



Significance of vitamin B₁₂ level as a risk factor metabolic syndrome in Saudi population

Ashgan Mohammed K Al-Manzlawi¹, Khalid O Abulnaja², Mazin A Zamzami³, Qari M⁴

^{1,2,3,5} Department of Biochemistry, Faculty of science, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia

^{2,5} Experimental Biochemistry Unit, King Fahad Medical Research center (KFMRRC), Jeddah, Kingdom of Saudi Arabia

² Bioactive Natural Products Research Group, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia

⁴ Department of Hematology, Faculty of medical science, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia

Abstract

Background: Metabolic syndrome (MetS) is a group of collective disease including obesity associated with diabetic and orhypertension. Therefore, the aim of the work is for monitoring plasma vitamin B₁₂ in association with BMI in Saudi subjects as a predictive biomarker for MetS. It was also our intention to provide a feasible approach for the early diagnosis of MetS.

Subjects and methods: This study was carried out on sixty subjects divided into four groups each 15 subjects: Group (I): Normal healthy subjects as control. Group (II): including patients diagnosed as type II diabetic Patients. Group (III): including hypertensive patients Group (IV): including patient's diabetic with hypertensive. Anthropometric analysis including BMI. Fasting blood samples was collected from all subjects for assay of glucose, HA1C and vitamin B₁₂.

Results: Data obtained showed that, vitamin B₁₂ level was significantly decreased in the diabetic group, hypertensive and the combined group (diabetic + hypertensive) ($P < 0.005$) compared to control group. While the diabetic group showed a non-significant ($P > 0.05$) difference versus hypertensive group, respectively. Moreover, a non-significant decrease in Vitamin B₁₂ level was occurred in the combined (diabetic + hypertensive) group ($P > 0.05$) compared to the diabetic group and hypertensive group. A negative correlation between HA1C and B₁₂ was recorded ($r = -0.62$) and with BMI ($r = -0.59$). It was concluded that, vitamin B₁₂ is a promising biomarker for differentiation between Met S and other diseases for management and prevent complications.

Keywords: metabolic syndrome: vitamin B₁₂: risk factor

Introduction

The prevalence of overweight or obesity in the world population has been rising rapidly, emerging as a major global challenge. Obesity contributes to the increased risk of other metabolic disease such as diabetes, cardiovascular disease (CVD), and certain types of cancer, thereby increasing global mortality [1-3]. Therefore, development of health food and natural nutraceuticals for prevention of overweight and obesity have received substantial attention because of their less side effect [4-6]. Since natural compounds derived from food material have been consumed by human for a long time, it is regarded safer than synthetic compounds. If their efficacy on obesity and metabolic diseases can be validated scientifically, it will be easily applicable to clinical use. Middle East is no exception in the growing obesity problem. Overweight and obesity have contributed greatly to the increase of non-communicable diseases (NCDs) in the Middle East [7]. The burgeoning rate of obesity is not only indicated in adult population, but also in children and adolescents [8]. This high prevalence of obesity has paralleled the rise of diabetes and hypertension. Therefore, the aim of the work is for monitoring plasma vitamin B₁₂, in Saudi subjects as a predictive biomarker for MetS. It was also our intention to provide a feasible approach for the early diagnosis of MetS.

Subjects and Methods

All participants gave informed consent according to the protocol approved by the local ethics committee and in accordance with the ethical standards of the bioethics and research committee of the King Abdulaziz University. Sixty adult patients were included in the present study, age ranging between (18-60) years; the samples were collected from King Abdulaziz hospital, Jeddah, Saudi Arabia.

Experimental design

The subjects were divided into four groups each 15 subjects: **Group (I):** Normal healthy subjects not suffering from any systemic diseases.

Group (II): including patients diagnosed as type II diabetic patients (fasting blood glucose FBG of 126 mg/dl, 5.5 mmol/l or higher).

Group (III): including hypertensive patients (BP \geq 130/85).

Group (IV): including patient's diabetic with hypertensive.

Fasting blood samples was collected from all subjects and serum was separated and stored at -80 °c till analysis. Glycated Hb (HbA1C) measurements were bought from Bio Vision® Milpitas, CA 95035 USA. Vitamin B₁₂ (V B₁₂) measurements

were bought from Aviva System Biology ® USA

Statistical analysis

One-way analysis of variance (ANOVA) and the least significant differences (LSD) were calculated. Statistical comparisons among the various groups were conducted using a (Graph Pad prism program and excel 2016 data analysis). Statistical significance is set at $\alpha < P = 0.05$.

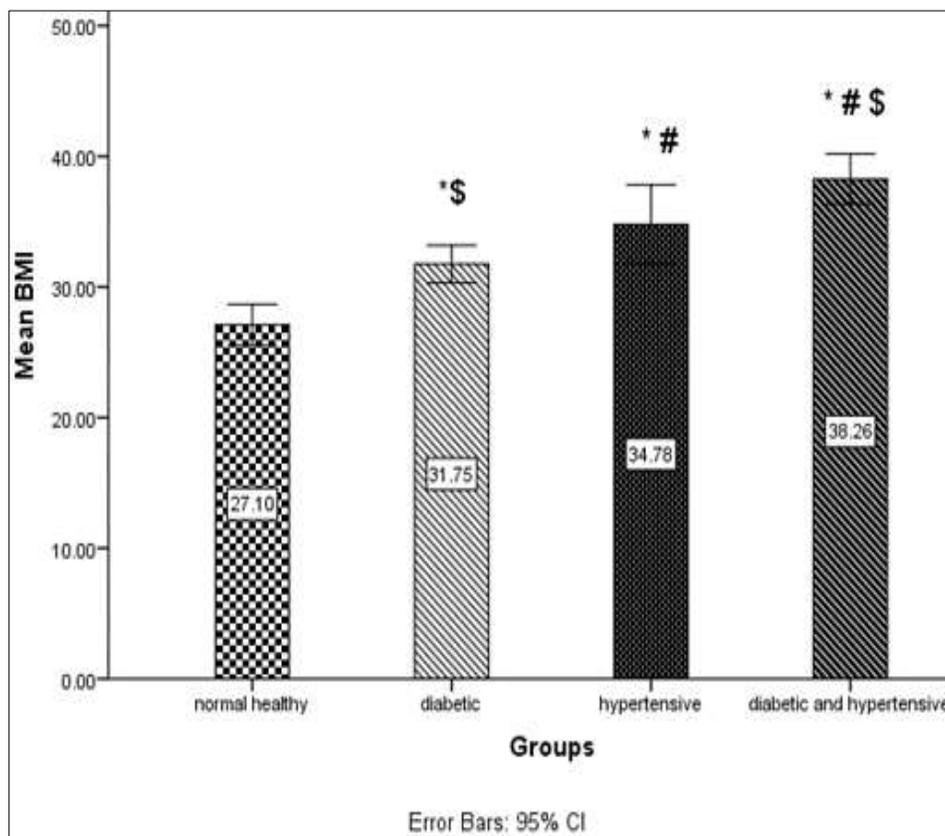
Results

Body mass index (BMI)

As shown in figure 1, a significant increase in body mass index ($P < 0.05$) of all tested groups diabetic group ($P < 0.00$), hypertensive group ($P < 0.00$) and the combined (diabetic + hypertensive) group ($P < 0.00$) compared to the control healthy group. Moreover, the combined (diabetic + hypertensive) group showed a significant ($P < 0.001$) increase in BMI compared to each diabetic group and hypertensive Group. As shown from

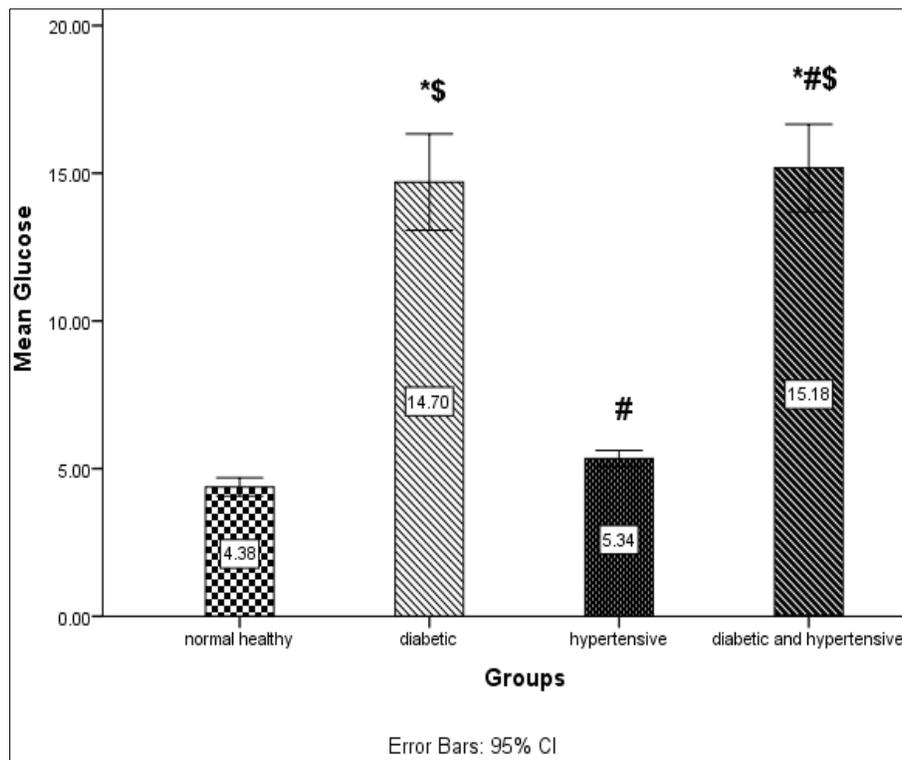
(Fig 2 and 3), a significant increase in glucose and HA1C levels ($P < 0.05$, 0.001) was found for the diabetic and the combined (diabetic + hypertensive) groups compared with the control group, respectively. Moreover, the combined group (diabetic + hypertensive) demonstrated a significant increase in glucose and HA1C levels ($P < 0.05$) compared with the hypertensive group. However, serum glucose level for the hypertensive group versus control group was non-significant changes ($P > 0.05$).

Figure (3) showed that vitamin B₁₂ level was significantly decreased in the diabetic group, hypertensive and the combined group (diabetic + hypertensive) ($P < 0.005$) compared to control group. While the diabetic group (+) group showed a non-significant ($P > 0.05$) difference versus hypertensive group, respectively. Moreover, a non-significant decrease in Vitamin B₁₂ level was occurred in the combined (diabetic + hypertensive) group ($P > 0.05$) compared to the diabetic group and hypertensive group. A negative correlation was found between BMI, glucose and HA1C levels and B₁₂ level.



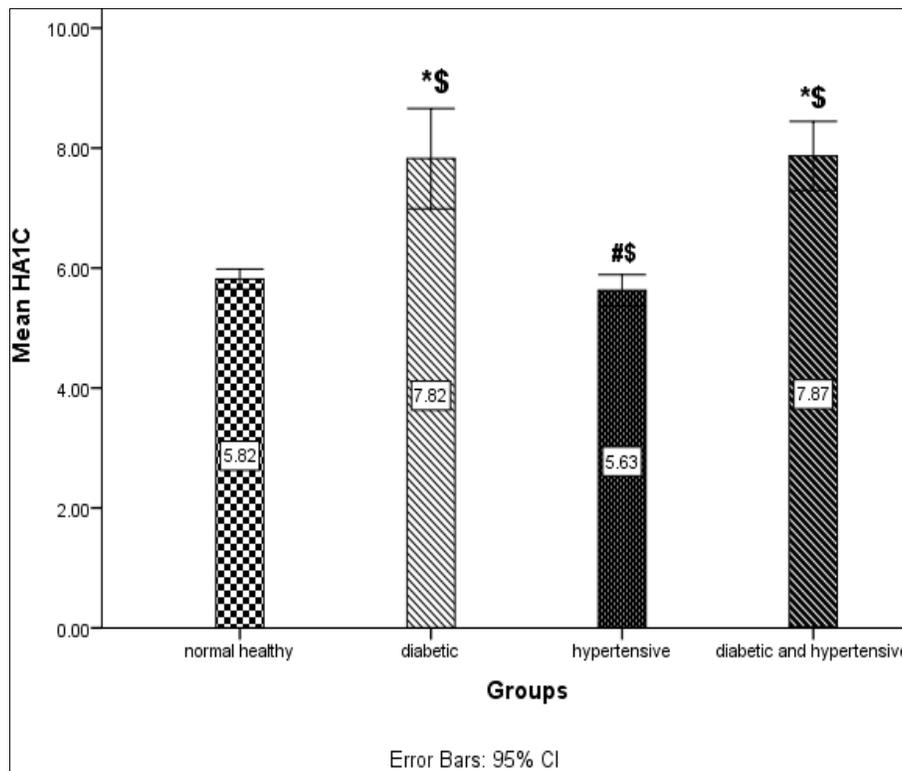
* Significant versus control group, # significant versus diabetic group, \$ significant versus hypertensive group.

Fig 1: Mean \pm S.E of body mass index (BMI) of control healthy, diabetic, hypertensive and (diabetic and hypertensive) groups.



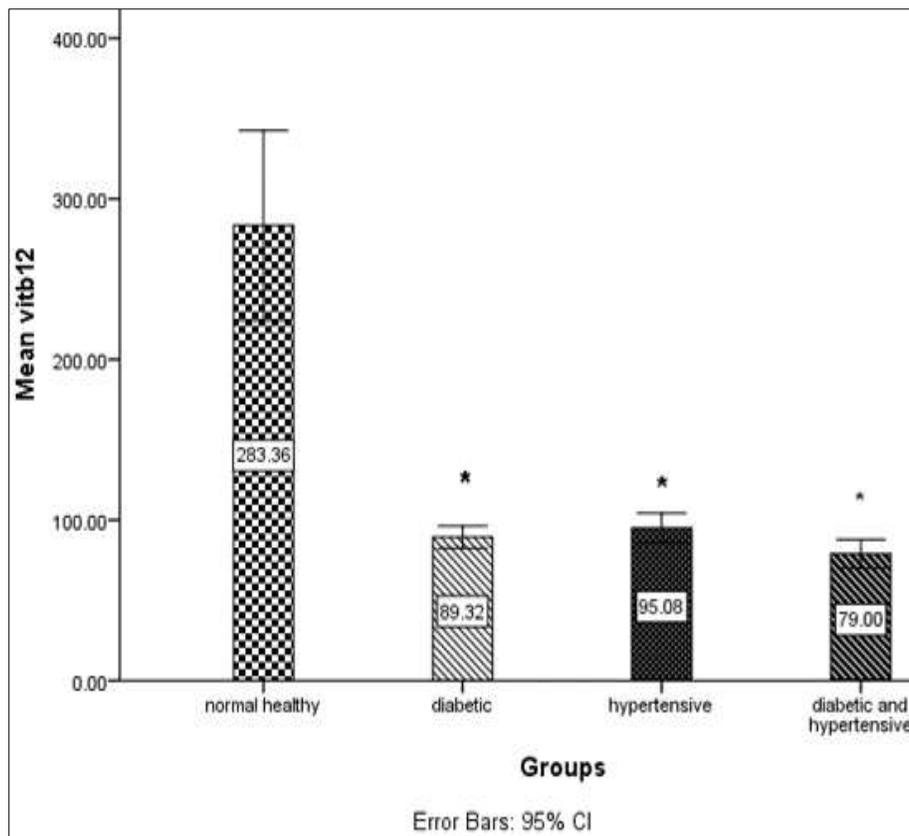
* Significant versus control group, # significant versus diabetic group, \$ significant versus hypertensive group.

Fig 2: Mean ± S.E of serum glucose level (mmol /l) of control healthy, diabetic, hypertensive and (diabetic and hypertensive) groups.



* Significant versus control group, # significant versus diabetic group, \$ significant versus hypertensive group.

Fig 3: Mean ± S.E of HA1c for control, control healthy, diabetic, hypertensive and (diabetic and hypertensive) groups.



* Significant versus control group, # significant versus diabetic group, \$ significant versus hypertensive group.

Fig 4: Mean \pm S.E of serum Vitamin B₁₂ level for control, control healthy, diabetic, hypertensive and (diabetic and hypertensive) groups.

Discussion

Middle East is no exception in the growing obesity problem. The obesity has contributed greatly to the increase of non-communicable diseases (NCDs) in the Middle East MetS [10-12]. The risk factors associated with MetS are considered as important biomarkers for early identification and diagnosis to fast intervention and management. The current study investigated the association of changes of serum level of vitamin B₁₂ with MetS as a good sensitive biomarker for early prediction of complication to manage it. It was found that, a significant increase in body mass index ($P < 0.05$) of all tested groups: diabetic group ($P < 0.00$), hypertensive group ($P < 0.00$) and the combined (diabetic + hypertensive) group ($P < 0.00$) compared to the control healthy group. Moreover, the combined (diabetic + hypertensive) group showed a significant ($P < 0.001$) increase in BMI compared to each diabetic group and hypertensive group. The BMI is a good indicator for obesity and overweighted subjects. Previous study revealed that, belly fat and BMI is higher in obese with diabetic or hypertensive subjects than that of diabetic or hypertensive only [16]. This is in accordance with our study. The results obtained showed that, a significant increase in HbA1c level ($P < 0.05$) was produced for the diabetic and the combined (diabetic + hypertensive) groups compared to the control group, respectively. Moreover, the combined group (diabetic + hypertensive) demonstrated a significant increase in glucose level ($P < 0.05$) compared to the hypertensive group. However, serum glucose level for the hypertensive group versus control group was non-significant ($P > 0.05$). Data obtained

showed that vitamin B₁₂ level was significantly decreased in the diabetic group, hypertensive and the combined group (diabetic + hypertensive) ($P < 0.005$) compared to control group. While the diabetic showed a non-significant ($P > 0.05$) difference versus hypertensive group, respectively. Moreover, a non-significant decrease in Vitamin B₁₂ level was observed in the combined (diabetic + hypertensive) group ($P > 0.05$) compared to the diabetic group and hypertensive group. Data from previous studies revealed that level of vitamin B₁₂ possibly reduced due to the glycation of hemoglobin with hyperglycemia and caused anemia. Serum vitamin B₁₂ levels of diabetic subjects were significantly reduced compared with control [13]. A negative correlation was observed between HbA1c and vitamin B₁₂ level ($r = -0.63$). These changes were correlated with the incidence of the disease and were of a higher significance with the genesis of complications, suggesting that hyperglycemia associated glycation may occur for early prediction of complications [14, 15]. The reduced level of vitamin B₁₂ may open a window in interpreting the anemic causes of diabetic complications [16-18].

References

- Aslinia F, Mazza J, Yale S. Megaloblastic Anemia and Other Causes of Macrocytosis. *Clinical Medicine & Research*. 2006; 4:236-41. doi: 10.3121/cm.4.3.236.
- Pflipsen M, Oh R, Saguil A, Seehusen D, Topolski R. The Prevalence of Vitamin B₁₂ Deficiency in Patients with Type 2 Diabetes: A Cross-Sectional.

3. Barakat H, Barakat H, Baaj MK. "CVD and obesity in transitional Syria: a perspective from the Middle East." *Vasc Health Risk Manag*. 2012; 8:145-150.
4. Fahed AC, El-Hage-Sleiman AK, Farhat TI, Nemer GM. "Diet, genetics, and disease: a focus on the Middle East and North Africa region." *J Nutr Metab*, 2012, 109037.
5. George M, Rajaram M, Shanmugam E. "New and emerging drug molecules against obesity." *J Cardiovasc Pharmacol Ther*. 2014; 19(1):65-76.
6. Hotamisligil GS. "Inflammation and metabolic disorders." *Nature*. 2006; 444(7121):860-867.
7. Jain R, Chung SM, Jain L, Khurana M, Lau SW, Lee JE, *et al*. "Implications of obesity for drug therapy: limitations and challenges." *Clin Pharmacol Ther*. 2011; 90(1):77-89.
8. Jiang Y, Wu SH, Shu XO, Xiang YB, Ji BT, Milne GL, *et al*. "Cruciferous vegetable intake is inversely correlated with circulating levels of proinflammatory markers in women." *J Acad Nutr Diet*. 2014; 114(5):700-708e702.
9. Kilpi F, Webber L, Musaigner A, Aitsi-Selmi A, Marsh T, Rtveldze K, *et al*. "Alarming predictions for obesity and non-communicable diseases in the Middle East." *Public Health Nutr*. 2014; 17(5):1078-1086.
10. Lam TK, Gallicchio L, Lindsley K, Shiels M, Hammond E, Tao XG, *et al*. "Cruciferous vegetable consumption and lung cancer risk: a systematic review." *Cancer Epidemiol Biomarkers Prev*. 2009; 18(1):184-195.
11. Lee JH, Moon MH, Jeong JK, Park YG, Lee YJ, Seol JW, *et al*. "Sulforaphane induced adipolysis via hormone sensitive lipase activation, regulated by AMPK signaling pathway." *Biochem Biophys Res Commun*. 2012; 426(4): 492-497.
12. Mirmiran P, Sherafat-KazemzadehR, Jalali-Farahani S, Azizi F. "Childhood obesity in the Middle East: a review." *East Mediterr Health J*. 2010; 16(9):1009-1017.
13. Morgen CS, Sorensen TI. "Obesity: Global trends in the prevalence of overweight and obesity." *Nat Rev Endocrinol*. 2014; 10(9):513-514.
14. Musaiger AO. "Diet and prevention of coronary heart disease in the Arab Middle East countries." *Med Princ Pract*. 2002; 11(2):9-16.
15. Shah R, Gayat E, Januzzi JL, Jr N, Sato A, Cohen-Solal S, *et al*. "Body mass index and mortality in acutely decompensated heart failure across the world: a global obesity paradox." *J Am Coll Cardiol*. 2014; 63(8):778-785.
16. Smith SR. "Drug treatment of obesity." *JAMA Intern Med*. 2014; 174(8):1414-1415.
17. Song MY, Kim EK, Moon WS, Park JW, Kim HJ, So HS, *et al*. "Sulforaphane protects against cytokine- and streptozotocin-induced beta-cell damage by suppressing the NF-kappaB pathway." *Toxicol Appl Pharmacol*. 2009; 235(1):57-67.
18. Thounaojam MC, Nammi S, Jadeja R. "Natural products for the treatment of obesity, metabolic syndrome, and type 2 diabetes." *Evid Based Complement Alternat Med*, 2013, 871018.