cells to express adhesion factors that prime monocytes and netruphile which facilitate inflammatory cells migration to site of inflammation. That is mechanism lead to elevate production of Cytokine [24]. Some study explain this by inflammation induce lipopolysaccharides increase the gene expression of cytokines and chemikines, which correlates with BNP gene expression in rates [25]. So, our study based on NT-proBNP more than BNP due to its advantages which includes BNP had short half-life

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around 20-30 minutes, but NT-proBNP has a longer half-life 60-120 minutes [26], (due to long half-life and circulating unchanged before excretion this is makes it useful to detect early onset of left ventricle dysfunction.NT-proBNP is stable at room temperature [27, 28]. 3) 0,1 ml of serum enough for NT-PROBNP measurement [29].

Firstly, the NT-proBNP defined as abnormal if above cut-off determined on Receiver Operator Characteristic (ROC) analysis, above the upper limit for age, or above 25 D Calculate from healthy children. High level of NT-proBNP in acute KD associated with systemic inflammatory response, and raise vascular permeability. NT-proBNP level was significant higher in those patients in acute phase of KD than in patients with other febrile illness. So, it is used as biomarker to diagnose early phase of KD and treated as soon as possible because the delay in treat leading to increase incidence of CAL and NT-proBNP concentration may be used as prediction key for systemic vasculitis in KD so it identify the patient who are at high risk of developing CAL [30], and resistance to IVIG. In table 1 of our study, there are 52 of TKD patients had a significant high level of NT-proBNP around 1049.0±283.4ng/L when compared with 40 cases of other febrile illness (control group)119.5±115.6ng/L , so in this study we can use level of NT-proBNP marker to help us to diagnose KD cases from other differential diagnosis. In addition, NT-proBNP marker can be used as tool to diagnose patient with incomplete clinical feature of KD. The IKD defined as patient with fever lasting for five days or more, with at least 2-3 of major clinical manifestation for KD, no other reasonable explanation for the illness and laboratory finding analogs with sever systemic inflammation. IKD is hard to discover, so recent work has been focused on laboratory test of NT-proBNP. In table 1, we have IKD 63 cases of 155 , when we measured their NT-proBNP , had a high level around 1441±467.4ng/L. On the other hand, the complete Kawasaki disease patients 52 of 155 their NT-proBNP around 1049.0±283.4ng/L,. IKD more risk to CAL especially young age [31], high incidence of CAL was described due to protocol of diagnoses because of use of echocardiogram in the diagnostic process, in addition due to delay in treatment , because in difficult making the diagnose. Therefore, in the presrnt study, we concentrate on laboratory tool to determine which children with significant NT-proBNP of KD is at risk to develop CAL, due to a significant difference between KD cases with or without CAL. The primary goal of recognizing and treating child with KD to prevent CAL, so can work on NT-proBNP as useful marker to predict the KD patient at great risk of CAL before initial IVIG, because it is important to detect who is risk for CAL, because recent therapeutic strategy used to treat KD steroid pulse therapy or with TNFα Antagonist. The goal of this study is how to detect high risk of coronary artery involvement in KD patients either TKD and IKD, and relationship between CAL in KD and NT-proBNP If we see table 2 and comparing two groups, CAL of KD group around 36 cases of 155 had high significant NT-proBNP around 2608.2±745.5 ng/l but on the other hand, we found 79 of 155 of non CAL of KD cases their NT-proBNP not significantly high 902.6±162.0 ng/l, so the NT-proBNP can predict cases of CALKD. But when we study the risk of CAL in which group of TKD and IKD, we make some Comparing in table 1, we found there are 40 of 52 case of TKD do not had CAL, while there are 13 of 52 cases of TKD had CAL. And we when looking to other group of IKD around 63 case, 38of them do not had CAL, while 24 of 63 had CAL. So, this study not enough to our hypothesis, due to less number of CAL IKD in comparing to number of NONCAL IKD. On the other hand, increase serum level of initial NT-proBNP before the initiation of treatment was associated with non response to IVIG around 10% to 20% of cases not respond to initial IVIG [32, 33]. In this study, we found there are no different

was significant when we do comparing between IVIG non-re-KD and IVIG sensitive groups.

5. Conclusions

This study adds additional evidence there are a relationship between the Kawasaki disease and coronary artery lesion with high level of NT-proBNP. So, it is used as prediction marker to early diagnosis of Kawasaki disease of patient who is risk of coronary artery lesion.

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