Comparison of Serum Uric Acid and Gamma-Glutamyltranspeptidase (GGT) Level in Obese Individuals and Non-Obese Individual

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ABSTRACT
Obesity is usually accompanied by excess presence of adipose tissue in the body which could cause excess xanthine oxidoreductase (XOR) production. Uric acid levels can increase with an excess of XOR production. Increased body fat also promotes fat deposition in the liver. Excess fat deposition induces the release of abundant reactive oxygen species (ROS) resulting in oxidative stress. Thus, this promotes an increase in serum gamma-glutamyltranspeptidase (GGT) level, which has potential anti-oxidative stress properties. This study aimed to identify the changes on serum uric acid and GGT level with association to waist to hip ratio (WHR) circumference in obese and non-obese individuals. A total number of 30 individuals aged between 20-45 years old participated. Data was analyzed using Mann Whitney U test and Spearman's rho test which was considered statistically significant at $P<0.05$. The variables in both male and female obese and non-obese individuals, the result shows significant, positive correlation even though all the variables showed positive correlation for both groups of obese and non-obese individuals, the strength of the relationship in obese individuals was much stronger than non-obese individuals. In the conclusion, increment of serum uric acid and GGT level were related with increased value of BMI and WHR as shown in previous studies.
Keywords: Serum uric acid, Gamma-glutamyltranspeptidase (GGT), Body mass index (BMI), Waist to hip (WHR) Xanthine oxidoreductase (XOR), Obesity

Introduction

Uric acid is the end product of purine degradation in human. Uric acid is synthesized in the liver and excreted in urine through the kidney. Uric acid is a by-product of the continual process in the body, where old cells are broken down and new one are formed (Yadav, Chhetri, Poudel, Sigdel, & Gyawali, 2009). Disorders of uric acid metabolism are often seen with factors associated with lifestyles such as an unbalanced diet abundant in purine, obesity and alcohol consumption. Uric acid can act as a pro-oxidant, particularly at increased concentrations may be a marker of oxidative stress (Karakurt, Maral, Lu, & Darcin, 2011).

The consumption of foods rich in purines and protein, obesity, alcohol and sweetened soft drinks could make serum uric acid level a dramatic increase. In addition, increased uric acid may also be closely associated with low-level lead intoxication, which causes a decline in renal function (Luo et al., 2014). A high uric acid level in obesity or also known as hyperuricemia, is an excess of uric acid in the blood. Uric acid is known as urate, where produced during the breakdown of purine from food of 30% and from the cell Deoxyribonucleic acid (DNA) of 70%. There is a clear link between body weight and uric acid levels. A high uric acid level may results in attack of the gout due to lifestyle pattern. It can be from family history and from high purine foods such as organ meats, herring, anchovies, mackerel, red meat and seafood such that tuna, lobster and scallops ("Wellness Talk," 2013).

The word 'obese' from which 'obesity' is derive, means to be 'stout, fat or plump'. The Dorland's Pocket Medical Dictionary defines 'obesity' as 'an increase in bodyweight beyond the limitation of skeletal and physical requirements, as the result of extreme accumulation of body fat'. In Malaysia, excess body fat gained during childhood and adolescence persists into adulthood there is an increased risk of developing chronic diseases in later life such as gout, liver disease, cardiovascular diseases, type-II diabetes and certain cancers (Teo, Nurul- Fadhilah, Aziz, Hills, & Foo, 2014). Obesity is a chronic disease that is increasing in prevalence worldwide (Achike, To, Wang, & Kwan, 2011). Obesity is defined as a condition of excess fat than the normal in the body, which reflected by Body Mass Index (BMI) more than 30kg/m². Normal individuals reflect Body Mass Index (BMI) of 18.5kg/m² to 24.99kg/m² (Muralidhara, US, & Swethadri, 2012).

Obese people are the individuals who suffer from psychological disorders such as depression, anxiety and eating disorder, may tend to have difficulty controlling food consumption and maintain a healthy weight. Food is often used as a coping mechanism by those with weight problems particularly when the individuals are sad, anxious, stressed, lonely and frustrated. In many obese individuals appear to be a perpetual cycle of mood disturbance and weight gain. This will cause guilty and may reactivate the cycle, leading to a continuous pattern of using food to cope with emotions (Collins & Bentz, 2009).

Adipose tissue includes distinct anatomic depots, a subcutaneous fat depot and an intra-abdominal fat depot, which can be divided into intra-peritoneal and retro-peritoneal depots.

The intra-peritoneal fat depot is also known as visceral fat. Subcutaneous fat is different from visceral fat in that venous drainage as subcutaneous fat is directed into the systemic circulation, whereas venous drainage from visceral fat is directed into the portal vein. The visceral fat releases free fatty acids and exposes the liver to fat accumulation (Ezzat et al., 2012).

Methods

A cross-sectional study was performed in 15 obese and 15 non-obese adults of aged 20 to 45 years old in Section 7, Shah Alam, Selangor. The study was conducted with the permission with ref no J150005E obtained from the Ethics Committee in the University of Selangor. A demographic data was done for the determination for inclusion and exclusion criteria. The respondents must be healthy, obese BMI >30kg/m² and non-obese respondents BMI 18kg/m² to 24.99kg/m². The informed consent has been taken from all the 30 respondents. Respondents were categorized into two groups as obese and non-obese respondents, according to the BMI classifications. The height and weight using a scale were recorded and BMI was calculated. The WHR circumference was measured by using a tape. Besides that, three ml of the blood was collected and serum was separated by centrifugation. Serum was stored in the freezer at -20ºC until the analysis was done. The samples were tested using biochemical analyzer in CLINIPATH MALAYSIA SDN BHD laboratory. All the statistical data analyzed by using SPSS Windows 22.0. The data was not normally distributed. It was analyzed by using the Mann-Whitney and spearman's rho correlation test, p value <0.05 was considered to be significant. The result for correlation coefficient was interpreted using Guilford Rule of Thumb.

Results

This study described the median (IQR) of 30 individuals of obese and non-obese individuals involving the age, BMI and WHR circumference in both male and female. In male obese individuals, the median age, BMI and WHR circumference were 26.5 years old (1.39), 32.0 kg/m² (2.50) and 0.91 (0.001) while for non-obese individuals were 24 years old (1.37), 24.0 kg/m² (3.00) and 0.86 (0.02). Whereas in female obese individuals, the median age, BMI and WHR circumference were 23.5 years old (1.35), 32.0 kg/m² (3.00) and 0.86 (0.01) respectively and for non-obese individuals were 22 years old (1.33), 21.5 kg/m² (2.50) and 0.76 (0.02). The P-value of age in male and female involving obese individuals and non-obese individuals were not statistically significant at P<0.05 while BMI and WHR circumference were statistically significant at P<0.05 (Table 3.6). The BMI and WHR circumference for obese individuals in both sexes showed in abnormal ranges while for non-obese individuals were in normal ranges.

Comparison of serum uric acid and gamma-glutamyltranspeptidase (GGT) level in obese individuals and non-obese individuals based on genders

The data analyzed by Mann Whitney U test. In male obese individuals, the serum uric acid and GGT level were 8.00 mg/dl (1.07) and 97.5 U/L (12.0) while for non-obese individuals were 5.50 mg/dl (1.50) and 13.0 U/L (13.0). Whereas in female obese individuals, the serum uric acid and GGT level were 6.70 mg/dl (0.50) and 66.0 U/L (22.0) respectively and for non-obese individuals were 3.90 mg/dl (1.30) and 12.0 U/L (1.75). The measurement of serum uric acid and GGT level in obese individuals were in abnormal range while in non-obese individuals showed within the normal range. The P-value serum uric acid and GGT level in both genders between the two groups showed statistically significant at P<0.05.

Association of body mass index (BMI), waist to hip ratio (WHR) circumference, serum uric acid and gamma-glutamyltranspeptidase (GGT) level in obese individuals and non-obese individuals

correlation coefficient value for BMI, WHR, serum uric acid and GGT level in female obese individuals were positive correlation. The correlation value between BMI and WHR circumference were 0.482, BMI and serum uric acid were 1.000, BMI and GGT level were 0.991, WHR circumference and serum uric acid were 0.482, WHR circumference and GGT level were 0.418 and serum uric acid and GGT level were 0.991. Therefore, they were statistically significant at P<0.05. The correlation coefficient value for BMI, WHR, serum uric acid and GGT level in male non-obese individuals were positive correlation. The correlation value between BMI and WHR circumference were 0.474, BMI and serum uric acid were 0.442, BMI and GGT level were 0.328, WHR circumference and serum uric acid were 0.701, WHR circumference and GGT level were 0.948 and serum uric acid and GGT level were 0.636. They were statistically significant at P<0.05 (Table 4.0). The correlation coefficient value for BMI, WHR, serum uric acid and GGT level in male non-obese individuals were positive correlation. The correlation value between BMI and WHR circumference were 0.566, BMI and serum uric acid were 0.571, BMI and GGT level were 0.768, WHR circumference and serum uric acid were 0.649, WHR circumference and GGT level were 0.663 and serum uric acid and GGT level were 0.644. Therefore, they were statistically significant at P<0.05. Individuals and non-obese individuals were 32.0 kg/m² (3.00) and 21.5 kg/m² (2.50), respectively. Both the gender were statistically significant at P<0.05 as p = 0.001.

Discussions

Anthropometric data

The age average of 20 to 45 years old was a suitable range to indicate obesity in the population. It's because of aging factor. As age increases, it increase the risk factor for the prevalent diseases. In include the higher level of GGT, uric acid and abdominal obesity. The obesity in Malaysian adults showed a serious problem (Azmi et al., 2009). The median age of obese and non-obese individuals were not statically significant in both male and female. This showed that there was no age factor that influence the result of this study. The samples were obtained non-randomly. The BMI median for male obese and non-obese individuals were 32.0 kg/m² (2.50) and 24.0 kg/m² (3.00) whereas for female obese individuals and non-obese individuals were 32.0 kg/m² (3.00) and 21.5 kg/m² (2.50), respectively. Both sexes were statistically significant at P<0.05 as p = 0.001.

The BMI for male and female obese individuals were in abnormal range while for non-obese individuals were in normal range. BMI was used as a standard indicator of obesity in adults (Oyama et al., 2006). The BMI was accepted as the most useful measure of obesity for adults, those who aged above 18 years old. In obese individuals, the correlation between the BMI and body fatness is fairly strong (Wu et al., 2013). The WHR circumference median for male obese individuals and non-obese individuals 0.91 (0.001) and 0.86 (0.02) whereas for female obese individuals and non-obese individuals were 0.86 (0.01) and 0.76 (0.02), respectively. Both sexes were statistically significant at P<0.05 as p = 0.001. The WHR circumference for male and female obese individuals were in abnormal range while for non-obese individuals were in normal range.

WHR is better indicator in obese because adipose tissue tends to accumulate around the mid-section (Khullar et al., 2014). It was found to be convenient tools to first screen for the subgroup of obese. The larger waistline has more abdominal fat than a lower waist. An increased waistline was associated with a greater accumulation of visceral adipose tissue (Després, 2012).

Comparison of serum uric acid and gamma-glutamyltranspeptidase (GGT) level in obese individuals and non-obese individuals based on genders

The serum uric acid median for male obese individuals and non-obese individuals were 8.00 mg/dl and 5.50 mg/dl whereas for female obese individuals and non-obese individuals were 6.70 mg/dl and 3.90 mg/dl, respectively. Both sexes were statistically significant at P<0.05 as p = 0.001. The serum uric acid for male and female obese individuals were in abnormal range while for non-obese individuals were in normal range. High serum uric acid level in the body defined as ≥ 7.0 mg/mL in male and ≥ 6.0 mg/mL in female (Cai et al., 2013). The high level of serum uric acid is closely related with abdominal obesity. Abdominal obesity lead to abundant XOR activity, in making excessive breakdown of cell which cause overproduction of uric acid in the body (You et al., 2014). XOR is an enzyme that responsible for purine degradation. Uric acid is elevated in obese adipose tissue. Abundant XOR activity lead to presence of oxidative stress. Oxidative stress is a condition of excessive free radicals production and ROS. Purine catabolism in adipose tissue could be enhanced in obesity (Tsushima et al., 2013). This result is expected as obesity with high level of uric acid. Its relationship with central obesity was confirmed with the WHR circumference results.

The GGT level median for male obese individuals and non-obese individuals were 97.5 U/L and 13.0 U/L whereas for female obese individuals and non-obese individuals were 66.0 U/L and 12.0 U/L, respectively. Both sexes were statistically significant at P<0.05 as p = 0.001. The GGT level for male and female obese individuals were in abnormal range while for non-obese individuals were in normal range. Excess abdominal obesity reflects high oxidative stress in the body, thus increase the GGT enzyme activity. It is known that GGT has a protective effect in maintaining appropriate intracellular glutathione levels, which is a powerful antioxidant. The generation of free radicals, which can occur in central obesity, may deplete intracellular glutathione and thus induce the activity of GGT into the circulation (Latha et al., 2015). The abdominal adiposity measure by WHR circumference is consistently stronger predictor of GGT level in both male and female. Moreover, it has been shown that central abdominal adiposity can correlate with the development of fatty liver (Stranges et al., 2004). The statement above showed for GGT level and its relationship to fatty liver can be confirmed to measurement of lipid profile, ultrasound of liver, liver profile and others, but not done in this study.

Association of serum uric acid and gamma-glutamyltranspeptidase (GGT) level in male and female obese individuals

There was significant moderate, positive correlation between BMI and WHR circumference in male obese individuals (r = 0.599, p = 0.011). Besides, there was significant low, positive correlation between BMI and WHR circumference in female obese individuals (r = 0.482, p = 0.027).

There was significant very high, positive correlation between BMI and serum uric acid in male obese individuals (r = 0.975, p = 0.001). Besides, there was significant very high, positive correlation between BMI and serum uric acid in female obese individuals (r = 1.000, p = 0.001). The BMI contribute to uric acid level in the body. As BMI increase with total fat, uric acid level increases in both male and female obese. Serum uric acid do have significant associations with BMI. In other words, it is associated with obesity based on the interaction of lifestyle modifications (N, M, Shetty, Bhandary, & Kathyayini, 2011). In adult obesity, with BMI growing the serum uric acid level increased (Oyama et al., 2006). Obesity is often accompanied by high uric acid level (Yin et al., 2014).

There was significant very high, positive correlation between BMI and GGT level in male obese individuals (r = 0.949, p = 0.001). Besides, there was significant very high, positive correlation between BMI and GGT level in female obese individuals (r = 0.991, p = 0.001). It is found that significant increment of BMI were directly related to increase of GGT level. The BMI accounts for body fat. GGT activities are associated with body fat in men and women, demonstrated that BMI is strongly associated with increased serum activities of GGT level (Choi, 2003).

There was significant very low, positive correlation between WHR circumference and serum uric acid in male obese individuals (r = 0.584, p = 0.012). Besides, there was significant low, positive correlation between WHR circumference and serum uric acid in female obese individuals (r = 0.482, p = 0.027). WHR circumference defines abdominal obesity. In male and female, the increment of abdominal fat related to increasing of serum uric acid (Zapolski et al., 2011). There is a significant connection between serum uric acid and WHR circumference, which is a manifestation of abdominal obesity in men and women. The reason is abdominal fat produce an excessive XOR enzyme that enhance in obesity. Thus, producing increase uric acid level in the body (You et al., 2014).

There was significant very low, positive correlation between WHR circumference and GGT level in male obese individuals (r = 0.423, p = 0.029). Besides, there was significant low, positive correlation between WHR circumference and GGT level in female obese individuals (r = 0.418, p = 0.035). It has found that there is a strong linear association between WHR circumference and GGT level as an indicator of fat distribution (Stranges et al., 2004). High liver fat content is associated with larger abdominal obesity, which reflected by a high WHR circumference value

(Després, 2012). Serum GGT levels are raised in obese individuals and are strongly associated with central obesity. It has been figured out that the high GGT level is a marker for abdominal fat (Latha et al., 2015).

There was significant very low, positive correlation between serum uric acid and GGT level in male obese individuals (r = 0.901, p = 0.002). Besides, there was significant low, positive correlation between serum uric acid and GGT level in female obese individuals (r = 0.991, p = 0.001). Increased serum uric acid level strongly reflect the increased level of GGT level in male and female obesity. There is significant association between serum uric acid level and the GGT level. Serum uric acid was independently related with GGT enzyme in obesity, as the adipose tissue release oxidative stress which disturb the normal mechanism in the body (Ryu et al., 2011).

Association of serum uric acid and gamma-glutamyltranspeptidase (GGT) level in male and female non-obese individuals

There was significant low, positive correlation between BMI and WHR circumference in male non-obese individuals (r = 0.474, p = 0.028). Besides, there was significant moderate, positive correlation between BMI and WHR circumference in female non-obese individuals (r = 0.566, p = 0.014). In non-obese individuals of male and female, indicates that decreased BMI related to decreased value of WHR circumference. BMI has been shown to be a good indicator of general fatness. WHR circumference has correlation to BMI. It has been said that WHR circumference has a positive effect independent of BMI (Vazquez, Duval, Jacobs, & Silventoinen, 2007). The BMI was found to be an adequate index of adiposity, where the simple anthropometric index of total adiposity had to be accompanied by indices of body shape such as the WHR (Després, 2012).

There was significant low, positive correlation between BMI and serum uric acid in male non-obese individuals (r = 0.442, p = 0.042). Besides, there was moderate, positive correlation between BMI and serum uric acid in female non-obese individuals (r = 0.571, p = 0.023). In non-obese individuals of male and female, indicates that decreased BMI related to decreased value of serum uric acid. Serum uric acid levels are positively correlated with BMI in men and women. (Oyama et al., 2006). Serum uric level is find to be in normal range along with BMI in non-obesity (Shetty, Bhandary, & Kathyayini, 2011).

There was significant low, positive correlation between BMI and GGT level in male non-obese individuals (r = 0.328, p = 0.049). Besides, there was significant high, positive correlation between BMI and GGT level in female non-obese individuals (r = 0.768, p = 0.012). In non-obese individuals of male and female, indicates that decreased BMI related to decreased GGT level. This reason is less or average body fat in healthy individual does not affect the serum GGT level (Choi, 2003). BMI is the measurement of body fat, widely used to assess the relationship between body fat distributions and have significant association with GGT enzyme activity (Stranges et al., 2004).

There was significant high, positive correlation between WHR circumference and serum uric acid in male non-obese individuals (r = 0.701, p = 0.042). Besides, there was significant moderate, positive correlation between WHR circumference and serum uric acid in female non-obese individuals (r = 0.649, p = 0.028). In non-obese individuals of male and female, indicates that decreased WHR circumference related to decreased serum uric acid. WHR circumference are the strongest factors correlated with the serum uric acid level in men and women. Lower abdominal obesity within the range of healthy individual may not affect the serum uric acid (You et al., 2014). It was also found that serum uric acid level was significantly positively associated with WHR circumference of non-obesity. The variables tends to decrease together with body fat distribution (Zhang, Zhang, Deng, & Chen, 2014).

There was significant very high, positive correlation between WHR circumference and GGT level in male non-obese individuals (r = 0.948, p = 0.049). Besides, there was significant moderate, positive correlation between WHR circumference and GGT level in female non-obese individuals (r = 0.663, p = 0.018). In non-obese individuals of male and female, indicates that decreased WHR circumference related to decreased GGT level. WHR circumference is a measurement of central adiposity. GGT was more strongly correlated with WHR circumference. The reduction of WHR circumference of abdominal fat is associated with decreasing level of GGT in men and women (Stranges et al., 2004). There is a solid evidence that WHR circumference is a best predictor correlated to the outcomes of GGT enzyme level (Després, 2012).

There was significant moderate, positive correlation between serum uric acid and GGT level in male non-obese individuals (r = 0.636, p = 0.012). Besides, there was significant moderate, positive correlation between serum uric acid and GGT level in female non-obese individuals (r = 0.644, p = 0.040). In non-obese individuals of male and female, indicates that there was no significant effect between serum uric acid and GGT level. Serum uric acid and GGT level have combined effect. GGT level and serum uric acid may decrease together or constant within range for non-obese people. It is because in the body of non-obese people, the mechanism functions well without disturbance from oxidative stress (Kong et al., 2013).
Even though there was positive correlation between the variables in non-obese individuals, however the strength of the relationship was comparable to the strength seen in obese individuals. The strength of relationship in obese individuals was stronger compared to non-obese individuals.

Conclusion and Future Recommendation

In the conclusion, this study has found that the increment of serum uric and GGT level were related with an increased value of BMI and WHR circumference in obese individuals than compare to non-obese individuals. It was demonstrated consistently strong associations of BMI and WHR circumference in obese individuals and non-obese individuals. Limitation in this study was time management. The materials arrival were delayed and yet started late. Recommend, earlier arrival of materials. There were insufficient number of respondents, thus more respondent are needed for better outcome. Recommendations for future study include refine sample selection including the diet history and exercise. In addition, instead of referring to the WHO international value of BMI and WHR circumference, it is best to refer to the Asian value of BMI and WHR circumference. To confirm liver health, additional tests such as liver ultrasound, liver function tests and lipid profile are suggested. Apart from that the measurement of fat distribution for participants which include skin-fold thickness and the body analyser will give a clearer picture on the presence of distribution of fat mass.

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