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Triglyceride Glucose Index and Triglyceride/ HDL Cholesterol as Predictors of Metabolic Syndrome in Adult Population in Mandya City, Karnataka

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Metabolic Syndrome, TG/HDL-C Ratio, TyGlu Index

ABSTRACT:

Background & Objectives: The diagnosis of Metabolic syndrome requires the presence of three or more of the five parameters which includes, Waist Circumference (WC), Blood Pressure (BP), Fasting Blood Sugar (FBS) and triglyceride (TG) level. These disorders stem from a common pathology that is insulin resistance. Instead of depending on costly tests like which also have problems of biological variability , it is important that cheaper and more reliable tests can be used which will help in diagnosing metabolic Syndrome faster. In this study TG/HDL-C and Triglyceride Glucose Index (TyGlu Index) are compared for use in predicting Metabolic Syndrome.

Methods: 600 adults (274 males and 326 females) were included in the study. Physical measurements like height, weight, Blood pressure were measured along with Biochemical parameters like FBS, TG, HDL-C. TG/HDL-C and TyGlu index were measured. The study population was divided into two groups, one with Metabolic Syndrome and one without Metabolic Syndrome. Frequency analysis, Comparison of Means, Correlation Analysis, ROC curves were analysed to get the results.

Results: Overall prevalence of MS was found to be 51.3%(52.3% in females and 49.6% in males). as the number of components of metabolic syndrome increased from 0 to 5, the mean value of both TG /HDL-C ratio and TyGlu index increased. A strong correlation was found between TyG index and TG/HDL-C (Spearman's rho coefficient 0.819 ($p<0.05$).

Larger Area Under the Curve (AUC) was obtained for TyG index (0.876;95%CI=0.81-0.88) compared to AUC for TG/HDL ratio (0.849;95% CI=0.84-0.90) with regards to discriminatory power for diagnosis of MS.The optimum cut off was found to be 8.6 (90.6% Sensitivity, 75% specificity) and 2.6 (90% sensitivity & 60 % specificity) respectively for TyG index and TG/HDL ratio.

Conclusion: In this study TyGlu index and TG/HDL-C were found to be better alternatives to diagnose Metabolic Syndrome. Amongst the two TyGlu Index with better AUC with the ROC curve and more reliable and standardized Analytical techniques for TG and FBS was better than TG/HDL in assessing Metabolic Syndrome.

I. INTRODUCTION

It was in the year 1988 that Reaven put forward a point that developing resistance to insulin action is an important feature in chronic diseases like Diabetes Mellitus and Ischemic Heart diseases. It was hypothesised that features like impaired tolerance to glucose, high blood pressure,

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dyslipidemias are congregated under the influence of insulin resistance.[1]

These risk factors clustering due to hyperinsulinemia was called Syndrome X which was renamed as Metabolic Syndrome(MS). With the International Statistical Classification of Diseases and Related Health Problems (10th Revison) , ICD 10 giving it the coding as e E88.81, Metabolic Syndrome has achieved acceptance from all over the world.[2]

Other than features like proinflammatory state ,female gender, genetic factors etc two main features which have been accepted as causation for metabolic syndrome are obesity and Insulin resistance.[2]

Insulin resistance refers to the state when body cells become resistant to the action of insulin which in turn leads to hyperinsulinemia.In due course beta cells can no longer produce insulin which in turn leads to Type 2 Diabetes Mellitus(DM). MS is a cluster of definite to coronary heart diseases and type 2 DM risk factors like increased accumulation of intraabdominal fat as can be measured using waist circumference (WC) or Waist Height ratio, increase in blood pressure (BP),Fasting blood sugar (FBS), triglycerides(TG) and decrease in High density lipoproteins Cholesterol (HDL-C). In order to diagnose this NCEP-ATP-III gives the following criterias,in which three of the five should be present.[3.]

1. WC $\geq$ 90 cm for males, $\geq$ 80 cm for females (revised for south Asians)
2. TG $\geq$ 150mg/dl
3. HDL-C <40mg/dl in males, < 50 mg/dl in females
4. SBP $\geq$130 mm Hg/ DBP $\geq$ 85 mm Hg
5. FBS $\geq$ 100 mg/dl

One way to prevent these risk factors from piling up would be to check for insulin resistance, insulin levels. But these methods are not conducive to be used in daily practice. The gold standard to measure insulin resistance is the Hyperinsulinemic -euglycemic clamp which has many practical issues with being used in day to day clinical practice. Hence many parallel markers have been put up for use. One most widely used being HOMA -IR or Homeostatic model assessment of IR. Although this is widely used but two attention drawing points against usage of same is the problem with insulin having very high biological variability and that measurement of insulin is not standardized yet. [4,5]

Hence it is essential that other indirect parameters which give indication about insulin resistance are used. It has been found that increased triglycerides and decreased alpha lipoproproteins are characteristic features of insulin resistance. A consistent finding that has been found is that increased triglyceride level interferes with metabolism of glucose at muscular level.[6,7]

Hence the connection between TG levels and HDL levels have been used as an alternative for estimating insulin action. In 2010 Guerrero et al proposed that triglyceride glucose index (TyGlu Index) can be used to evaluate insulin resistance.[8]In this study it was found that this index was well in line with the hyperinsulinemic- euglycemic clamp and was shown to have comparable sensitivity and specificity.In a study by Reaven et al it was found that this index was also comparable to TG /HDL-C ratio using fasting insulin levels as standard method.[9]

II. MATERIALS & METHODS

This was a cross sectional observational study conducted in Mandya city, Karnataka.

According to a review article by Rajvir Bhalwar, wherein the Indian perspective of Metabolic Syndrome was studied, the prevalence of Metabolic syndrome in India was stated at 25%.[2] On calculating the sample size with the formula $4pq/l^2$ and 15 % margin of error, the sample size comes out to be 533. To this 10% non response rate is added which brings the sample size to 586. Hence a sample size of 600 was taken.

600 participants included 326 women and 274 Men aged between 20-70 years of age. This study was started after receiving institutional ethics committee clearance. The ethics committee clearance number being MIMS/IEC/01-05/2012-13. Informed consent was taken from the participants. They were informed about the study and ensured regarding confidentiality and anonymity.

The data collected included basic details like age, gender, medication. Anthropometric measurements like weight, height, BMI, WC, BP were done applying standard procedures. WC was measured between the last rib lower lateral margin of last rib and superior region of iliac crest using a non distensible flexible measuring tape. Blood pressure was measured using sphygmomanometer. At least two measurements were taken,one minute apart, and average of two was considered. Fasting Blood samples were collected

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in the morning for measuring fasting plasma glucose,Triglycerides and HDL. Glucose GOD POD method was used for estimation of Plasma Glucose. Triglyceride estimation was done by GPO-PAP end point method and HDL estimation by Immunoinhibition method. Natural logarithm (Ln) of the product of plasma glucose and TG was done to calculated TyGlu index. TG/HDL-C ratio was also calculated. The study participants were divided in two categories- Without MS and With MS using criteria by NCEP II according to which Metabolic Syndrome is diagnoses as presence of three or more of risk factors like abdominal obesirty (WC ≥ 90 cm for males, ≥ 80 cm for females (revised for south Asians),Triglycerides ≥ 150mg/dl,HDL-C <40mg/dl in males, < 50 mg/dl in females,SBP ≥130 mm Hg/ DBP ≥ 85 mm Hg and Fasting Plasma Glucose ≥ 100 mg/dl.The TyGlu index was calculated as the natural logarithm (Ln) of the product of plasma glucose and TG using the formula: Ln (TG [mg/dL] × glucose [mg/dL]/2).[8]The TG/HDL-C ratio was calculated.

The data was entered in excel sheet and cleaned. It was then transferred to Statistical Package for Social Sciences for Windows (SPSS software ,version 21,IL,USA) Frequency distributions were analysed. Mean values of variables were analysed using Students t test and ANOVA test. Spearman's Rho was used to study correlation between TyG index and TG/HDL ratio . ROC curves were used to study area under the curves for both the indices. Best Cut off points for males, females and whole study population were obtained with regards to sensitivity and specificity.

III. RESULTS

This study was a cross sectional study which had total of 600 participants out of which 326 were females and 274 were males. The average age of our study participants was 45.5±12.8 years in case of females and 44.4 ± 12.5 years in case of males. The difference was not found to be statistically significant. An alarmingly high prevalence (51.3%) of metabolic Syndrome was found amongst study participants(52.3% in females and 49.6% in males).

The Mean Values of Triglycerides, FBS, HDL , WC, TG/ HDL-C Ratio, TyGlu index were found to be different in males and females and this difference was statistically significant with regards to FBS, TG /HDL-C ratio, WC and HDL-C(Table 1).

TABLE I-Mean±SD of variables in males and females.

S No	Variable	Males(274)	Females(326)
1	WC*	91.9±13.74	82.1±12.5
2	SBP	129.8±15.3	131.8±22.5
3	DBP	84.8±9.6	83.1±11.1
4	TG	171.8±93.9	163.1±81.1
5	HDL-C*	44.4±17.5	48.8±14.4
6	FBS*	122.1±55.8	112.1±53.8
7	TG /HDL-C*	4.4±3.3	3.7±2.5
8	TyGlu Index	9.0±0.7	8.9±0.6

*p Value <0.05

It was found that as the number of components of metabolic syndrome increased from 0 to 5, the mean value of both TG /HDL-C ratio and TyGlu index increased. One test ANOVA proved that there was a statistically significant difference between groups.

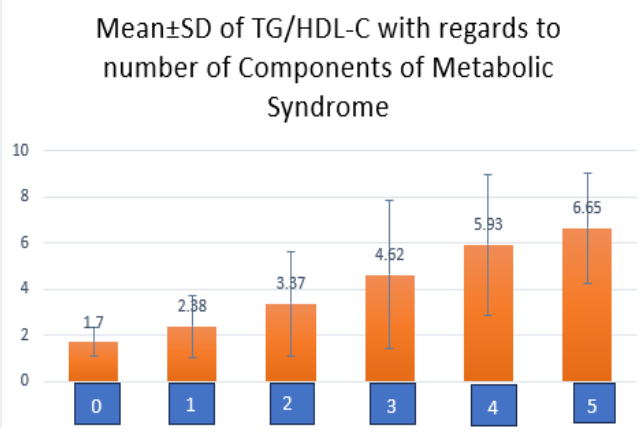

Fig. 1. Mean±SD of TG/HDL ratio with regards to number of components of Metabolic Syndrome.

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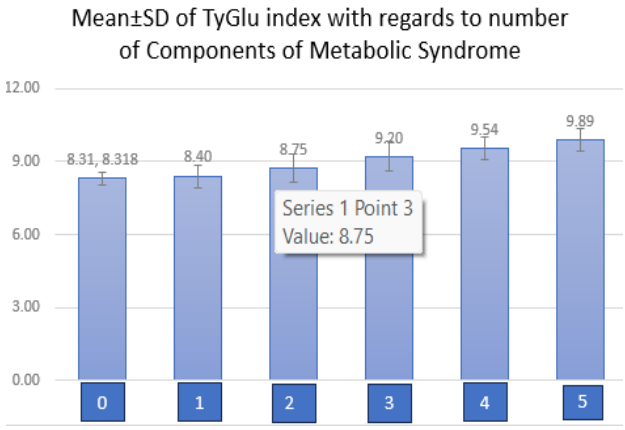

Fig. 2. Mean±SD of TG/HDL-C ratio with regards to number of components of Metabolic Syndrome.

The mean values of TG/HDL-C Ratio and TyGlu Index were found to be significantly different in males and females with regards to presence or absence of Metabolic Syndrome.(Table 2).

TABLE II- Mean±SD of TG/HDL-C ratio and TyGlu Index in males and females with regards to Metabolic Syndrome.

TG/HDL-C Ratio			
	Without MS (Mean±SD)	With MS (Mean±SD)	P Value
Total Population(n=600)	2.6±1.8	5.3±3.1	0.01
Males	2.9±2.0	6.0±3.5	0.01
Females	2.5±1.6	4.8±2.6	0.01
TyGlu Index			
Total Population	8.5±0.58	9.4±0.6	0.01
Males	8.5±0.6	9.5±0.6	0.01
Females	8.5±0.4	9.3±0.6	0.01

It was found that only 8.8% of females and 8.4% of males had no component of metabolic syndrome. Rest of the 91.2% of females and 91.6% males had one or more positive components of metabolic syndrome. Table 3 shows the percentage distribution of males and females with regards to number of components positive for metabolic syndrome.

TABLE III- Percentage distribution of males and females with regards to number of components positive for metabolic syndrome.

Number of Components of Metabolic Syndrome	Percentage of Males	Percentage of Females
0	8.8	8.4
1	19.8	17.9
2	18.5	24.1
3	26.7	27.0
4	18.8	15.0
5	6.4	7.6

A strong correlation was found between TyG index and TG/HDL-C wherein Spearman's rho coefficient was found to be 0.819 ($p<0.05$) in the whole study population.
Larger Area Under the Curve (AUC) was obtained for TyG index (0.876;95%CI=0.81-0.88) compared to AUC for TG/HDL ratio (0.849;95% CI=0.84-0.90) with regards to discriminatory power for diagnosis of MS(Figure 3).The optimum cut off was found to be 8.6 (90.6% Sensitivity, 75% specificity) and 2.6 (90% sensitivity & 60 % specificity) respectively for TyG index and TG/HDL ratio.

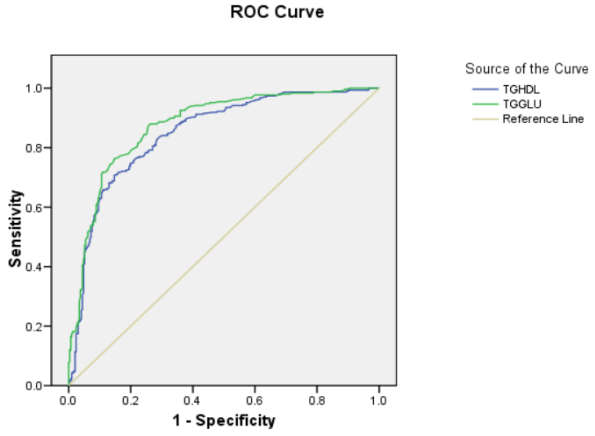

Fig. 3. ROC curves depicting Area Under the curves for TG/HDL-C ratio and TyGlu Index.

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When analysed for males and females separately it was found that a statistically significant strong correlation was present between TG /HDL-C ratio and TyGlu Index.In case of Males spearman rho was found to be 0.800 ($p<0.05$) and in case of females it was found to be 0.829 ($p<0.05$). AUC for TG/HDL-C ratio was found to be 0.846 in females and 0.858 in case of females. With regards to TyGlu index the AUC for males and females were found to be 0.880 and 0.875 respectively. Here also on stratification with gender higher AUC was found for TyGlu index compared to TG/HDL-C ratio in both males and females. The cut off point for discriminating MS for TyGlu index was found to be 8.9 in both males (Sensitivity- 91%, Specificity- 70%) and females (Sensitivity- 80%, Specificity- 81%) For Tg/HDL ratio it was found to be 2.8 and 2.9 in males (Sensitivity- 90%, Specificity- 60%)and females (Sensitivity- 80%, Specificity- 74%) respectively.

IV. DISCUSSION

In this study an effort was made to find the credibility of use of indices like TryGlu Index and TG/HDL-C ratio in diagnosis of Metabolic Syndrome. Our study found that as the number of components of metabolic syndrome increased from 0 to 5 the values of these indices increased with a statistically significant difference between each group. Based On the ROC curves , significant areas were found for TG/HDL-C ratio and TyGlu index. A statistically significant difference was found between males and females with and without Metabolic Syndrome with regards to both the indices. Unger G et al found in their study amongst adults from Argentina that cut off values for MS in the overall population was 8.8 for Tyg index and 2.4 for TG/HDL ratio.[10]This was comparable to our study wherein we found the overall cut off for Tyg index to be 8.6 and 2.6 for TG/HDL-C ratio.

In a study by Abbasi F et al wherein Steady State Plasma Glucose was correlated with Triglyceride glucose index and triglyceride HDL ratio. It was found that these correlated well with SSPG concentration to a similar degree.[9]

In a study by Guerrero-Romero F et al the cut off point with sensitivity of 96.5% and specificity of 85 % for TyGlu index was found to be 4.68.[8]

In a study by Lewis B et al wherein serum lipoproteins were quantitatively compared in different European communities it was found that Cholesterol and Triglyceride concentrations showed significant interpopulation differences . In contrast High Density lipoproteins showed little to nil differences between populations.[11] If this is the case then it is more than obvious that cut offs for tyGlu Index and TG/HDL ratio will have to be specific for a specific populations. This could be the reason for difference in cut offs in different population studies.For example in an elderly Chinese population a cut off of 1.49 for TG/HDL-C has been suugested to be the critical value for diagnosis of metabolic syndrome.[12]

In a study done on obese adolescents in turkey it was found that Both TyGlu index and TG/HDL-C ratio were better markers than HOMA-IR to ascertain the risk of metabolic syndrome. In this population the cut off values for MS were TG/HDL ratio> 2.16 for sensitivity of 88.8% and specificity of 57% , TyG index >8.50 for sensitivity of 85.6% and specificity of 57%.[13]

Various study in the past reported HOMA -IR to be a good indicator for MS. [14]

But this parameter has some disadvantages like requirement of fasting insulin, standardization requirement and high costs. Hence its use at a large scales in population studies mainly in low income groups is questionable. To give a diagnosis it is said that three out of Five parameters should be positive. Out of these five parameters , two are non invasive measurements that is waist circumference and Blood pressure. The other three being Serum triglycerides, HDL Cholesterol levels and Fasting Blood Sugar Levels.It has been found that TG levels correlate well with insulin secretion in prediabetic as well as normoglycemics. Increase in triglyceride levels due to visceral adiposity increases free fatty acids in the liver.This in turn causes reduced sensitivity to insulin in liver which leads to increased glucose output from liver.It has been reported that beta cell dysfunction may be caused by increased triglyceride levels by production of nitric oxide and ceramide formation. [15]

The tyG index depends on triglycerides and Glucose compared to triglyceride /HDL ratio which depends on HDL-C levels too. HDL-C have various methodological principles which need more clarification and standardization. As stated above triglycerides might be having interpopulation difference. It is also seen that triglycerides have a huge variability intra subject of 19.9 % and inter subjects of 32.7%. compared to insulin measurement though estimation of TG by enzymatic methods is standardized and most importantly it is

accessible to all clinical laboratories both with regards to analysis and finanances. [4]

Instead of waiting or looking out for three or more parameters becoming positive to diagnose Metabolic syndrome, it is more important that the root pathogenesis of Metabolic syndrome that is insulin resistance is identified soon. To do so parameters which are economical, standardized and can be used at a large scale in population studoes need to be sought. This study shows that TG/HDL-C ratio as well as TyGlu index are good surrogates for assessing insulin resistance and hence onset of Metabolic syndrome. Out of TG/HDL-C ratio, TyGlu index is more promising with regards to the analytical component with less biological variability and not causing much financial burden compared to TG/HDL ratio. Large population studies to determine the correct cut off for these indices is the need of the hour. This might hold the key for early discovery of risk factors which will prevent the onset of full fledged diseases like cardiovasucar diseases, stroke etc.

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