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A comparison of the cardiometabolic profile of black South Africans with suspected non-alcoholic fatty liver disease (NAFLD) and excessive alcohol use

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ABSTRACT

Excessive alcohol use and non-alcoholic fatty liver disease (NAFLD) are putative cardiovascular disease risk factors. In order to ease the identification of these conditions on primary health care level, we aimed to determine and compare the demographic and cardiometabolic characteristics of excessive alcohol users and those with suspected NAFLD in black South Africans. In the Prospective Urban Rural Epidemiology study (North West Province, South Africa, $N = 2021$, collected in 2005) we selected 338 participants, namely: 1) alcohol users ($N = 143$) reporting 'yes' to alcohol intake, with high gamma-glutamyl transferase (GGT) $\geq$80 U/L and a percentage carbohydrate deficient transferrin (%CDT) $\geq$2%; 2) non-alcohol users ($N = 127$) self-reporting 'no' to alcohol intake with GGT $\leq$30 U/L and %CDT $\leq$2%; and 3) NAFLD group ($N = 68$) who were non-drinkers with GGT levels $\geq$60 U/L and %CDT $\leq$ 2%. The demographics indicated that the alcohol users were mostly men (73%) with a body mass index (BMI) of 19.8 (15.2–27.3) kg/m^2, 90% of which were smokers. Systolic blood pressure (SBP) of alcohol users significantly correlated with high-density lipoprotein cholesterol (HDL-C) ($\beta = 0.24$; $p = 0.003$) and waist circumference (WC) ($\beta = 0.22$; $p = 0.006$). Non-alcohol users were mostly women (84%) with a BMI of 26.0 (18.0–39.2) kg/m^2 and blood pressure in this group related positively with triglycerides. The NAFLD group were also mostly women (72%) with a comparatively larger WC ($p < 0.001$) and an adverse metabolic profile (total cholesterol: 5.55 ± 1.69 mmol/L; glycosylated hemoglobin: 6.03 (4.70–9.40) %). Diastolic blood pressure in the NAFLD group associated positively with WC ($\beta = 0.27$; $p = 0.018$). We therefore found disparate gender and cardiometabolic profiles of black South Africans with suspected NAFLD and excessive alcohol use. The described profiles may aid health care practitioners in low resource settings when using these crude screening measures of gender, obesity indices (and self-reported alcohol use) to identify individuals at risk.

Introduction

Cardiovascular disease (CVD) remains one of the leading causes of morbidity and mortality in sub-Saharan Africa (Opie & Seedat, 2005; Sliwa et al., 2008; Twagirumukiza et al., 2011). South Africa experiences a rapid rate of urbanization which leads to lifestyle changes that contributes to the high prevalence of hypertension and type 2 diabetes (Stewart et al., 2011; Van Rooyen et al., 2000). The levels of alcohol intake and abuse have increased in Africans over the last decade and is considered one of the main contributors to hypertension (Schutte et al., 2012) and liver injury (Nguyen & Thuluvath, 2008) in this ethnic group.

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Gamma-glutamyl transferase (GGT) is a well-known marker of alcohol intake and GGT levels are elevated in individuals who use alcohol excessively (Tsai, Ford, Li, & Zhao, 2012). GGT is also known to relate strongly with the development of CVD and may also predict cardiovascular outcomes (Mason, Starke, & Van Kirk, 2010). Apart from the association of GGT with excessive alcohol intake, it is also influenced by other factors including age, obesity and liver injury (Mason et al., 2010; Puukka et al., 2006; Torrente, Freeman, & Vrana, 2012). GGT is also elevated in patients with non-alcoholic fatty liver disease (NAFLD) even in the absence (or during very low intake) of alcohol (Bhatia, Curzen, Calder, & Byrne, 2012; Hall & Cash, 2012).

The prevalence of NAFLD has been shown to be positively associated with body weight (Bayard, Holt, & Boroughs, 2006) and is recently receiving significant attention as a putative CVD risk factor (Bhatia et al., 2012; Targher, Day, & Bonora, 2010; Tsuzaki, Kotani, Fujiwara, Sano, & Sakane, 2014). Obesity is common among black South Africans, contributing to the onset of hypertension (Puoane et al., 2002; Schutte et al., 2008). Although obesity is associated with NAFLD, a study carried out in South Africa did not find any association between the degree of obesity and severity of NAFLD in Africans (Kruger et al., 2010), possibly due to the low number of Africans ($N = 12$) used in their study. Additionally, patients with NAFLD are mostly asymptomatic, making it difficult to accurately characterize these individuals with NAFLD (Scaglioni, Ciccia, Marino, Bedogni, & Bellentani, 2011). Despite the availability of various tests used for indicating excessive alcohol use (percentage carbohydrate transferrin (%CDT), ethyl glucuronide (EtG), ethyl sulphate (EtS) and phosphatidylethanol (PEth)), they are rather costly and not necessarily viable options for use in developing countries (Junghanns et al., 2009; Viel, Boscolo-Berto, Cecchetto, Fais, & Nalesso, 2012).

In a large African population cohort of 2021 participants, we characterized 3 subgroups for the purpose of this investigation: (1) self-reported excessive alcohol users and (2) abstainers (both the latter confirmed with %CDT and GGT), and (3) individuals with characteristics of NAFLD, who reported no or low alcohol intake, with low %CDT and elevated GGT. We aimed to compare the cardiovascular and metabolic characteristics of these three groups in order to obtain a better understanding regarding the risk factors contributing toward elevated blood pressure in each group.

Materials and methods

Study population

This is a sub-study of the international PURE (Prospective Urban and Rural Epidemiology) study and the detailed methodology has been described elsewhere (Schutte et al., 2012; Teo, Chow, Vaz, Rangarajan, & Yusuf, 2009). This South African leg of the PURE study is based in the North West Province, where data was collected in 2005 from 2021 participants. We identified 338 individuals who complied with the inclusion criteria of the predetermined groups, namely, (1) those who reported 'yes' to alcohol intake, confirmed with a GGT $\geq$80 U/L and %CDT $\geq$ 2% (named "alcohol users") ($N = 143$); (2) those that self-reported 'no' to alcohol intake, confirmed by low GGT $\leq$ 30 U/L and %CDT $\leq$ 2% (named "non-alcohol users") ($N = 127$); and (3) those who presented with the characteristics of NAFLD, i.e. reported 'no' to alcohol intake but accompanied with GGT $\geq$60 U/L and %CDT levels $\leq$2% (named "NAFLD group") ($N = 68$).

The study was approved by the Ethics Committee of the North-West University, South Africa and complied with the Helsinki Declaration of 1975, as revised in 2008. Permission was obtained from the Department of Health of the North West Province, community leaders, tribal chiefs and mayors in this area to conduct the study. All subjects were informed about the objectives and procedures of the study and gave written informed consent prior to voluntary participation. Participants were asked to fast for 10 h prior to blood sample collection. Field workers were available to do the translation in the participant's native language. Confidentiality and anonymity of all the results were assured. Participants identified with chronic illnesses such as hypertension and Human Immunodeficiency Virus (HIV) were referred to their local clinics and hospitals with which prior arrangements were made. Afterward participants received a light meal. If any health risk was identified, they received counseling and a referral letter. Moreover, remuneration was offered to ensure they could go to clinics if referred.

Questionnaires

The participants were requested to complete structured demographic, socio-economic, lifestyle and physical activity questionnaires, conducted by trained African fieldworkers, developed and standardized for the international PURE study (Teo et al., 2009). The questions on alcohol consumption included a no/yes question on alcohol use (yes, current or former use; no, never used).

Anthropometric measurements

Each participant had height, body weight, waist and hip circumferences measured (Precision Health Scale, A & D company, Tokyo, Japan; Invicta Stadiometer, IP 1465, Leicester, UK; Holtain unstretchable metal tape) using standardized methods (Marfel-Jones, Olds, Stewart, & Cartel, 2006).

Cardiovascular measurements

Cardiovascular measurements were executed after a 10-min rest period once BP had stabilized. Systolic and diastolic blood pressure (SBP, DBP) and heart rate were measured in duplicate, 5 min apart, with the validated Omron HEM-757 apparatus (Omron Healthcare, Kyoto, Japan), while the participants were seated upright with the right arm at heart level. Appropriate sized cuffs were used for obese participants. Pulse pressure (PP) was then calculated by subtracting DBP from SBP.

Blood, serum and plasma samples

As indicated earlier, each participant was requested to fast for approximately 10 h before blood sampling commenced. A registered nurse took a blood sample from the ante-brachial vein branches. Samples were prepared according to appropriate methods. In the rural area, samples were immediately frozen and stored at -18 °C for no longer than five days, transported to a laboratory facility and stored at -80 °C until analysis.

Biochemical analyses

From the collected blood samples, liver enzymes (GGT, alanine aminotransferase (ALT), aspartate aminotransferase (AST)), high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), triglycerides (TG), uric acid, C-reactive protein (CRP) and serum glucose (Konelab20i auto analyser; Thermo Scientific, Vantaa, Finland) were determined. Serum iron was determined using immunological, colorimetric and high-performance liquid chromatography methods and glycosylated hemoglobin (HbA1c), in the EDTA-treated whole blood, using the D-10 Hemoglobin testing