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RELATION BETWEEN BETA 2 MICROGLOBULIN LEVELS AND CARDIAC PERFORMANCE IN PATIENTS ON REGULAR HAEMODIALYSIS

By

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ABSTRACT

Background: B2-microglobulin (B2M) is recognized as a surrogate marker of middle-molecule uraemic toxins and is a key component in the genesis of dialysis-associated amyloidosis.

Objectives: To investigate the relation between hidden cardiac dysfunction in one side and B2M levels, conventional risk factors low hemoglobin levels, and aging on the other side.

Subjects and methods: This was a case control study conducted on 50 patients aged 20-60 years with ESRD on regular HD and 50 apparently healthy individuals at El- Mokattam Insurance Hospital from September 2019 till March 2020.

Results: There were statistically significant differences between groups regarding B2M, EF, LVMI, intraventricular septal thickness and LVEDD.

There were no statistically significant differences between groups. Patient's B2- microglobulin in Group (A) ranged between 76.00-109.70 with mean±S.D. 94.162±9.735, while in Group (B) ranged between 0.78-3.29 with mean±S.D. 1.956±0.704. There were statistically significant differences between groups. Patient's LVMI in Group (A) ranged between 111.87-131.59 with mean±S.D. 123.41±5.675, while in Group (B) ranged between 82.02-104.84 with mean±S.D. 91.63±7.236. There were statistically significant differences between groups. Patient's LVEDD in Group (A) ranged between 5.94-7.56 with mean±S.D. 6.79±0.505, while in Group (B) ranged between 3.27-5.25 with mean±S.D. 4.25±0.571. There were statistically significant differences between groups. Patient's LVESD in Group (A) ranged between 4.80-5.73 with mean±S.D. 5.34±0.250, while in Group (B) ranged between 2.87-3.65 with mean±S.D. 3.27±0.243. There were no statistically significant differences between groups.

Conclusion: Plasma B2M level was significantly and directly correlated with some cardiac performance factors such as LVMI, LVEDD, and LVESD. It was also significantly and inversely associated with GFR, albumin and Hb.

Keywords: Beta-2 microglobulin, cardiovascular disease, chronic kidney disease, mortality, uremic toxins, haemodialysis.

INTRODUCTION

Beta-2 microglobulin (B2M) is a low-molecular-weight polypeptide (11800 Da), which is present on the surface of all nucleated cells, expressing the major histocompatibility class I. Under physiologic conditions, B2M is produced at a constant rate and is eliminated from circulation by kidneys. In patients with a range of inflammatory, hematologic, immunodeficiency, and renal diseases, plasma B2M levels are elevated *(Jasim et al., 2019)*.

In patients with chronic kidney disease (CKD), plasma B2M levels are elevated, especially in patients on hemodialysis (HD) in whom glomerular filtration rate (GFR) is almost completely absent. B2M is also a surrogate marker of middle-molecular-weight uremic toxins in patients on HD, which is cleared only by high-flux membrane. In some studies, predialysis serum B2M level predicted mortality and increase of B2M clearance during HD was associated with improved outcomes. In addition, elevated plasma B2M level is a potential risk factor for the development of dialysis-related amyloidosis *(Wong et al., 2016)*.

B2-microglobulin (ß2-m), the non-polymorphic chain of the major histocompatibility Class I complex (MHC-I), is found on the surface of all nucleated cells and plays a central role in cellular immunology. Its synthesis rate normally ranges from 2-4 mg/kg/day with a half-life of 2-5 hours. In healthy individuals, the plasma concentration varies from 1 to 3 mg/L which varies inversely with the glomerular filtration rate (GFR). More than 95% of ß2-m is eliminated by degradation in the proximal tubule. Since this compound cannot be removed fromthe serum by the kidney or certain dialysis membranes in patients with renal dysfunction on dialysis, ß2-m concentration is increased by up to 60-fold in patients with end-stage renal disease (ESRD). Accumulations of ß2-m in these patients lead to Dialysis-Related Amyloidosis (DRA) *(Hoang et al., 2019)*.

In general, it becomes apparent only after more than 5-7 years of renal replacement therapy. This type of amyloid may be seen even in patients with long-standing, severe renal failure who are not yet treated by dialysis or related procedures. 3 Age above 40- years at the start of dialysis, 4 duration of dialysis, 5 use of cuprophane and low-flux membranes and use of low purity dialysate are identifiable risk factors. ß2-m-related amyloid has a marked affinity for joint tissues (cartilage, capsule, synovium). The main signs and symptoms of DRA are musculoskeletal disorders such as carpal tunnel syndrome, joint arthro-pathy, and bone cysts leading occasionally to pathologic bone fractures *(Singh et al., 2017)*.

It is still unclear whether B2M is an important factor of cardiovascular mortality in patients with CKD. In some clinical studies, B2M had an active role in vascular damage by up regulation of interleukin-1 (IL-1) and tumor necrosis factor α (TNF-α) expression. In addition, it might cause cardiovascular disease by amyloid formation. However, in the other studies, higher serum B2M levels were associated with better nutritional status and survival in patients with CKD *(Fatima et al., 2018)*.

The aim of this study was to investigate the relation between hidden cardiac dysfunction in one side and B2M levels, conventional risk factors low hemoglobin levels ,and aging on the other side.

PATIENTS AND METHODS

This was a case control study conducted on 50 patients aged 20-60 years with ESRD on regular hemodialysis and 50 apparently healthy individual at El-Mokattam Insurance Hospital from September 2019 till March 2020.

Target population: Fifty patients aged 20-60 years with ESRD on regular HD and 50 apparently healthy individuals matched for age and sex.

Inclusion criteria:

1. Patients with ESRD on regular HD for at least 3 months.
2. Informed consents from all individuals studied.
3. Age ranged from 20 to 60 years old.

Exclusion criteria:

1. Hospitalization due to non-renal causes.
2. Heart failure or any acute cardiac events within 3 months.
3. Ejection fraction less than 50 %.
4. Pregnancy.
5. Uncontrolled hypertension and Diabetics.
6. Malnutrition.
7. Active malignancy.

All individuals are subjected to clinical assessment and laboratory assessment.

Ethical committee: Permission from the Faculty of Medicine ethical committee was also obtained and approval from institutional review board was taken, with written consents from every subject sharing in this work.

Statistical analysis:

Analysis of data was done using Statistical Program for the Social Science version 20 (SPSSInc., Chicago, IL, USA). Quantitative variables were described in the form of mean and standard deviation. Qualitative variables were described as number and percent. In order to compare parametric quantitative variables between two groups, Student t test was performed or Mann-Whitney test. Qualitative variables were compared using chi-square (X2) test or Fisher's exact test when frequencies were below five. Pearson correlation coefficients were used to assess the association between two normally distributed variables. P value < 0.05 was considered significant.

RESULTS

Patients were classified into 2 groups: Group (A): 50 patients aged 20-60 years with ESRD on regular HD and Group (B): 50 apparently healthy individual matched for age and sex. Age in Group (A) ranged between 20-60 years with mean±S.D. 43.94±12.363 years while in Group (B) was ranged between 21-59 years with mean±S.D. 40.96±12.638 years. There was no statistically significant differences between groups where P=0.212. Patient's sex in Group (A) showed that 27(54%) were males and 23(46%) were females while in Group (B) 25(50%) were males and 25(50%) were females. There was no statistically significant difference between groups where P=0.841 **(Table 1)**.

Table (1): Comparison between two groups as regard to patient's age (years)

Groups / Parameters	Group (A) (n=50)		Group (B) (n=50)		P-Value
Age: Min.-Max.	20-60		21-59		0.212
Mean± S.D	43.94±12.363		40.96±12.638		
	No.	**%**	**No.**	**%**	
Sex: Males	27	54	25	50	0.841
Females	23	46	25	50	

Patient's Cause of ESRD in Group (A) showed that the major cause of ESRD was diabetes mellitus 34(68%) followed by hypertension 13(26%). Duration on dialysis ranged between 4-16 months with a mean of value 10.20±3.574 months **(Table 2)**.

Table (2): Distribution of studied cases as regard to patient's cause of ESRD and duration on dialysis

Group (A) (n=50) / Parameters	No.	%
Causes of ESRD		
DM	34	68
Hypertension	13	26
Chronic Glomerulonephritis	3	6
Duration on dialysis years		
Min.-Max.	4-16	
Mean± S.D	10.20±3.574	

Patient's urea in Group (A) ranged between 73.57-144.99 with mean±S.D. 109.646±20.085, while in Group (B) ranged between 24.39-30.50 with mean±S.D. 27.524±1.876. There were statistically significant differences between groups where P<0.001. Patient's creatinine in Group (A) ranged between 3.10-8 with mean±S.D. 5.902±1.633, while in Group (B) ranged between 0.65-0.92 with mean±S.D. 0.771±0.080. There were statistically significant differences between groups where P<0.001 **(Table 3)**.

Table (3): Comparison between the two studied groups according to Kidney Function Test

Parameters \ Groups	Group (A) (n=50)	Group (B) (n=50)	P
Urea (mg/dL)			
Min.-Max.	73.57-144.99	24.39-30.50	<0.001
Mean± S.D	109.646±20.085	27.524±1.876	
Creatinine (mg/dL)			
Min.-Max.	3.10-8	0.65-0.92	<0.001
Mean± S.D	5.902±1.633	0.771±0.080	

Patient's iron in Group (A) ranged between 28.61-133.11 with mean±S.D. 83.372±31.297, while in Group (B) ranged between 62.87-169.94 with mean±S.D. 102.968±30.887. There were statistically significant differences between groups where P=0.005.

Patient's ferritin in Group (A) ranged between 159.51-539.92 with mean±S.D. 379.44±120.359, while in Group (B) was ranged between 13.09-289.08 with mean±S.D. 347.77±58.245. There were statistically significant differences between groups where P<0.001.

Patient's TIBC in Group (A) ranged between 180.61-291.70 with mean±S.D. 239.16±35.905, while in Group (B) ranged between 245.39-444.42 with mean±S.D. 3.246±0.188. There were statistically significant differences between groups where P=0.010.

Patient's transferrin saturation in Group (A) ranged between 11.11-53.27 with mean±S.D. 30.85±12.248, while in Group (B) ranged between 25.04-35.00 with mean±S.D. 29.81±2.893. There were no statistically significant differences between groups where P=0.915 **(Table 4)**.

Table (4): Comparison between the two studied groups according to Iron study

Parameters \ Groups	Group (A) (n=50)	Group (B) (n=50)	P
Iron μg/Dl			
Min.-Max.	28.61-133.11	62.87-169.94	0.005
Mean± S.D	83.372±31.297	102.968±30.887	
Ferritin (ng/ml)			
Min.-Max.	159.51-539.92	13.09-289.08	<0.001
Mean± S.D	379.44±120.359	170.39±79.378	
TIBC μg/dL			
Min.-Max.	180.61-291.70	245.39-444.42	<0.001
Mean± S.D	239.16±35.905	347.77±58.245	
Transferrin (%) **saturation**			
Min.-Max.	11.11-53.27	25.04-35.00	0.915
Mean± S.D	30.85±12.248	29.81±2.893	

Patient's PTH in Group (A) ranged between 70.50-95 with mean±S.D. 82.02±7.390, while in Group (B) ranged between 10-64 with mean±S.D. 34.37±17.529. There were statistically significant differences between groups where P<0.001.

Patient's β2- microglobulin in Group (A) ranged between 76.00-109.70 with mean±S.D. 94.162±9.735, while in Group (B) ranged between 0.78-3.29 with

mean±S.D. 1.956±0.704. There were statistically significant differences between groups where P<0.001.

Patient's EF (%) in Group (A) ranged between 35-56 with mean±S.D. 44.82±6.278, while in Group (B) ranged between 51-65 with mean±S.D. 57.46±4.072. There were statistically significant differences between groups where P<0.001 **(Table 5)**.

Table (5): Comparison between two groups as regard to patient's PTH and β2-macroglobulin

Groups / Parameters	Group (A) (n=50)	Group (B) (n=50)	P-Value
PTH (pg/mL)			
Min.-Max.	70.50-95	10-64	<0.001
Mean± S.D	82.02±7.390	34.37±17.529	
β2-microglobulin mg/L			
Min.-Max.	76.00-109.70	0.78-3.29	<0.001
Mean± S.D	94.162±9.735	1.956±0.704	
EF %			
Min.-Max.	35-56	51-65	<0.001
Mean± S.D	44.82±6.278	57.46±4.072	

Patient's LVMI in Group (A) ranged between 111.87-131.59 with mean±S.D. 123.41±5.675, while in Group (B) ranged between 82.02-104.84 with mean±S.D. 91.63±7.236. There were statistically significant differences between groups where P<0.001.

Patient's Intraventricular septal thickness in Group (A) ranged between 1.17-2 with mean±S.D. 1.62±0.267, while in Group (B) ranged between 0.40-1.13 with mean±S.D. 0.775±0.225. There were statistically significant differences between groups where P<0.001.

Patient's LVEDD in Group (A) ranged between 5.94-7.56 with mean±S.D. 6.79±0.505, while in Group (B) ranged between 3.27-5.25 with mean±S.D. 4.25±0.571. There were statistically significant differences between groups where P<0.001.

Patient's LVESD in Group (A) ranged between 4.80-5.73 with mean±S.D. 5.34±0.250, while in Group (B) ranged between 2.87-3.65 with mean±S.D. 3.27±0.243. There were no statistically significant differences between groups where P<0.001 **(Table 6)**.

Table (6): Comparison between the two studied groups according to echocardiography

Parameters \ Groups	Group (A) (n=50)	Group (B) (n=50)	P
LVMI g/m^2			
Min.-Max.	111.87-131.59	82.02-104.84	<0.001
Mean± S.D	123.41±5.675	91.63±7.236	
Intraventricular septal thickness, cm			
Min.-Max.	1.17-2	0.40-1.13	<0.001
Mean± S.D	1.62±0.267	0.775±0.225	
LVEDD, cm			
Min.-Max.	5.94-7.56	3.27-5.25	<0.001
Mean± S.D	6.79±0.505	4.25±0.571	
LVESD, cm			
Min.-Max.	4.80-5.73	2.87-3.65	<0.001
Mean± S.D	5.34±0.250	3.27±0.243	

There was a significant correlation between plasma B2M level and echocardiographic data in patients with CKD **(Table 7)**.

Table (7): Correlation between Plasma B2M Level and Echocardiographic data in patients with CKD

Parameters \ Values	r	P value
Ejection fraction, %	-0.622	<0.001
LVMI, g/m2	0.438	<0.001
Interventricular septal thickness, cm	0.330	0.004
LVEDD, cm	0.41	0.021
LVESD, cm	0.319	0.024

DISCUSSION

As regard sociodemographic data, age in Group (A) ranged between 20-60 years Group (B) ranged between 21-59 years. There were no statistically significant differences between groups where P=0.212. Patient's sexes in Group (A) 54% were male and 46% were females while in Group (B) 50% were male and 50% were females. There were no statistically significant differences between groups. There were no statistically significant differences between groups regarding working status.

The accumulation of middle molecular weight solutes, such as beta-2 microglobulin (b2M), is toxic to various body tissues and has been associated with adverse cardiovascular and infectious outcomes among patients with end-stage renal disease (ESRD) *(Cheung et al., 2010)*.

In the present study, that the major cause of ESRD in Group (A) was diabetes mellitus, hypertension and chronic glomerolsclerosis. Duration on dialysis ranged between 4-16 months.

Our results were in line with study of *Mumtaz et al. (2010)* as they reported that

the main causes of ESRD in the studied group were diabetes mellitus followed by hypertension and the mean duration on dialysis was 13.82 months with a range of three to sixteen months.

Those results were in line with study of *Mumtaz et al. (2010)* and *Dung et al. (2019),* the present study showed that there were statistically significant differences between groups iron, ferritin and TIBC and PTH.

The current study showed there was β2- microglobulin statistically significant difference between groups.

Our results were in agreement with study of *Cheung et al. (2010), Mumtaz et al. (2010), Kim et al. (2011), Sedighi et al. (2015)* and *Malik et al. (2018)* as they reported that mean plasma B2M level was significantly higher in patients with CKD than control group.

The major reason for such a high level of ß2- m in the previous study was that the dialyzer used for HD in their patients was of the low-flux type. As ß2-m is a middle molecule of molecular weight of 12000 Da, conventional, low-flux dialyzers do not clear these molecules which lead to accumulation of this silent killer in the body. Financial constraints are the major reason for using low-flux dialyzers in their patients. The cost of dialysis when low-flux dialyzers are used is about US Dollars 400 as against the cost for using high-flux HF dialyzers, which is about 50 US Dollars more. This factor is the major reason for using low-flux dialyzers and accumulation of ß2-m in these patients *(Sedighi et al., 2015).*

Liabeuf et al. (2012) confirms that plasma B2M levels are elevated in CKD patients and that these levels progressively increase with decreasing GFR and peak in hemodialysis patients. More interestingly, B2M levels were independently associated with overall and cardiovascular mortality and cardiovascular events in the entire cohort and with cardiovascular events in predialysis patients. Moreover, they show that circulating B2M is a better predictor of overall and cardiovascular mortality for the whole cohort and of cardiovascular events for predialysis patients, compared with well-established factors associated with outcomes in this population, including eGFR, inflammation biomarkers, and others factors included in a propensity score.

The present study showed that EF (%) was statistically significant differences between groups. Patient's LVMI intraventricular septal thickness there were statistically significant differences between groups.

LVEDD showed statistically significant differences between groups, no statistically significant difference in LVESD between groups.

Our results were supported by study of *Amighi et al. (2011)* who showed a strong association between serum B2M level and cardiovascular events in patients with prevalent asymptomatic carotid atherosclerosis, with comorbidity severity similar to patients with CKD, even after adjustment for CRP and GFR. *Cheung et al. (2013)* reported serum B2M level as a novel risk marker for all-cause and cardiovascular mortality in patients with diabetes mellitus, regardless of renal function. *Shinkai et al. (2012)* suggested that, in old age population, the predictive value of plasma B2M level was superior

to other established prognostic factors for mortality such as GFR, cystatin C, and CRP. Furthermore, *Wu et al. (2017)* found that in those with CKD, serum B2M was more sensitive than creatinine in predicting CVEs and MIA syndrome.

Regarding *Dung et al. (2019)*, during the follow-up period of 5 years, there were 75 all-cause deaths (23.0%). Kaplan–Meier analysis revealed that all-cause mortality in the higher β2-M group was significantly higher compared to that in the lower β2-M groups. Serum β2-M level was a significant predictor for all-cause mortality.

The role of B2M in patients with CKD is unclear. Uremic milieu has a harmful effect on the cardiovascular system. In an in vitro study, high serum B2M and indole-3-acetic acid levels were with low CD34+ and CD133+ endothelial progenitor cells that contribute to vessel repair and neovascularization *(Jourde-Chiche et al., 2011)*. Moreover, other uremic toxins such as P-cresyl sulfate and guanidine compounds might disturb endothelial proliferation and vascular repair mechanism *(Schepers et al., 2010)*.

CONCLUSION

Plasma B2M level was significantly and directly correlated with some cardiac performance factors such as LVMI, LVEDD, and LVESD. It was also significantly and inversely associated with GFR, albumin and Hb. Thus, B2M might have an important role in the development of cardiovascular diseases in patients on regular hemodialysis.

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العلاقة بين مستوى الميكرو غلوبيولين بيتا 2 وأداء القلب فى مرضى الاستصفاء الدموى المنتظم

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خلفيـــة البحـــث: تعـــد بيتـــا2 ميكروجلوبيـــولين سلســـلة غيـــر متعـــددة الأشـــكال لمركـــب التوافـــق النســـيجي الرئيســـي مـــن الفئـــة الأولـــى، وتوجـــد علـــى ســـطح جميـــع الخلايـــا المنـــواة وتلعـــب دورًا مركزيًـــا فـــي علـــم المناعـــة الخلـــوي. يتـــراوح معـــدل التوليـــف عـــادة مـــن 2-4مجـــم/ كجـــم/ يـــوم مـــع نصـــف عمـــر 2-5 ســـاعات. يختلـــف تركيـــز البلازمـــا مـــن 1 إلـــى 3ملغـــم / لتـــر فـــي الأفـــراد الأصـــحاء والـــذي يختلـــف عكسًـــا مـــع معـــدل الترشـــيح الكبيبـــي. يـــتم الـــتخلص مـــن أكثـــر مـــن 95٪ مـــن بيتـــا2 ميكروجلوبيـــولين عـــن طريـــق التحلـــل فـــي الانابيـــب القريبـــة. نظـــرًا لأنـــه لا يمكـــن إزالـــة هـــذا المركـــب مـــن المصـــل عـــن طريـــق الكلـــى أو بعـــض أغشـــية الغســـيل الكلـــوي فـــي المرضـــى الـــذين يعـــانون مـــن الفشـــل الكلـــوي فـــي غســـيل الكلـــى، يـــتم زيـــادة تركيـــز بيتـــا2 ميكروجلوبيـــولين بمـــا يصـــل إلـــى 60مـــرة فـــي المرضى الذين يعانون من مرض كلوي في المرحلة النهائية.

الهـــدف مـــن البحـــث: تهـــدف هـــذه الدراســـة اليمراجعـــه العلاقـــة بـــين الخلـــل القلبـــي الخفـــي فـــي جانـــب ومســـتويات بيتـــا2 ميكروجلوبيـــولين، وعوامـــل الخطـــر مثـــل انخفـــاض مستويات الهيموغلوبين، والشيخوخة على الجانب الآخر.

المرضـــي وطـــرق البحـــث: تـــم إجـــراء الدراســـة علـــى 50 مريضًـــا تتـــراوح أعمـــارهم بـــين 20 و60 عامًـــا مصـــابون بمـــرض كلـــوي فـــي المرحلـــة النهائيـــة ويتعرضـــون للغســـيل الكلـــوي بشـــكل منـــتظم و 50 فـــرد ســـليم فـــي مستشـــفى المقطـــم للتـــأمين مـــن ســـبتمبر 2019 حتى مارس 2020.

نتـــائج البحـــث: تراوحـــت نســـبة الفيـــريتين فـــي المجموعـــة (أ) بـــين 159.51-539.92 بمتوســـط 379.44 ± 120.359 بينمـــا فـــي المجموعـــة (B) تراوحـــت بـــين 13.09-

289.08 بمتوسط 347.77 ± 58.245. كانت هناك فروق ذات دلالة إحصائية بين المجموعتين. تراوحت قدره ربط الحديد بالترانسفرين في المجموعة (أ) بين 180.61-291.70 بمتوسط 239.16 ± 35.905 بينما في المجموعة (ب) تراوحت بين 245.39-444.42 بمتوسط 3.246 ± 0.188. كانت هناك فروق ذات دلالة إحصائية بين المجموعتين. تراوحت نسبة بيتا2 ميكروجلوبيولين في المجموعة (أ) بين 76.00-109.70 بمتوسط 94.162 ± 9.735 بينما في المجموعة (B) تراوحت بين 0.78-3.29 بمتوسط 1.956 ± 0.704. كانت هناك فروق ذات دلالة إحصائية بين المجموعتين. تراوح مؤشر البطين الأيسر في المجموعة (أ) بين 111.87-131.59 بمتوسط123.41 ± 5.675 بينما في المجموعة (B) تراوحت بين 82.02-104.84 بمتوسط 91.63 ± 7.236. كانت هناك فروق ذات دلالة إحصائية بين المجموعتين. تراوحت سماكة الحاجز داخل البطين في المجموعة (أ) بين 1.17-2 بمتوسط1.62 ± 0.267 بينما في المجموعة (ب) تراوحت بين 0.40-1.13 بمتوسط 0.775 ± 0.225. كانت هناك فروق ذات دلالة إحصائية بين المجموعتين. تراوحت قيمة قطر انبساط البطين الأيسر النهائي للمرضى في المجموعة (أ) بين 5.94-7.56 بمتوسط 6.79 ± 0.505 بينما في المجموعة (ب) تراوحت بين 3.27-5.25 بمتوسط 4.25 ± 0.571. كانت هناك فروق ذات دلالة إحصائية بين المجموعتين. تراوحت قيمة قطر انقباض البطين الأيسر النهائي للمرضى في المجموعة (أ) بين 4.80-5.73 بمتوسط 5.34 ± 0.250 بينما في المجموعة (ب) تراوحت بين 2.87-3.65 بمتوسط 3.27 ± 0.243. لم تكن هناك فروق ذات دلالة إحصائية بين المجموعتين.

الاستنتاج: ارتبط مستوى البلازما B2M بشكل كبير ومباشر ببعض عوامل الأداء القلبي مثل LVMI و LVEDD و .LVESD كما ارتبط بشكل كبير وعكسي مع GFR والألبومين وHb.

الكلمات الدالة: بيتا 2 مكروغلوبولين، أمراض القلب والأوعية الدموية، أمراض الكلى المزمنة، الوفيات، السموم البوليسية، غسيل الكلى.