ejpmr, 2019,6(3), 367-373

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

AN ASSOCIATIVE STUDY OF NON-LIPID RISK FACTORS (HIGH SENSITIVE-CRP, URIC ACID AND THYROID STIMULATING HORMONE) WITH PARAMETERS OF TYPE 2 DIABETES MELLITUS, BLOOD PRESSURE IN METABOLIC SYNDROME

V. Srinivasa Babu[1]*, V. Kalyan Chakravarthy[2], C. Ramaswamy[3], S. Srikanth[4], M. Karthik[5]

[1]Department of Research, Saveetha University, Thandalam, Chennai, Tamilnadu, India.
[2]Professor, Department of Pathology, Pinnamaneni Institute of Medical Sciences and Research Foundation, Chinnautapalli, Gannavaram, Andhra Pradesh, India.
[3]Professor, Department of Physiology, Saveetha Medical College, Thandalam, Chennai, Tamilnadu, India.
[4]Assistant Professor, Department of Community medicine, Nimra Institute of Medical Sciences, Ibrahimpatnam, Vijayawada, Andhra Pradesh, India.521456.
[5]Assistant Professor, Department of Physiology, Nimra Institute of Medical Sciences, Ibrahimpatnam, Vijayawada, Andhra Pradesh, India. 521456.

***Corresponding Author: Dr. V. Srinivasa Babu**

Department of Research, Saveetha University, Thandalam, Chennai, Tamilnadu, India.

Article Received on 27/12/2018 **Article Revised on 16/01/2019** **Article Accepted on 05/02/2019**

ABSTRACT

Background: Metabolic syndrome is the huddle of diseases for atherosclerotic cardiovascular disease (ASCVD) which arises due to excess of plasma glucose, cholesterol, fatty acids, blood pressure and obesity. The role of lipids in the development of MetS had been extensively studied. Some non-lipid factors like hsCRP, uric acid and TSH level also remain elevated in the serum of the MetS patients the correlation of the same with the MetS not fully determined. **Aim and Objectives**: Hence in this study our aim and objectives was to assess the significance of non-lipid risk factors in determining the severity of MetS with the association of type 2 diabetes and blood pressure parameters. **Methods**: A total of 450 subjects (211 men and 239 women) aged ≥ 35 years attending the hospital were divided based on the components of MetS as control (CS), Metabolic syndrome (MS) and severe (SMS) MetS groups. Comparative study was done by one way ANOVA and variables with significant associations were included in regression analysis to determine the future prediction with non-lipid risk factors hs-CRP, serum uric acid and TSH as dependent variables. The cardiovascular and T2DM related parameters FPG, HbA1c, serum fasting insulin, HOMA-IR, SBP, DBP, PR were independent variables in this study. **Results**: All the T2DM and BP variables had highly significant relation (P<0.001) when compared MetS and severe Mets group with control group. In this study, the value of participants HbA1C, PR, FPG, DBP and IR had significant Adjusted OR [3.03 P<0.001; 2.10 P 0.004; 1.86 P 0.033; 0.17, P <0.001 and 0.08, P <0.001 respectively] high positive correlation with the hs-CRP values. It was found that HbA1c, SBP, DBP, FPG and PR had significant predictive AOR [5.829 P<0.001; 2.789 P 0.007; 0.098 P<0.001; 0.383 P 0.008 and 0.543 P 0.053 respectively] in association with Uric acid values. Also, PR, FPG and DBP had significant AOR significance [1.96 P 0.001; 1.41 P <0.001; 1.37 P 0.026 respectively] in association with TSH values. **Conclusion:** It can be concluded that reducing the above T2DM and cardiovascular variables by various lifestyles or other means can reduce the levels of non-lipid risk factors and thereby arrest susceptibility of the development of MetS and severe MetS.

KEYWORDS: T2DM; HTN; Metabolic syndrome; Non-lipid risks; hs-CRP; Uric acid; TSH.

INTRODUCTION

Metabolic syndrome is the huddle of diseases for atherosclerotic cardiovascular disease (ASCVD) which arises due to excess of plasma glucose, cholesterol, fatty acids, blood pressure and obesity.[1,2] Around the world it is appraised that one out of four people suffers from MetS in spite of the competing on its definition.[2] Individual constellation of epidemic risk factors of the pervasiveness of Mets, is intensifying with different regions of all over the world, and specifically there is a sign for high incidence of MetS in other South Asian countries and India.[3-5]

An environmental, metabolic and genetic aspects, evidently signifies a multidimensional interface of etiology of this syndrome but it is mostly unspecified.[6,7] For myocardial infarction (MI), cerebrovascular accident (CVA) and incidence of type 2 diabetes mellitus (T2 DM) are allied and amplified risk by frequent manifestations of prothrombotic and proinflammatory condition of the subjects with these characteristics.[8-10]

Although in previous cross-sectional studies elevated high sensitivity C-reactive protein (hs-CRP) levels had significant association with individual modules of MetS like adiposity, hyperinsulinemia, insulin resistance, hypertriglyceridemia, and low HDL cholesterol[11,12], but not in relation to severity of MetS. MetS and Thyroid Disorders (TD) comparison and association is complex and uncertain.[13] Studies showed a significant relationship of SCH (subclinical hypothyroidism) with components of MetS.[14,15] Shantha et al. study[16], showed the association of primary hypothyroidism in the urban population with MetS. So, the design of TD in MetS and its components differs in unlike studies. There is a evidence that many studies have concentrated on the serum uric acid (SUA), MetS, and carotid atherosclerosis relationship.[17-20] The atherosclerotic vascular disease and SUA is leftovers contradictory.[21] Some studies experiential that relationship between SUA and atherosclerotic vascular disease is assign to an indirect association of increased levels of SUA with cardiovascular risk factors or constellation of these metabolic and hemodynamic risk factors, projected MetS.[22,23]

The elevated levels of the inflammatory markers like hs-CRP and serum uric acid levels are associated with increased risk for development of cardiovascular disease and diabetes mellitus. Adding hs-CRP values in the diagnostic criteria for metabolic syndrome has shown to improve future prediction of development of these diseases.[24] In present study, one step forward we tried to see the association between non lipid risk factors of MetS like hs-CRP, Uric acid and TSH and the Type 2 DM, BP parameters in relation to severity of Metabolic syndrome.

Here is a significant evidence that type 2 diabetes and cardiovascular parameters influences non-lipid risks in MetS and severe MetS and by reducing levels of these factors by life style changes thus decrease susceptibility of MetS. Further, helps to decrease morbidity micro and macro vascular diseases of vital organs like brain, heart, and kidneys and the metabolic diseases HTN and Type 2 Diabetes Mellitus.

AIM AND OBJECTIVES

Our aim is to study of significance of non-lipid risk factors (hs-CRP, Uric acid and TSH) in severity of MetS and the association of type 2 diabetes and blood pressure parameters.

MATERIALS AND METHODS

A total of 450 participants (211 men and 239 women) aged ≥35 years attending our institute hospital from 2nd December, 2015 to 4th August, 2017 were included in this study. The study protocol was approved by the Institutional Ethics Committee. All the participating subjects in the study gave written informed consent. Criteria for choosing the subjects: As per the guidelines issued by the following international organizations: MetS is defined according to the 2009 harmonizing definition set by a joint statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; Word Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity, as the presence of three or more of the following five criteria.[25]

1) Waist circumference in South Asians >90 cm in men and >80 cm in women.
2) Serum triglycerides levels >150 mg/dl.
3) Serum HDL cholesterol levels < 40 mg/dl in men and < 50 mg/dl in women, under treatment is an alternate indicator.
4) Systolic blood pressure >130 mmHg and/or diastolic blood pressure >85 mmHg) under treatment is an alternate indicator, and.
5) Fasting serum glucose levels >100 mg/dL under treatment.[26]

The same standard is also stated in the modified NECP ATP III definition.[27]

The inclusion criteria for patients: Insulin resistance, hypertension, type II diabetes mellitus, increased BMI, is ≥ 23, Increased waist circumference ≥ 36 inches (90cm) in males and ≥32 inches (80cm) in females and age limit is ≥35. Exclusion criteria: Any recent infections, Active lifestyle, PCOD in women and fatty liver disease.

Baseline parameters

•Blood pressure and anthropometric data including height, weight, waist circumference were measured using standard techniques.

•Blood Pressure was measured using a Mercury Sphygmomanometer (Diamond, Mumbai, India) with the patients in a sitting position, legs uncrossed. After 5 minutes of rest in the sitting position, BP was measured on both arms and the higher of the two is taken into consideration. If the systolic and diastolic blood pressure were in different categories, the higher of the two was used in the classification and on that visit; fasting blood samples was drawn from the subjects.

•Biochemical analysis: Fasting blood samples were obtained from the subjects and centrifuged at 2000×g for 10 min. Samples were analyzed for MetS component of fasting plasma glucose, uric acid using by ERBA EM-360 fully automated analyzer. Also MetS non-lipid risk factors such as serum TSH, high sensitive C-reactive protein (hs-CRP) and serum fasting Insulin were assessed by Enzyme Linked Immuno Sorbent Assay (ELISA) method. HbA1c is assessed by High performance liquid chromatography (HPLC), and Homeostatic model for assessment of Insulin Resistance (IR) was calculated (HOMA- IR (µmol/L) = FI mIU/L X FPG (mmol/L) / 22.5 and conversion of FPG mg/dl to mmol/L divided by 18 if mmol/L to mg/dl is multiply by 18 and pulse rate is assessed by pulse meter.

Further the groups were divided into three groups (150 participants in each group), according to the number of components of Metabolic syndrome risk factors mentioned above they acquired.

Group I: Subjects with less than any of the three components of metabolic syndrome (Control group),
Group II: Subjects with any three components of metabolic syndrome (MS group),
Group III: Subjects with more than three components of metabolic syndrome (Severe MS group {SMS})

Statistical analysis: Data were entered on Excel and imported for analysis on SPSS v 16.

To find out the descriptive study of mean and standard error was done by one way ANOVA analysis. MetS variables FPG, HOMA-IR, Hb A1c %, S F Insulin,, SBP, DBP, PR, hs-CRP and Uric acid were highly significant (P <0.001) and TSH was not significant. Regression analysis (Multiple) was done with non-lipid risk factors hs-CRP, serum uric acid and TSH individually taken as dependent variables. The cardiovascular and biochemical parameters FPG, HbA1c, serum fasting Insulin, HOMA-IR, SBP, DBP, PR are independent variables for all the participants used to investigate future predictive study of our three non-lipid risks. Statistical significance was considered if the P value is less than 0.05.

RESULTS

Analysis of the Results

The results of the different parameters in there groups of MS were represented in Figure.1 In this Type 2 Diabetes mellitus in the severity of MetS were compared between the controls and MS and SMS and the statistical analysis showed that the values of Insulin resistance [HOMA-IR] were significantly higher among MS (3.3±0.2) and SMS (5.3±0.2) groups when compared to controls (1.9±0.1). The values of the following in control, MS and SMS were respectively: mean fasting plasma glucose (6.8±0.2, 8.9±0.3 and 4.5±0.1), glycosylated hemoglobin (6.4±0.1, 7.4±0.1 and 5.9±0.1) and serum fasting insulin (9.6±0.5, 13.1±0.6 and 8.9±0.3) and the statistical analysis of these values showed that it was significantly higher (P <0.001) in MS and SMS groups when compared with Controls (8.9±0.3).

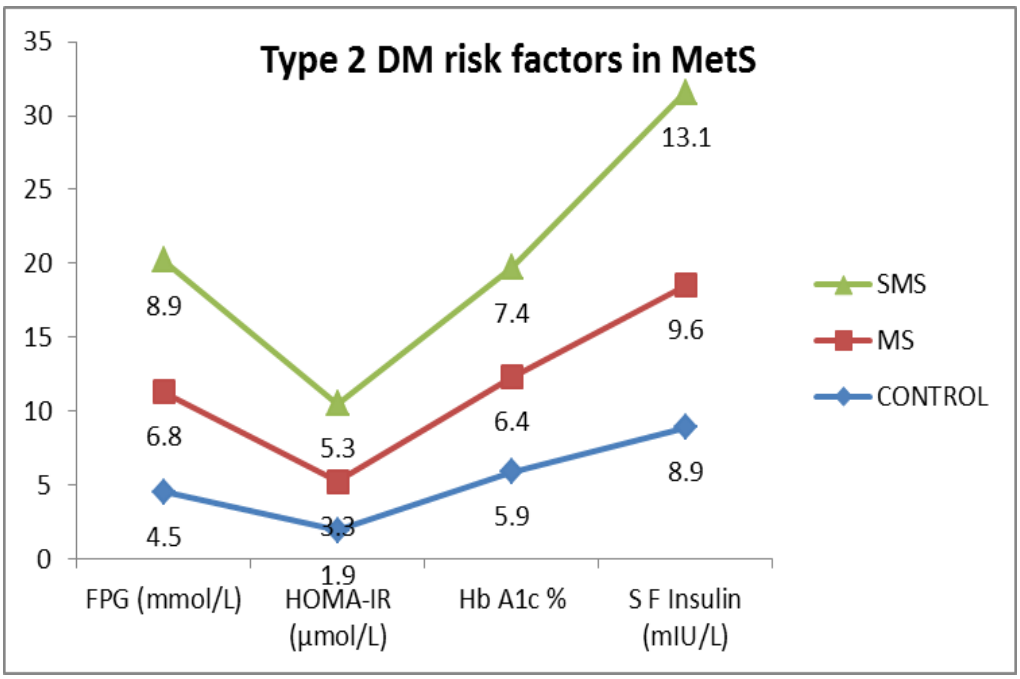

Figure.1: Comparison of mean and SE of Fasting plasma glucose (FPG), HOMA index of insulin resistance (HOMA-IR), Glycosylated hemoglobin (HbA1c) and Serum fasting insulin (SFI).

Group I: Control
Group II: MS group and
Group III: Severe MS

Likewise, the values of the Blood pressure parameters of the participants were given in Figure.2 and result showed that the systolic blood pressure mean and SE had significantly higher among MS (137.9±1.3) and SMS (146.7±1.3) groups when compared to controls (122.5±1.0). This was statistically highly significant P<0.001. Same as diastolic blood pressure (82.9±0.7, 86.5±0.8 and 78.1±0.6), Mean pulse rate (78.3±0.7, 79.1±0.9 and 74.4±0.7) was significantly higher in MS and SMS groups when compared with Controls and all these blood pressure parameters also statistically highly significant P<0.001.

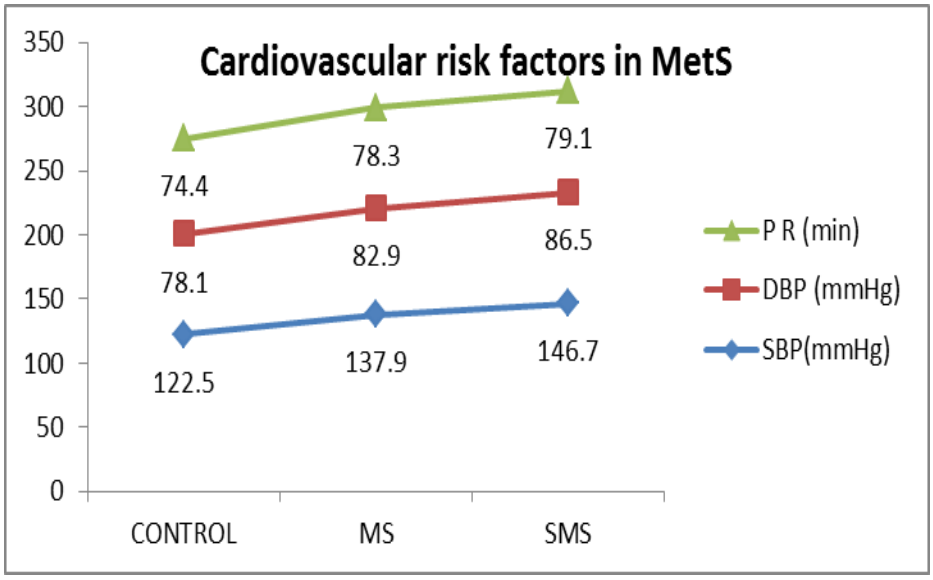

Figure 2: Comparison of mean and SE of Systolic blood pressure (SBP-mmHg), Diastolic blood pressure (DBP-mmHg) and Pulse rate (PR -min).

Group I: Control
Group II: MS group and
Group III: Severe MS

Figure.3 shows non-lipid risk factors hs-CRP mean and SE of MS group (2.2 ± 0.2), SMS group (2.1 ± 0.1) and control group (1.5 ± 0.1) and Uric acid MS (5.0 ± 0.1) SMS (5.2 ± 0.1) Controls (4.6 ± 0.1) were highly significant but only the values of TSH showed [MS (3.2 ± 0.2) SMS (3.0 ± 0.2) and controls (2.6 ± 0.1)] not significant P 0.66 among themselves.

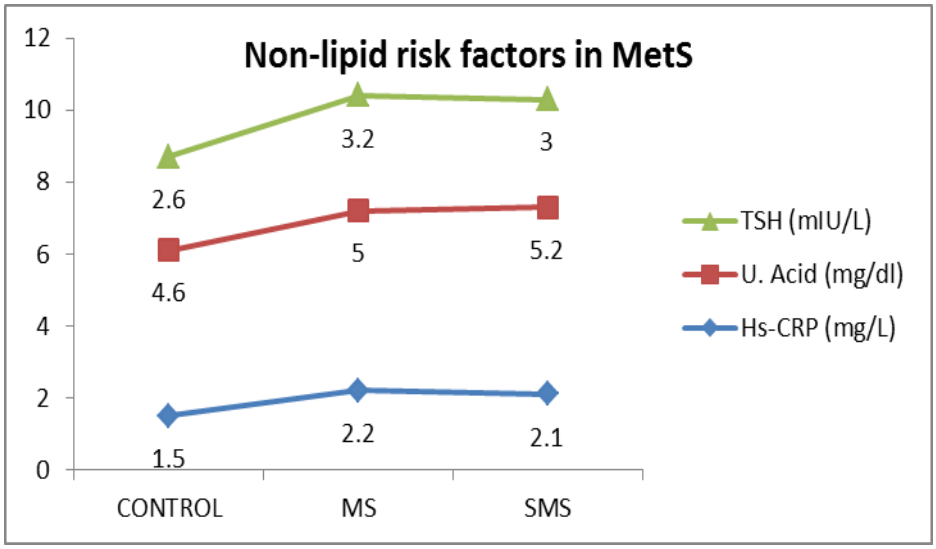

Figure 3: Comparison of mean and SE of Non-lipid risk factors high sensitive C-reactive protein (hs-CRP-mg/L), serum Uric acid (SUA-mg/dl) and TSH (mIU/L) in controls, MS and SMS group.

Group I: Control
Group II: MS group and
Group III: Severe MS

The results of the association of the non-lipid risk factors with the components of MetS were represented in Table. 1, 2 and 3. All the above variables were recorded during the study period and were tabulated to find the association with a change in Hs-CRP. The factors with significant associations were then included in a regression analysis to determine the regression coefficient of change in hs-CRP. The results are represented in Table 1 and it was found that independent variables of IR Adjusted Odds Ratio (AOR 0.08, P <0.001) and DBP (0.17, P <0.001) were independently correlated with dependent variable hs-CRP; HbA1C, PR and FPG which showed positive correlation of AOR 3.03 P<0.001, 2.10 P 0.004, 1.86 P 0.033 respectively. Here, HbA1C having highest predictor with the proinflammatory marker hs-CRP values among the study subjects.

Table 1: Non-lipid risk factor Hs-CRP regression analysis with the variables IR, DBP, FPG, PR and HbA1C in Metabolic syndrome.

Variables	Hs-CRP Adjusted OR	P-value
IR (µmol/L)	0.08	**<0.001**
DBP (mmHg)	0.17	**<0.001**
FPG (mg/dL)	1.86	0.033
PR (min)	2.10	**0.004**
HbA1c **%**	3.03	**<0.001**

Adjusted to HOMA-IR, DBP, FPG, PR and HbA1c
Unadjusted to SBP, Serum fasting Insulin
Bold letters indicates high significance

It was found that independent variables adjusted to DBP (AOR 0.098 P<0.001), FPG (0.383 P 0.008) and PR (0.543 P 0.053) had significant relation with dependent variable Uric acid; while independent variables HbA1c, and SBP with respective positive association AOR of 5.829 P<0.001, 2.789 P 0.007. Thus the study showed that the metabolic end product Uric acid level in the blood had highest future predictor relation with HbA1c and to certain extent SBP.

Table 2: Non-lipid risk factor Uric acid regression analysis with the following variables DBP, FPG, PR, SBP and HbA1c in Metabolic syndrome.

Variables	Uric acid Adjusted OR	P-value
DBP(mm/Hg)	0.098	**<0.001**
FPG (mg/dL)	0.383	**0.008**
PR (min)	0.543	0.053
SBP (mmHg)	2.789	**0.007**
HbA1c %	5.829	**<0.001**

Adjusted to DBP, FPG, PR,SBP and HbA1c
Unadjusted to IR, and Serum fasting Insulin
Bold letter s indicates high significance

The table 3 showed that PR, FPG and DBP had all significant positive adjusted odds (AOR 1.96 P 0.001, 1.41 P <0.001, 1.37 P 0.026) respectively with increasing the endocrinal hormone TSH values among the study subjects. Here also TSH is a dependent variable and all others are independent variables. In this, PR was the highest predictor next to it FPG.

Table 3: Non-lipid risk factor TSH regression analysis with the following variables DBP, FPG and PR in Metabolic syndrome.

Variables	TSH Adjusted OR	P-value
DBP (mmHg)	1.37	0.026
FPG (mg/dL)	1.41	**<0.001**
PR (min)	1.96	**0.001**

Adjusted to DBP, FPG and PR
Unadjusted to HOMA-IR, Serum fasting Insulin and HbA1c and SBP.
Bold letters indicates significance.

DISCUSSION

MS is associated with an increased risk of diabetes, and a number of cardiovascular events, such as myocardial infarction, stroke, and heart failure[28]. The cost of treatment for metabolic diseases is infinite. In present study we found significant association of many risk factors among MetS cases and controls could help to prevent the progression of MetS.

The severity of MetS increases proportionate to DM related factors like FPG, HOMA-IR, S F Insulin and HbA1c and also blood pressure parameters like SBP, DBP and PR. Regitz-Zagrosek V et al showed SBP and DBP are the predictors of MetS.[29] The findings of Patrick H Dessein et al recognize the association of CRP as an proinflammatory marker with CVD in Rheumatoid arthritis and patients with increased waist circumference, was significant regression analysis for the independent variable of HOMA-IR and hs-CRP.[30] In present study we found that HOMA-IR, DBP, FPG, PR and HbA1c were significantly associated with hs-CRP levels in MetS cases. Some study by Devraj *et al* it was suggested that the patients at high risk for future prediction of Type 2 DM and CVD can be identified better by the addition of hs-CRP to the present definition of the MetS may help identify at high risk for future prediction of Type 2 DM and CVD.[28]

Association between serum uric acid levels and the components of MetS showed that as independent variables DBP, FPG PR, SBP, and HbA1c had significant predictors with dependent variable Uric acid. Also, when compared to patients with normal serum uric acid level it was predicted that hyperuricemic patients have higher risks of having hypertension, hyperglycemia and low HDL cholesterol. A number of previous studies also had reported such findings[31] Hyperuricemia predicts the development of hypertension, obesity, and type 2 diabetes mellitus.[32] A strong correlation between serum uric acid and MetS components showed in studies by Nejatinamini et al. and Lee et al.[33,34] Same predictor results were found in correlative study of FBG and DBP shows positive correlation with salivary uric acid.[35]

Thyroid dysfunction is well known cause abnormal glucose level and lipid profile; which in turn are important factors of metabolic syndrome.[36] In our study, it was found that PR, FPG and DBP all had significant increase with increase in the hormone (TSH) values among the study subjects. Similar results were found in a study by Jang J et al.[37] In the present study, non-lipid risk factors of MetS like hs-CRP and SUA levels were significantly more in cases when compared to controls, but no significant association was noted with TSH levels. In contrast to our study, Zhou YC et al concluded that TSH levels had a strong association with incident MetS.[38]

CONCLUSION

It can be concluded that reducing the independent variables like IR, DBP, FPG, PR and HbA1C with the non-lipid inflammatory marker hs-CRP, variables like DBP, FPG, PR, SBP and HbA1C with the dependent non-lipid metabolic end product serum uric acid values and independent factors like DBP, FPG and PR with the endocrinal factor TSH values by various lifestyle or other means can help to reduce and there by the development of MetS.

Thus reducing all these three non-lipid risk factors values reduces the susceptibility of MetS, thus the prevention (the development) of MetS and severe MetS.

Future studies would include the association study of other non-lipid factors such as T3, T4 levels, urine microalbumin levels, serum creatinine and albumin-creatine ratio with parameters of Type 2 DM and BP in Mets.

ACKNOWLEDGEMENTS

The author would like to thank the faculty members of Department of Research, Saveetha University, Chennai, India and the Department of Physiology, Nimra Institute of Medical Sciences, Vijayawada, Andhra Pradesh, India (working as Assistant Professor) for their valuable advice, guidance and constructive criticism. I also acknowledge the subjects for their consent and participation in this study.

Funding: *No funding sources.*
Conflict of interest: *None declared.*

Ethical approval: *The study was approved by the Institutional Ethics Committee of Saveetha University, Chennai, India***.**

REFERENCES

1. International Diabetes Federation: The IDF consensus worldwide definition of the metabolic syndrome. Available from: http://www.idf.org/webdata/docs/MetSyndrome FINAL.pdf (updated 2014 Dec 17).
2. Tehrani FR, Tohidi M, Dovom MR, Azizi F. A population based study on the association of thyroid status with components of the metabolic syndrome. J Diabetes Metab, 2011; 2: 156-62.
3. Sharma SK, Ghimire A, Radhakrishnan J, Thapa L, Shrestha NR, Paudel N, Gurung K, R M, Budathoki A, Baral N, Brodie D. Prevalence of hypertension, obesity, diabetes, and metabolic syndrome in Nepal. Int J Hypertens, 2011; 2011: 821971.
4. Misra A, Khurana L. The metabolic syndrome in South Asians: epidemiology, determinants, and prevention. Metab Syndr Relat Disord, 2009; 7: 497-514.
5. Misra A, Misra R, Wijesuriya M, Banerjee D. The metabolic syndrome in South Asians: continuing escalation & possible solutions. Indian J Med Res, 2007; 125: 345-54.
6. Groop L: Genetics of the metabolic syndrome. Br J nutr, 2000; 83(suppl 1): S39-S48.
7. Lidfeldt J, Nyberg P, Nerbrand C, Samsioe G, Scherstén B, Agardh CD: Sociodemographic and psychological factors are associated with features of the metabolic syndrome: the Women's Health in the Lund Area (WHILA) study. Diabetes Obes Metab, 2003; 5: 106-112.
8. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM: C-reactive protein, interleukin 6, and the risk of developing type 2 diabetes mellitus. JAMA, 2001; 286: 327-334.
9. Freeman DJ, Norrie J, Caslake MJ, Gaw A, Ford I, Lowe GD, O'Reilly DS, Packard CJ, Sattar N: C-reactive protein is an independent predictor of risk for the development of diabetes in the West of Scotland Coronary Prevention Study. Diabetes, 2002; 51: 1596-1600.
10. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH: Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men. N Engl J Med, 1997; 336: 973-979.
11. Mendall MA, Patel P, Ballam L, Strachan D, Northfield TC: C-reactive protein and its relation to cardiovascular risk factors: a population based cross sectional study. BMJ, 1996; 312: 1061-1065.
12. Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW: C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? Arterioscler Thromb Vasc Bio, 1999; 19: 972-978.
13. Gyawali P, Takanche JS, Shrestha RK, Bhattarai P, Khanal K, Risal P, Koju R. Pattern of thyroid dysfunction in patients with metabolic syndrome and its relationship with components of metabolic syndrome. Diabetes & metabolism journal, 2015; 39(1): 66-73.
14. Uzunlulu M, Yorulmaz E, Oguz A. Prevalence of subclinical hypothyroidism in patients with metabolic syndrome. Endocr J, 2007; 54: 71-6.
15. Dessein PH, Joffe BI, Stanwix AE. Subclinical hypothyroidism is associated with insulin resistance in rheumatoid arthritis. Thyroid, 2004; 14: 443-6.
16. Shantha GP, Kumar AA, Jeyachandran V, Rajamanickam D, Ra-jkumar K, Salim S, Subramanian KK, Natesan S. Association between primary hypothyroidism and metabolic syndrome and the role of C reactive protein: a cross-sectional study from South India. Thyroid Res, 2009; 2: 2.
17. Ishizaka N, Ishizaka Y, Toda E-I, Nagai R & Yamakado M. Association between serum uric acid, metabolic syndrome, and carotid atherosclerosis in Japanese individuals. Arteriosclerosis, Thrombosis, and Vascular Biology, 2005; 25: 1038–1044.
18. Ishizaka N, Ishizaka Y, Toda E-I, Hashimoto H, Nagai R & Yamakado M. Higher serum uric acid is associated with increased arterial stiffness in

Japanese individuals. Atherosclerosis, 2007; 192: 131–137.
19. Kawamoto R, Tomita H, Oka Y & Ohtsuka N. Relationship between serum uric acid concentration, metabolic syndrome and carotid atherosclerosis. Internal Medicine, 2006; 45: 605–614.
20. Iribarren C, Folsom AR, Eckfeldt JH, McGovern PG & Nieto FJ. Correlates of uric acid and its association with asymptomatic carotid atherosclerosis: the ARIC Study. Atherosclerosis Risk in Communities. Annals of Epidemiology, 1996; 6: 331–340.
21. Lippi G, Montagnana M, Franchini M, Favaloro EJ & Targher G. The paradoxical relationship between serum uric acid and cardiovascular disease. Clinica Chimica Acta, 2008; 392: 1–7.
22. Nagahama K, Isei K, Inoue T, Touna T, Ikemiya Y & Takishita S. Hyperuricemia and cardiovascular risk factor clustering in a screened cohort in Okinawa, Japan. Hypertension Research, 2004; 27: 227–233.
23. Bonora E, Kiechl S, Willeit J, Oberhollenzer F, Egger G, Bonadonna RC & Muggeo M. Bruneck study. Carotid atherosclerosis and coronary heart disease in the metabolic syndrome: prospective data from the Bruneck study. Diabetes Care, 2003; 26: 1251–1257.
24. Srinivasa Babu V, Ramaswamy C, Kalyan Chakravarthy V. "Role of non-lipid risk factors like hs-CRP, uric acid and thyroid stimulating hormone in metabolic syndrome," Int J Res Med Sci, 2019; 7(1): 272-277.
25. K. G. M. M. Alberti, R. H. Eckel, S. M. Grundy., "Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; National heart, lung, and blood institute; American heart association; World heart federation; International atherosclerosis society; and international association for the study of obesity," Circulation, 2009; 120(16): 1640–1645.
26. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al; International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; International Association for the Study of Obesity. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation, 2009; 120(16): 1640-5.
27. S. M. Grundy, J. I. Cleeman, S. R. Daniels et al., "Diagnosis and management of the metabolic syndrome: an American Heart Association/NationalHeart, Lung, and Blood institute scientific statement," Circulation, 2005; 112(17): 2735–2752.
28. Devaraj S, Singh U and Jialal I. Human C-reactive protein and the metabolic syndrome. Curr Opin Lipidol, 2009 Jun; 20(3): 182–189.
29. Regitz-Zagrosek V, Lehmkuhl E, Weickert MO. Gender differences in the metabolic syndrome and their role for cardiovascular disease. Clin Res Cardiol, 2006; 95: 136–147.
30. Patrick H Dessein, Gavin R Norton, Angela J Woodiwiss, Barry I Joffe and Ahmed Solomon. "Independent role of conventional cardiovascular risk factors as predictors of C-reactive protein concentrations in rheumatoid arthritis," The Journal of Rheumatology, April 2007; 34(4): 681-688.
31. Lin SD; Tsai DH, Hsu SR, Association between Serum Uric Acid Level and components of the Metabolic Syndrome. J Chin Med Assoc, 2006; 69(11): 512-516.
32. Billiet L, Doaty S, Katz JD, and Velasquez MT. Review of Hyperuricemia as New Marker for Metabolic Syndrome. ISRN Rheumatology, 2014; 7.
33. Nejatinamini S, Jafani AA, Qorbani M, Nikoohemat S, Kelishadi R, Asayesh H, Hosseini S. Association between salivary uric acid and metabolic syndrome components. Journal of diabetes and metabolic disorders, 2014; 70: 1-7.
34. Lee JM. Kim HC, Cho HM, Oh SM, Choi DP, Suh, Association between serum uric acid level and metabolic syndrome. J Prev Med Public Health, 2012; 45(3): 181-187.
35. Mrs, Bhagasree. N, Dr.C.Ramaswamy, Dr. Ganesh. M. "A correlative study showing the relationship of salivary uric acid level with the Metabolic syndrome components and its severity," Int J Pharm Bio Sci, 2017; (July - September), 8(3): 665-668.
36. Rizos C, Elisaf M, Liberopoulos E. Effects of thyroid dysfunction on lipid profile. Open Cardiovasc. Med. J, 2011; 5: 76.
37. Jang J, Kim Y, Shin J, Lee SA, Choi Y, Park EC. Association between thyroid hormones and the components of metabolic syndrome. BMC endocrine disorders, 2018 Dec; 18(1): 29.
38. Zhou YC, Fang WH, Kao TW, Wang CC, Chang YW, Peng TC, Wu CJ, Yang HF, Chan JY, Chen WL. Exploring the association between thyroid-stimulating hormone and metabolic syndrome: A large population-based study. PloS one, 2018 Jun 21; 13(6): e0199209.