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Habitual Alcohol Consumption and Changes in Markers of Insulin Resistance and Cardio-Renal Function

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Abstract

***Introduction:** Higher rates of alcohol consumption have been reported in most parts of the world including Nigeria, which could suggest a future increase in alcohol related ill-health and shorter life expectancy. Even so, the clinical consequences of heavy/habitual alcohol consumption on cardio-renal endpoints and markers of insulin activity are unclear and unreported in some regions of the world. The aim of the present study was to assess the effect of habitual alcohol consumption on markers of insulin resistance (IR) and cardio-renal endpoints.*

***Methods:** One hundred and twenty six adult men and women were examined between July 2016 and January 2018 using standard assessment methods including socio-demographic/lifestyle and alcohol consumption assessment questionnaires and assessment of bio-chemical indices of IR and markers of cardio-renal function.*

***Results:** Habitual alcohol consumption was associated with significant ($p<0.05$) higher values of WC only in male drinkers, however, significant ($p<0.05$) increase in MAP, TG-C, AIP, ALT, AST, fasting SUA and HOMA-IR were found in drinkers than non-drinkers in both male and female participants.* SCr *level was significantly higher in male drinkers than non-drinkers (105.00 ± 11.03 versus (vs) 94.67 ± 11.88) and leading to a significant reduction in eGFR in male drinkers than non-drinkers (88.40 ± 7.78 vs 99.10 ± 6.36). In females,* SCr *level was lower in drinkers than non-drinkers (92.32 ± 14.10 vs 97.02 ± 12.96) and leading to a significant increase in eGFR in female drinkers than non drinkers (93.30 ± 4.95 vs72.00 ± 2.83).*

***Conclusion:** Habitual alcohol consumption could be associated with adverse cardio-renal endpoints and impaired insulin sensitivity.*

Keywords: *Chronic alcohol drinking, hyperinsulinemia, heart, kidney, effect.*

Introduction

Recreational alcohol consumption is increasingly common globally [1]. Recent reports indicate changing pattern of alcohol consumption in sub-saharan Africa including Nigeria, with regards to the quantity, quality, reasons for consumption and demographics of consumers [2].

A recent population based study showed that age at first use of alcohol beverage is also changing, with more teenagers engaging in binge alcohol drinking than previously, and worst still, a large proportion of the population (26.7%) drinks above the World Health Organization-established cut-off [3], which could suggest a future increase in alcohol use disorders. Historical, societal factors,and lack of information to make informed health decision contribute to the current trends.

A study by Oshodin [4] evaluating the alcohol drinking status of teenagers in a Nigerian city found that 85% of them were currently drinking. Bridging of gender gaps in alcohol consumption and eroding of societal values with respect to female alcohol intake have also been reported. More women are now consuming alcohol than before [5]. Guerini et al [6] studied a sample of

three Italian communities and reported a consistent pattern of female predominance in heavy alcohol drinking than their male counterparts. Among other factors, economic development, gender roles and lack of awareness and knowledge on the adverse health effects of binge alcohol drinking drive the increase use of alcohol found among women [2, 7]. Although mild-to-moderate alcohol consumption is assumed to have some health benefits and therefore recommended [8], it is well established that binge/habitual alcohol consumption is detrimental to health and contributes to a significant increase in chronic disease burdens such as hypertension, stroke, liver disease and cancers in most regions of the world [9, 7]. Alcohol consumption caused some 3.3 million deaths in 2012 equivalent to 5.9% of all deaths globally [10]. Also, 3million deaths have been recorded yearly globally due to harmful use of alcohol [11]. Cardiovascular diseases and diabetes contributed to a third of these alcohol related deaths,

Several studies examined the effect of alcohol on cardio-renal system in different parts of the world and populations, however, the observed effects have been inconsistent across studies [12]. Some studies report direct association between alcohol consumption and cardio-renal disorders [13, 9], while others report either inverse [14, 15], or no association between alcohol consumption and adverse cardio-renal endpoints [14, 16].

These conflicting findings underscore the need for more population-based studies and data to scientifically justify these claims as ethnic differences have been reported by previous investigators [17, 15, 9]. No study has hitherto been reported on the effect of chronic/heavy alcohol consumption on markers of IR and cardio-renal function in Southern Nigeria despite the recent report on changing patterns of use, the users and reason for consumption of alcohol in Nigeria [17].

The recent increase in alcohol consumption in Nigeria and the absent of a consistent information on the effect of alcohol on cardio-renal endpoints may indicate the burden of alcohol related health problems including cardio-renal disorders will be greater in the future, because current risk factors eventually manifest as diseases and public health burdens. Knowledge of risk factors can therefore be used to shift the population burden.

The aim of the present study was to assess the effect of self reported habitual alcohol consumption on markers of IR and cardio-renal endpoints in a group of enrollees and others accessing care at a primary care center.

Materials and Methods

Study Participants

A total of 126 adult subjects aged 18 to 40 years participated in this survey carried out between July 2016 and January 2018 among participants particularly the enrollees attending a primary care center for medical care. The study was cross-sectional and was also opened for anybody who resides within the study area (Uyo metropolis) and met the inclusion criteria, such as those who currently engage in regular heavy drinking defined as alcohol consumption of greater than or equal to 40g/day for males and greater than or equal to 20g/day for females according to WHO definition of heavy alcohol consumption [6], or maintains regular drinking habits (3 to 4 times standard per day equivalence to 30 to 40g of alcohol per day for 6months or more) [18], however, before the study commenced detail explanation of the aims/objectives and procedures of the study was made to the participants.

Exclusion applied if individual engaged in mild to moderate drinking habits or those diagnosed of any metabolic disorder or on medication for any of the metabolic syndrome clusters (hypertension, type 2 diabetes mellitus (T2DM)), dylslipidemia or not falling within the study age bracket, inappropriately completed the questionnaire.

Others were recent consumption of red wine, missing data, or inconsistent responses. Written informed consent was obtained from participants and the study was conducted according to the guidelines laid down in the declaration of Helsinki and all protocols involving human subjects were approved by the institutional research Ethics Committee.

Assessment Measures

Survey instruments used to assess the participants who were classified into 2 groups (drinkers and non-drinkers) included a socio-demographic/alcohol drinking habits assessment questionnaire adapted from previous studies [19] and assessment of clinical and biochemical markers of insulin resistance and cardio-renal function.

The socio-demographic section of the questionnaire contained information on the socio-demographic/life style profile of the participants including age (years), gender, marital status, educational level, occupation and ethnicity. Participants were asked to state the quantity of alcohol ingested per time and per day using different sizes of drinking containers of known volume and how often they drink alcohol (daily and weekly). Questions were also asked about the participants' life-style characteristics including physical activity status, dietary habits, smoking status and night clubbing habits. Past medical and family history of any of the metabolic syndrome clusters (e.g., T2DM, hypertension, dyslipidemia) was also enquired about. History of kidney, liver or hematological disorders was also elicited. The main index of assessment was heavy/habitual alcohol consumption defined as the consumption of greater than or equal to 20g for females and >40g for males for at least 1 day per week and for 6months. The main outcome measures were markers of insulin resistance (IR) (Fasting insulin, fasting blood sugar (FBS) and serum uric acid (SUA) levels as well as homeostatic Model Assessment of insulin resistance (HOMA-IR)) and serum level of liver enzymes (alanine amino transaminase (ALT),aspartate amino transaminase (ASP) and alkaline Phosphatase (AIP)). Markers of cardio-renal function; blood pressure (BP) indices (systolic BP, diastolic BP, Pulse rate (PR), Mean arterial pressure (MAP and pulse pressure (PP). Lipid sub-fraction (triglycerides-cholesterol (TG-C), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), total cholesterol (T-Chol) and atherogenic index of plasma (AIP) were measured. Serum insulin level was determined by Radio-immune assay (RIA) (Diagnostic Product Corp Los Angeles CA)

Renal function assessment including serum creatinine (SCr) level, urea (UA), bicarbonate (HCO3), electrolytes (sodium (Na), potassium (K), chloride (Cl^-)) and estimated glomerular filtration rate (eGFR) were determined. Values were compared between drinkers and nondrinkers.

Results

In this cross-sectional study, 209 participants were initially invited to participate in the survey, but 126 were finally included giving a response rate of 60.3%, reasons for exclusion ranges from decline participation, missing data and failure to meet other inclusion criteria. Among those who participated, 47.6% were heavy drinkers while 52.4% were non-drinkers.

The socio-demographic variables (age, educational level, occupation and ethnicity) were not significantly different between the two groups. However, marital status and physical activity status showed significant ($P<0.05$) differences between drinkers and non-drinkers (Table 1).

Table 2 shows that WC was significantly higher ($P<0.05$) in male drinkers than non-drinkers. In females, WC did not show any significant difference between drinkers and non-drinkers. Significant higher values of MAP and PP were also found in drinkers than non-drinkers. Although BMI and other blood pressure indices were higher in drinkers than non-drinkers, the differences did not reach level of statistical significance.

Table 3 shows that among all lipid sub-fractions, only TG-C, HDL-C and calculated AIP showed significant ($p<0.05$) differences between drinkers and non-drinkers.

Table 4 shows that SCr was significantly higher in male drinkers than none-drinkers, whereas in females, SCr was higher in non-drinkers than drinkers but the difference was below level of statistical significance. Serum levels of urea, K^+ and Cl^- were significantly ($P<0.05$) higher in both male and female drinkers than non-drinkers. eGFR decreased significantly ($P<0.05$) in male drinkers compared with non-drinkers. In females, eGFR was significantly higher in drinkers than none drinkers.

Furthermore, habitual alcohol consumption caused significant ($p<0.05$) higher values of some hepatic enzymes (AST and ALT) in drinkers than non-drinkers (Table 5).

Table 6 shows higher values of markers of insulin resistant (fasting insulin, fasting blood sugar, and fasting serum uric acid (SUA) levels and HOMA-IR) in drinkers than non-drinkers. However, only SUA and HOMA-IR reached statistical significant levels.

Statistical Analysis

Mean ± standard deviations were computed for quantitative variables as frequencies and percentages for qualitative variables. Univariate relationships between qualitative variables were established using chi-square and differences in quantitative variables between drinkers and non-drinkers were compared for statistically significance using independent t-test. Statistical package for social sciences (SPSS version 22.0) was employed to enhance data analysis and statistical significance was established at $P<0.05$.

Table 1. *Socio-demographic Characteristics of the Study participants*

Variables	Drinkers (n=60)	Non-Drinkers (n=66)	P-value
Age	37.62 ± 12.22	38.59 ± 8.01	0.2729
Sex Male Female	 48 (80.0) 12 (20.0)	 52 (78.8) 14 (21.2)	0.999
Marital status Single Married	 112 (80.0) 28 (20.0)	 34 (51.5) 32 (48.5)	<0.0001**
Educational status Primary Secondary Tertiary	 10 (16.7) 36 (60.0) 14 (23.3)	 18 (27.3) 38 (57.6) 10 (15.2)	0.256
Occupation Employed Unemployed	 31 (51.7) 29 (48.3)	 42 (63.6) 24 (36.4)	0.239
Ethnicity Ibibio Annang Ibo Yoruba	 27 (45.0) 20 (33.3) 10 (16.7) 03 (5.0)	 32 (48.5) 21 (31.8) 09 (13.6) 04 (6.1)	0.949
Physical activity status Active Inactive	 23(38.3) 37(61.7)	 39(59.1) 27(40.9)	0.032*
Dietary habits Good Poor	 21(35.0) 39(65.0)	 35(53.0) 31(47.0)	0.064
Smoking habits Current Ex-smoking Non-smoking	 25(41.7) 12(20.0) 23(38.3)	 23(34.8) 19(28.8) 24(36.4)	0.496

**Significant at 5% (P<0.05)*

Table 2. *Effect of habitual alcohol consumption on anthropometric indices and cardiovascular parameters of participants*

Variables	**Drinkers (n=60)**	**Non-Drinkers (n=66)**	**P-value**
BMI(kg/m)	31.80 ± 14.88	29.20 ± 9.22	0.2361
WC(cm) Men Women	 82.02 ± 10.09 81.43 ± 10.78	 75.05 ± 12.33 77.03 ± 13.90	 0.0008** 0.0509
SBP(mmHg)	138.05 ± 30.33	132.33 ± 37.90	0.3545
DBP(mmHg)	85.88 ± 20.89	79.67 ± 29.80	0.1965
PR(mins)	77.60 ± 3.94	78.87 ± 4.29	0.0870
MAP	103.27 ± 10.22	87.22 ± 9.42	< 0.0001*
PP	52.17 ± 5.89	49.66 ± 8.05	0.0499*

**Significant at 5% (p<0.05), **Significant at 1% (p<0.01). BMI=Body Mass Index,*

WC=Waist Circumference, PR=Pulse rate, MAP=Mean arterial pressure, PP=Pulse pressure

Table 3. *Habitual Alcohol intake and changes in lipid sub-fractions of participants*

Lipid sub-fractions	Drinkers (n=60)	Non-Drinkers (n=66)	P-value
TG-C(mg/dl)	172.2 ± 30.22	158.5 ± 26.42	0.0076**
HDL-C(mg/dl)	48.6 ± 10.90	52.3 ± 9.89	0.0479
LDL-C(mg/dl)	135.5 ± 30.22	136.3 ± 28.78	0.8793
AIP (Log TG/HDL)	0.55 ± 0.01	0.42 ± 0.03	<0.0001**

TG-C=Triglyceride-cholesterol, HDL-C=High density lipoprotein-cholesterol, LDL-C=low density lipoprotein-cholesterol, AIP=Atherogenic index of plasma

**Significant at 5% (p<05), **Significant at 1% (p<0.01)*

Table 4. *Effect of Habitual alcohol consumption on renal function indices of participants*

Renal function indices	Drinkers (n=60)	Non-Drinkers (n=66)	P-value
Serum Cr(µmol/L)			
Male	105.00 ± 11.03	94.67 ± 11.88	<0.0001**
Female	92.32 ± 14.10	97.02 ± 12.96	0.0535
Urea(mmol/L)	4.47 ± 0.90	4.02 ± 0.80	<0.0036*
Na^+ (mmol/L)	136.40 ± 4.37	136.93 ± 2.45	0.3972
K^+ (mmol/L)	5.71 ± 2.08	5.09 ± 0.89	0.0289*
Cl^- (mmol/L)	105.53 ± 1.81	104.07 ± 2.60	<0.0001**
eGFR (MDRD-4 variable version)			
Men	88.40 ± 7.78	99.10 ± 6.36	< 0.0001**
Women	93.30 ± 4.95	72.00 ± 2.83	< 0.0001**
HCo_3(MEq/L)	21.87 ± 2.03	23.33 ± 12.32	0.3664
Serum Anion Gap(mE/L)	14.71 ± 2.27	14.62 ± 3.01	0.8512

**Significant at 5% (p<0.05), **Significant at 1%*

Na=Sodium, K=Potassium, CL=chloride, eGFR=estimated glomerular filtration, MDRD=Modification of Diet in Renal Disease, HCO3=Serum bicarbonate concentration

Table 5. *Habitual alcohol consumption and changes in liver function indices of participants*

Liver function indices	Drinkers (n=60)	Non-Drinkers (n=66)	P-value
ALT(iu/L)	14.00 ± 5.12	8.91 ± 3.51	<0.0001**
AST(iu/L)	13.12 ± 8.88	7.81 ± 5.23	<0.0001**
AIPtase(iu/L)	24.0 ± 8.99	21.02 ± 12.01	0.1203

**Significant at 1% (p<0.01)

ALT=Alanine amino transaminase, AST=Aspartate aminotransaminase, ALPtase Alkaline phosphatase.

Table 6. *Effect of habitual alcohol intake on markers of insulin resistance in participants*

Insulin Resistance Indices	Drinkers (n=60)	Non-Drinkers (n=66)	P-value
Fasting Insulin Level (µU/mL)	7.03 ± 3.09	6.82 ± 2.44	0.6714
Fasting Blood Sugar (mmol/L)	7.3 ± 2.23	5.73 ± 2.81	0.0008**
Fasting Serum Uric acid level (mmol/L)	8.41 ± 4.44	6.02 ± 3.23	0.0007**
HOMA-IR	2.27 ± 0.99	1.70 ± 0.83	<0.0006**

***Significant at 1% (p<0.01)*

Discussion

Results of the present study showed that habitual consumption of alcohol could be associated with changes in markers of cardio-renal function and insulin sensitivity. This notion is supported by the observed significant differences in cardio-renal endpoints between drinkers and non-drinkers. The relevant cardio-renal indices and markers of IR that demonstrated significant differences between drinkers and non-drinkers in the present study were WC (in men) MAP, PP, serum TG-C, HDL-C, AIP, Cr concentration, eGFR, fasting SUA concentration, FBS, HOMA-IR and liver enzymes.

Consistent with results of the present study, several previous studies [20, 21] report that acute and chronic alcohol consumption are related to higher values of insulin-level, and markers of IR including fasting insulin level, FBS level, serum UA and HOMA-IR. It is posited that binge drinking could be associated with the induction of hepatic IR by impairing insulin action in adipose tissue and leading to lipolysis, free fatty acid and glucose generation and ultimately hepatic gluconeogenesis [22], and causing the above observed biochemical changes. It is also associated with autonomic dysfunction through the attenuation of insulin receptor signaling in the hypothalamus. Likewise increased sympathetic discharge and associated lipolysis have been reported among heavy alcohol drinkers [23]. Chronic alcohol drinking can cause inflammation of the hypothalamus and poor insulin signaling [24] and insulin activities. For instance, IR caused by the consumption of >60g/dl of alcohol was found to be associated with acute hyper-triglyceridemia and lower HDL-C level, probably due to the associated IR-induced decrease in lipoprotein lipase activity as previously reported by Defronzo and Ferrannini [25].

The higher mean values of TG-C, AIP, glucose, insulin, hepatic enzymes, BMI and WC and the lower serum levels of HDL-C among drinkers in the present study suggest the presence of alcohol-induced IR [26]. Higher mean values of BP indices found among drinkers (although within normal ranges) compared with non-drinkers corroborate with previous studies that showed that habitual intake of alcohol has a causal relationship with raised BP [27]. Several studies [26, 28] implicate IR in hypertension. It is posited that IR causes hypertension by various mechanisms including increase in Na re-absorption, alteration of transmembrane ion transport, hypertrophy of resistance vessels, activation of sympathetic nervous system and up regulation of angiotensis II receptor by a posttranslational mechanism [25, 29].

Raised serum ALT and AST levels found among drinkers compared with nondrinkers could probably be due to disorders of hepatic function in the former. This finding is consistent with previous studies that showed that acute/chronic alcohol consumption could adversely affect the liver [30]. Also, altered hepatic enzymes found among heavy alcohol drinkers depicted a state of insulin insensitivity [31]. Heavy/long term alcohol intake was also associated with abnormal serum lipid sub-fractions including significant increase in TG-C and calculated AIP and non- significant decrease in serum HDL-C and LDL-C levels. The decrease in LDL-C is probably due to the associated oxidative stress-induced formation of acetaldehyde adducts of apo-B which is associated with a reduction in the conversion of VLDL-C to LDL-C [32].

Furthermore, drinkers had moderate increase in BMI compared with non-drinkers, however similar increase in WC among drinkers was found but more significant in men than women. One study found that although alcohol intake caused increase in WC in men, a small positive association was found in women [33]. Several studies indicate positive association between chronic alcohol intake and weight gain [34, 35]. One plausible explanation is that, IR following alcohol consumption is associated with increased adipose mass due to low insulin action in adipose tissue, liver and skeletal muscle. However, mixed results have been demonstrated in other studies [36], likely due to the confounding effect of several covariates including physical activity status, low study power and the frequency and quantity of alcohol consumed.

Also, the influence of alcohol on some appetite modulating hormones such as leptin and ghrelin [37] and leading to increase food consumption and weight gain is well documented. SCr level was higher in male than female drinkers but showed significant difference with nondrinkers only in males. eGFR was significantly lower in male drinkers than non-drinkers whereas in female drinkers eGFR was significantly higher in drinkers than non-drinkers, evidence of decrease renal function in male but not female habitual alcohol drinkers.

Collectively, these findings are consistent with previous studies that showed various degrees of renal function impairments or improvements following exposure to moderate to heavy alcohol consumption [38]. Alcohol is posited to exert either a direct [39, 40] or indirect nephrotoxic or nephroprotective effects [13]. Indirectly through the effects of its association with important risk factors of renal dysfunction such as hypertension, diabetes mellitus, stroke, IR, dyslipidemia [41], hyperuricemia [42], electrolyte disturbances [41] and Obesity.

The findings of a significant higher serum UA level among alcohol drinkers support previous studies with similar results. The mechanisms relating alcohol consumption to hyperuricemia include the following; (1) Alcohol is metabolized into adenine monophosphate (AMP), which is used as a precursor for synthesis of UA. (2) lacticacidemia formed during alcohol metabolism can raise SUA level either by decreasing excretion through the urine [43] or by increasing UA re-absorption by the renal tubule.

Furthermore, alcohol induced-IR is etiologically related to hyper-uricemia through 2 major processes including IR-induced depletion of nitric oxide bio-availability and supply, and activation of nicotin adenine dinucleotide phosphate hydrogen (NADPH) oxidase and leading to increase generation of ROS.

The postulated pathophysiological mechanisms underlying the association between heavy alcohol intake and changes in the above mentioned cardio-renal endpoints is through the IR path. Existing research indicates that heavy/long term alcohol consumption is etiologically related to induction of OS, decreased serum adiponectin level, inflammation and immune system dysfunction [44, 45]. Evidence has been garnered indicating that chronic consumption of alcohol increases the induction of liver cytochrome P-450, generation of ROS and increases OS and leading to hepatic damage and hepatic IR. There is also a significant association between OS and disorders of insulin activity and cardio-renal endpoints. Therefore, chronic alcohol intake-induced depletion of adiponectin and induction of OS appear to form the central etio-pathogenic links in alcohol-induced IR. However, controversies exist about which one precedes the other. Available data suggest that adiponectin level might be decreased in OS and vice versa [46]. Adiponectin is a plasma glycoprotein secreted only by adipocytes. It has anti-inflammatory, anti-atherogenic and anti-oxidative properties [47], and is a major regulator of insulin action and IR and its levels correlate directly with insulin activity [48].

Low plasma level of adiponectin is implicated in hepatic IR and by extension whole body IR [48]. It has been posited that adiponectin mediates its effect through adiponectin 1&2 receptors to induce signal transduction pathways mediated by Adenosine Monophosphate Kinase (AMPK) and peroxisom proliferator-activated alpha (PPARα) in target tissues including adipose tissue, hepatic cell and muscle cells [49].

In a study to assess the correlation between serum adiponectin and HDL-C, serum lipid, lipoprotein and IR profiles among young healthy men, Kazumi et al [50] found that serum adiponectin level was positively correlated with HDL-C and negatively correlated with TG, BMI, percent body fat and IR (HOMA-IR). A parallel study among Japanese subjects found a similar pattern, negative correlation between serum adiponectin and BMI, SBP, DBP, FBS, insulin, HOMA-IR total cholesterol, triacylglycerols, LDL-C and UA and positive correlation with HDL-C. This relationship was significant even after adjusting for known covariates [51]. Administration of adiponectin particularly the high molecular weight sub-type caused improvement in markers of IR and cardio-renal function [52]. Therefore without any contrary evidence, habitual alcohol intake-induced decrease in serum adiponectin and insulin sensitivity may be etiologically related to the observed abnormal values of cardio-renal indices among chronic alcoholics in the present study.

Habitual alcohol consumption could be associated with adverse cardio-renal endpoints and impaired insulin sensitivity. Some limitations of the present study should be considered in the interpretation of the results especially those associated with the cross-sectional nature of the study design. Also, self reported personal characteristics and alcohol consumption habits are prone to over and under estimation.

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References

[1] Traversy, G., & Chaput, J-P. (2015). Alcohol consumption and Obesity: an update. *Current Obesity Report*, 4, 122-130.

[2] Dumbill, E. (2013). Changing patterns of alcohol consumption in Nigeria: An exploration of responsible factors and consequences. *Journal of BSA Medical Society,* 7(1), 20-33.

[3] Chikere, E. I. C., & Mayowa, M. O. (2011). Prevalence and perceived health effect of alcohol use among male undergraduate students in Owerri, South-east Nigeria: A descriptive cross-sectional study. *BMS Public Health,* 11, 118.

[4] Oshodin, O. (1984). Parental influences upon alcohol use by teenagers in Benin City Nigeria. *The Journal of the Royal Society for the promotion of Health*, 104, 106-107.

[5] Adelekan, M. L., Abiodun, O. A., Imouokhome, A. O., Oni, G. A., Ogunremi, O. O. (1993). Psychosocial correlates of alcohol, tobacco and cannabis use: findings from a Nigerian University. *Drug-alcohol Dependence*, 33(3), 247-256.

[6] Guerini, I., Gentili, C., Guazzelli, M. (2006). Alcohol consumption and heavy drinking; Asurvey in three Italian villages, *Alcohol and Alcoholism,* 41(3), 336-340.

[7] World Health Organization (WHO). (2004). Global status report. Alcohol policy, Geneva: World Health Organization.

[8] Schrieks, I. C., Heil, A. L. J., Hendriks, H. F., Mukaml, K. J., Beulens. (2015). The effect of alcohol consumption on insulin sensitivity and glycemic status; A systemic review and meta-analysis of intervention studies. *Diabetes care* 2015:38:723-732.

[9] White, S. L., Polkinghorne, K. R., Cass, A., Shaw, J. E., Atkins, R. C., Chadban, S. (2009). Alcohol consumption and 5-year onset of chronic kidney disease: the AUSDiab study. *Nephrol Dial Transplant,* 24, 2464-2472.

[10] Gullard A. Alcohol consumption kills 3.3million people a year, WHO calculates BMJ 2014; 348: g3335. Doi: https://doi.org/10,113/bmj.g3335.

[11] World Health Organization: Global status report on alcohol and health 2018.

[12] Kim, H. N., Kim, S. H., Song, S. W. (2014). Is alcohol drinking associated with renal impairment in the general population of South Korea.

[13] Vanthiel, D. H., Gavaler, J. S., Little, J. M., Lester R (1977). Alcohol its effect on the kidney. *Metabolism,* 26; 857-866.

[14] Hsu, Y. H., Pai, H. C., Chang, Y. M., Liu, W. H., Hsu, C. C. (2013). Alcohol consumption is inversely associated with stage 3 chronic kidney diseases in middle-aged Taiwanese men. *BMC Nephrology,* 14, 254. http://www.biomedcentral.com1471-2369/14/254.

[15] Schaeffner, E. S., Kurth, T., de Jong, P. E. et al., (2005). Alcohol consumption and the risk pf renal dysfunction in apparently healthy men. *Archives of Internal Medicine,* 165, 1048-1053.

[16] Menon, V., Katz, R., Mukamal, K., Kestenbaum, B., deBoer. I. H., Siscovick, D. S., Sarnak, M. J., Shilipak, M. G. (2019). Alcohol consumption and kidney function decline in the elderly. *Nephrology Dialysis Transplant,* 25, 3301-3307.

[17] Dumbili, E. W. (2013). Changing patterns of alcohol consumption in Nigeria. An exploration of responsible factors and consequences. *Medial Sociology. Online,* 7 (1), 20-33.

[18] Mori, T. A, Burke, V., Zilkens, R. R., Hodgson, J. M., Beilin, L. J., Puddey, L. B. (2016). The effects of alcohol on ambulatory blood pressure and other cardiovascular risk factors in type 2 diabetes: a randomized intervention. *Journal of Hypertension,* 34 (3), 421-428.

[19] Ashok, N. G. (2018). Dhanraj Ganapathy status of alcoholism among dental students: A questionnaire based study. *International Journal of Orofacial Biology*, 1 (2), 66-69.

[20] Avogaro, A., Valerio, A., Miola, M., Crepaidi, C., Pavan, P., Tiengo,A., del Prato, S. (1996). Ethanol impairs insulin-mediated glucose uptake by an indirect mechanism. *International Journal of Clinical Endocrinology Metabolism*, 81, 2285-2290.

[21] Boden, G., Chen, X., DeSantis, R. A., Kendrick, Z. (1993). Ethanol inhibits insulin action on lipolysis and on insulin resistance in elderly men. *American Journal of Physiology,* 265, E197-E202.

[22] Lewis, G. F., Varnic, M., Harley, P., Giacca, A. (1997). Fatty acids mediate the acute extrahepatic effects of insulin on hepatic glucose production in humans. Diabetes, 46,111-1119.

[23] Lindtner, C., Scherer, T., Zielinski, E., Fllatova, N., Fasshauer, M., Tonks, N. K., Puchowikz, M., Buettner, C. (2013). Binge drinking indices whole-body insulin resistance by impairing hypothalamic insulin action. *Science Translational Medicine*, 50 (170), 170ra14. Doi.10.1126/scitranslmed.3005123.

[24] Schenk, S., Saberi, M., Olefsky, J. M. (2008). Insulin sensitivity: Modulation by nutrition and inflammation. *Journal of Clinical Investigation*, 188: 2992-3002.

[25] DeFronzo, R. A., Ferrannini, E. (1991). Insulin resistance for NIDDM, obesity, hypertension dyslipidemia and atherosclerotic cardiovascular disease. *Diabetic Cardiovascular disease. Diabetic care,* 14: 173-194.

[26] Reaven, G. (2002). Metabolic syndrome: patho physiology and implications for management of cardiovascular disease. *Circulation*, 106-28-38.

[27] Friedman, G. D., Selby, J. V., Quesenberry, C. P., Jr Armstrong, M. A., Klatsky, A. L. (1988). Precursors of essential hypertension: body weight, alcohol and salt use, and parental history of hypertension. *Preventive Medicine,* 17(4), 387-402.

[28] Swislocki, A. L. M., Hoffman, B. B., Reaven, G. M. (1989). Insulin resistance, glucose intolerance and hyperinsulinemia in patients with hypertension. *American Journal of Hypertension*, 2 (2), 419-423.

[29] Salvetti, A., Brogi, G., Dilegge, V. (1993). Bernini GP. The interrelationship between insulin resistance and hypertension. *Drugs*, 46, 149-159.

[30] Dey, A., Cederbaum, A. (2006). Alcohol and toxidative liver injury. *Hypertology,* S63-S74.

[31] Ekpenyong, C. E. (2018). Micronutrient deficiency, a novel nutritional risk factor for insulin resistance and syndrome X. *Archive of Food and Nutrition Science* 17-30.

[32] Wehr, H., Rodo, M., Lieber, C. S., Baraona, E. (1993). Acetaldehyde addicts and auto-antibodies VLDL and LDL in alcoholics. *Journal of Lipid and Research,* 34, 1237-1247.

[33] Romaguera, D., Angquist, L., Du, H., Jakobsen, M. U., Forouhi, N. G., Halkjaer, J., Feskens, E. J., van der, A. D. L., Masala, G., Steffen, A., Palli, D., Wareham, N. J., Overvad, K., Tjønneland, A., Boeing, H., Riboli, E., Sørensen, T. I. (2010). Dietary determinations of changes in waist circumference adjusted for body mass index-a proxy measure of visceral adiposity. *PLOS one*, 5:e11588.

[34] Lahti-Koski, M., Pietinen, P., Heliovaara, M., Vartiainen, E. (2002). Associations of body mass index and obesity with physical activity, food choices, alcohol intake, and smoking in the 1982–1997 FINRISK Studies. *American Journal Clinical Nutrition*, 75, 809–17.

[35] Wannamethee, S. G., Shaper, A. G., Whincup, P. H. (2005). Alcohol and adiposity: effects of quantity and type of drink and time relation with meals. *International Journal of Obesity (Lond),* 29, 1436–44.

[36] Wannamethee, S. G., Shaper, A. G. (2003). Alcohol, body weight, and weight gain in middle-aged men. *American Journal Clinical Nutrition*, 77, 1312–7.

[37] Wurst, F. M., Rasmussen, D. D., Hilemacher, T., Kraus, T., Ramskogler, K., Lesch, O., Baylein, K., Schanze, A., et al. (2007). Alcoholism, Craving, and Hormones: The role of leptin, ghrelin, prolactin, and the Pro-opiomelanocortin system in modulating ethanol intake. *Alcoholism Clinical and Experimental Research*, 31 (13), 1963-1967.

[38] Knight, E. l., Stampfer, M. J., Rimm, E. B., et al. (2003). Moderate alcohol intake and renal function decline in women. A prospective study. *Nephrology, Dialysis, Transplantation,* 18(8), 1549-1554.

[39] Heidland, A., Holt, W. H., Schaefer, R. M., Teschner, M., Weipert, J., Heidbreder, E. (1985). Role of alcohol in clinical nephrology. *Klinische Wachenschrift,* 63, 948-958.

[40] Vamvakas, S., Teschner, M., Bahner, U., Heidland, A. (1998). Alcohol abuse. Potential in electrolyte disturbances and kidney disease. *Clinical of Nephrology,* 49, 205-213.

[41] Parekh, R. S., Klag, M. J. (2001). Alcohol: role in the development of hypertension and end-stage renal disease. *Current Opinion in Nephrology Hypertensive,* 10, 385-390.

[42] Yamanaka, H. (1996). Alcohol ingestion and hyperuricemia. *Nippon Rinsho*, 54:3369-3373.

[43] Estimond, C. J., Gaiton, M., Robins, S., Riddoch, S. (1995). The effects of alcohol beverage on urate metabolism in gout sufferers. *British Journal of Rheumatology*, 34, 756-759.

[44] Xu, A., Wang, Y., Keshaw, H., Xu, L. Y., Lam, K. S., Cooper, G. J. (2003). The fat-derived hormone adiponectin alleviates alcoholic and nonalcoholic fatty liver diseases in mice. *Journal of Clinical Investigation,* 112, 91-100.

[45] You, M., Considine, R. V., Leone, T. C., Kelly, D. P., Grabb, D. W. (2005). Role of adiponectin in the protective action of dietary saturated fat against alcoholic fatty liver in mice. Hepathology, 42, 568-577.

[46] Tang, H., Sebastian, B. M., Axhemi, A., Chen, X., Hillian, A. D., Jacobsen, W. D., Nagy, L. E. (2012). Ethanol-Induced Oxidative Stress via the CYP2E1 Pathway Disrupts Adiponectin Secretion from Adipocytes. *Alcoholism Clinical & Experimental Research,* 36(2), 214-222.

[47] Jeong, J. E., Kwak, S. M., Bang, S. G., Lim, S. G., Kim, D. J. (2014). The effect of chronic alcohol consumption on adiponectin and insulin resistance. *Alcohol and Alcoholism*, 48(1), 158 http//doi.org/10.1093/alcalc/aguo54.27

[48] Li, Y., Ding, L., Hassan, W., Abdelkader, D., Shang, J. (2013). Adipokines and hepatic insulin Resistance. *Journal of Diabetes Research,* http://dx.doi.org/10.1155/2013/170552.

[49] Yamauchi, T., Kadowaki, T. (2013). Adiponectin receptor as a key player in healthy longervity and obesity related diseases. *Cell Metabolism,* 17: 185-196.

[50] Kazumi, T., Kawaguchi, A., Hirano, T., Yoshino, G. (2004). Serum adiponectin is associated with higher density liprotine cholesterol, triglycorides, and low density lipoprotine particle size in young healthy men. *Metabolism,* 53 (5), 589-593.

[51] Yamamoto, Y., Hirose, H., Saito, I., Tomita, M., Taniyama, M., Matsubara, K., Okazaki, Y., Ishii, T., Nishikai, K., Saruta, T. (2002). Correlation of the adipocyte-derived protein-cholesterol independent of body mass index n the Japanese population *Clinical Science,* 103 (2), 137-142.

[52] Hirose, H., Yamamoto, Y., Seino-Yashihara, Y., Kawabe, H., Saito, I. (2010). Serum high-molecular weight adiponectin as a marker for the evaluation and care of sunjects with metabolic syndrome and related disorders. *Journal Atherosclerosis and Thrombosis,* 17 (12), 1201-11.

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