Cardiovascular risk factors in rural Kenyans are associated with differential age gradients, but not modified by sex or ethnicity

Dirk L. Christensen1,2 Daniel Faurholt-Jepsen3,4, Louise Birkegaard1, David L. Mwaniki5, Michael K. Boit6, Beatrice Kilonzo5, Søren Brage7, Henrik Friis3, Inge Tetens8, Knut Borch-Johnsen9, and Dorte Vistisen2

1Department of Public Health, University of Copenhagen, Copenhagen, Denmark, 2Steno Diabetes Center, Gentofte, Denmark, 3Department of Nutrition, Exercise and Sports, University of Copenhagen, Frederiksberg, Denmark, 4Department of Infectious Diseases, National University Hospital (Rigshospitalet), Copenhagen, Denmark, 5KEMRI, Nairobi, Kenya, 6Department of Recreation Management and Exercise Science, Kent State University, Akron, Ohio, USA, 7Medical Research Council Epidemiology Unit, University of Cambridge, Cambridge, UK, 8National Food Institute, Technical University of Denmark, Søborg, Denmark, and 9Holbæk Hospital, Holbæk, Denmark

Abstract

Background: The relationship between metabolic disease and the non-modifiable risk factors such as age and ethnicity in Africans is not well-established.

Aim: This study aimed to describe sex, age and ethnicity differences in blood pressure (BP) and lipid levels in rural Kenyans.

Subjects and methods: A cross-sectional study was undertaken among rural Kenyans. BP and pulse rate (PR) were measured while sitting and fasting blood samples were taken for analysis of standard lipid profile. Standard anthropometric measurements were collected. Physical activity expenditure was calculated objectively and lifestyle data were obtained using questionnaires.

Results: In total, 1139 individuals (61.0% women) participated aged 17–68 years. Age was positively associated with BP and plasma cholesterol levels. Sitting PR was negatively associated with age in women only (sex-interaction p < 0.001). Ethnicity did not modify any of the age-associations with haemodynamic or lipid outcomes. Differences in intercept between women and men were found in all parameters except for diastolic BP (p = 0.154), with men having lower HDL-C but higher values in all other cardiovascular risk factors.

Conclusion: BP and plasma cholesterol levels increase with age at a similar gradient in men and women, but absolute levels of the majority of the risk factors were higher in men.

Introduction

Metabolic diseases are on the increase in sub-Saharan Africa (SSA) and morbidity and mortality from cardiovascular disease (CVD) has become highly prevalent in black Africans (Seedat, 1999; Steyn et al., 2005). According to the most recent World Health Organization report in 2011 on CVD, significant increases in coronary diseases in SSA are expected over the next decades (WHO/WHF/WSO, 2011). The current mortality rates from cerebrovascular and ischaemic heart disease for both men and women have an approximate range of 85–295 per 100 000 (age standardised) in most SSA countries, which is higher than for most of the high-income countries in Europe, the Americas, and Australia (WHO/WHF/WSO, 2011).

The main known risk factor for CVD is hypertension, which is estimated to be prevalent in around half of the adult population ≥25 years of age in several countries in SSA (WHO/WHF/WSO, 2011). In the east African region, this development has been going on since the 1940s (Williams, 1944), as prior to this decade the limited available studies showed no hypertension as well as little or no increase in blood pressure with increasing age (Donnison, 1929; Vint, 1936). In the Luo Migration Study from the 1980s, higher age seemed to be associated with 10 mmHg higher blood pressure (BP) (Poulter et al., 1984). More recently, among rural Kenyans >55 years of age, half were hypertensive (Hendriks et al., 2012). In addition to hypertension, dyslipidaemia is associated with CVD, e.g. dyslipidaemia causes atherosclerosis (Keys, 1970), which is a precursor for severe outcomes such as stroke or myocardial infarction. Obtaining a blood lipid profile is not routinely done in SSA populations and in research settings it has only become common practice in more recent years. It has been reported that individuals of black African descent have relatively high levels of high-density lipoprotein cholesterol (HDL-C) and low triglyceride (TG) levels (Ervin, 2009). However, compared to individuals of European descent, black African individuals with insulin resistance have a different lipid profile with low levels of HDL-C and normal TG levels rather than combined low HDL-C/high TG levels (Sumner & Cowie, 2008).
A so-called rural protection factor has been emphasised as an explanation of low prevalence of metabolic disease in rural African populations (Steyn & Damasceno, 2006). Whether diverse lifestyles due to gender differences as well as behaviour (agro-fishing, agriculturalist, agro-pastoralist) determined by ethnic origin affect the age-associated risk of CVD remains unknown. We have previously reported substantial differences in living conditions and anthropometric as well as biochemical outcome parameters by ethnicity. Thus, the agro-pastoral Maasai had a substantially higher dietary intake of fat compared to the agro-fishing Luo and agricultural Kamba (30% vs 15%) (Hansen et al., 2011) and the Maasai were more physically active than the two other ethnic groups (Christensen et al., 2012). We have also reported that the Maasai had a higher visceral fat accumulation (Christensen et al., 2008), as well as higher insulin resistance and lower beta cell function compared to the two other ethnic groups (Christensen et al., 2014). We aimed at studying the association between age and blood pressure and plasma lipids in a rural Kenyan population, to assess how sex and ethnicity (Luo, Kamba and Maasai) affect this association, whilst controlling for differences in lifestyle factors.

Research design and methods

Study design, site and population

A cross-sectional study was conducted in the districts of Bondo, Kitui and Transmara in rural Kenya among the Luo, Kamba and Maasai ethnic groups during the period August–November 2005. They were chosen to represent societies of agro-fishing, agriculture and agro-pastoralism, respectively. The study participants were randomly selected at weekly village meetings (n = 648) and non-randomly selected volunteers (n = 91) among the Luo and Kamba. All adult Maasai within a radius of 20 km from the study site were invited to participate. All resided in rural villages, but some commuted regularly to the nearest town for business and were, thus, exposed to an urban lifestyle. A more detailed account of the selection procedure has been presented elsewhere (Christensen et al., 2008). All participants gave written or oral informed consent. Ethical approval was given by the National Ethical Review Committee in Kenya and consultation (Christensen et al., 2003). All participants were seated for at least 15 minutes. If the systolic or diastolic blood pressure differed by more than 5 mmHg, a third measurement was made. Mean blood pressure was calculated from the two lowest measurements. Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg (Whitworth, 2003) or being on anti-hypertensive drug treatment. Pulse pressure (PP, mmHg) was defined as SBP - DBP.

Anthropometry

With the participants wearing undergarments, body weight was measured to the nearest 0.1 kg using a portable high precision scale (Tanita, type BWB-800S MA, Tokyo, Japan) and height was measured twice to the nearest 0.1 cm with a portable stadiometer (Meterex II, D97, UNICEF, Copenhagen, Denmark). Body mass index (BMI) was calculated as weight/height² (kg/m²). For further methodological details, see Christensen et al. (2008).

Physical activity and sitting heart rate

Physical activity measurements were carried out using a combined uniaxial accelerometer and heart rate (HR) sensor (Actiheart, CamNtech Ltd, Cambridge, UK). HR was pre-processed (Stegle et al., 2008) and average daily physical activity energy expenditure (PAEE) was estimated using branched equation modelling (Brage et al., 2004), to combine torso acceleration with individually (step) calibrated HR into an activity intensity time-series (Brage et al., 2007), and then integrated with respect to time, whilst minimizing potential diurnal information imbalance bias. The Actiheart monitor was worn an average of 3.9 (range = 1.0–8.1) days, as described elsewhere (Christensen et al., 2012).

Dietary intake, alcohol consumption and smoking

The dietary intake for each participant was estimated using a repeated 24-hour recall method. The first 24-hour recall was conducted Monday through Saturday and the subsequent
24-hour recall 4 days later. The dietary assessment was conducted by trained staff members who were recruited locally. The dietary intake data were entered into the programme General Intake Estimation System (GIES) (National Food Institute, Søborg, Denmark). Subsequently, data were linked to an ad-hoc food composition database for calculation of nutrient intakes, as described in detail elsewhere (Hansen et al., 2011).

Statistics

The following outcome variables were considered: SBP, DBP, PP and sitting PR; TG, HDL-C, LDL-C, VLDL-C, total cholesterol and total cholesterol:HDL-C ratio. The proportion of missing data ranged from 0% for age, sex and ethnicity up to 7% for physical activity. Missing data on outcomes and explanatory variables were imputed using the Multivariate Imputations by Chained Equations (MICE) method in R software (van Buuren, 2007) with missing-at-random assumptions. Fifty copies of the data, each with missing values suitably imputed, were independently assessed in the analyses described below. Estimates of parameters of interest were averaged across the copies to give a single mean estimate. Standard errors and $p$ values were adjusted according to Rubin’s rules (Rubin, 1987).

Associations between age and outcomes were assessed through linear regression analysis. We explored different levels of adjustment for potential confounders in the analyses; as a first step we adjusted only for sex and ethnicity; second, analyses were additionally adjusted for BMI and third, further adjustment for average daily PAEE, alcohol intake, smoking and daily total energy intake. For systolic and diastolic blood pressure, pulse pressure and sitting PR, we additionally adjusted for haemoglobin level. In each of the models, a modifying effect on age by sex was tested as well as deviation from a linear trend of age. In addition, we used change point analysis to assess any significant changes in the linear associations across age. In the last model, we further tested for a modifying effect of ethnicity on age. Prior to analysis, we log-transformed outcomes with highly skewed distributions (TG, VLDL-C and total cholesterol:HDL-C ratio). In the analyses of haemodynamic markers, we excluded two participants on anti-hypertensive treatment. Figures illustrating the found associations between haemodynamic markers and lipids with age were provided for a hypothetical but representative Luo study participant, i.e. with characteristics corresponding to the median or most frequent value in the studied population. Statistical analyses were performed in R (version 9.15.2) and SAS (version 9.2).

Results

The study population included 1139 individuals consisting of 391 Luo (56% women), 387 Kamba (74% women) and 361 Maasai (53% women) with an age range of 17–68 years. No differences were found in age, sex distribution or BMI between the randomly and non-randomly selected participants (data not shown). Background information is represented in Tables 1 and 2.

Of 97 (8.5%) participants with hypertension, two (2.1%) were on anti-hypertensive treatment at the time of the study.

Of the remaining 95 participants with a blood pressure measurement commensurate with a diagnosis of hypertension, 58 (61.1%) had isolated high SBP, seven (7.2%) had isolated high DBP and 30 (30.9%) had both. None of the study participants were taking lipid-lowering drugs.

A total of 397 (37.3%) individuals had dyslipidaemia, of which 24 (6.1%) had isolated high TG, 344 (86.7%) had isolated low HDL-C and 29 (7.3%) had both. Overall, high TG was seen in 5.3% (4.1; 6.9) of the participants and in 4.2% (2.8; 6.1) vs 7.0% (4.8; 9.9) ($p < 0.0485$) of women vs men, respectively. Low HDL-C was found in 35% (32.2; 38.0) of...
the participants and in 36.2% (32.5; 40.0) vs 33.3% (28.8; 38.0) (p = 0.333) of women vs men, respectively.

In all models, we found linear associations with age, except for PP, where a statistically significant deviation from linearity was present. However, for none of the associations with age did we find a significant change point in the linear associations. Furthermore, because the non-linear effect for PP was tiny and not clinically relevant, we present results from the more parsimonious linear model for this association. Only for sitting PR did we find a modifying association with age by sex (p < 0.001). None of the associations with age were modified by ethnicity in the model adjusted for age, sex, BMI, PAEE, alcohol intake, smoking and total energy intake and with further adjustment for haemoglobin level in the models for the haemodynamic markers (Table 3, Model 3). Except for DBP (p = 0.154), we found significant differences in the estimated levels of haemodynamic markers and lipids between men and women across age (p < 0.001) (Figures 1 and 2). To further investigate the age-related decrease in sitting PR in women, we tested for possible change points in the linear slope by age in women, but none were found to be statistically significant (data not shown). Furthermore, we found no differences in hypertension or dyslipidaemia between the randomly and non-randomly selected individuals (data not shown). Background characteristics of the study population by ethnicity are shown in Supplementary Table S1.

Discussion
This study showed that systolic blood pressure and plasma cholesterol concentrations as well as sitting PR (in women) were higher in older individuals, irrespective of differences in clinical and lifestyle parameters. Furthermore, we found no modifying effect of age by sex or ethnicity in any of the blood pressure or plasma cholesterol parameters, except for sitting PR for which the association differed in men and women.

When considering absolute numbers, sex differences in blood pressure are well-documented (Ong et al., 2008), with women exhibiting lower blood pressure levels than their age-matched male counterparts up to about the seventh decade of life, as shown in different UK cohorts (Wills et al., 2011). Similarly, we show that differences in blood pressure by sex seem to persist, at least up to the end of the sixth decade of life in Kenyan populations. Furthermore, prevalence of hypertension was twice as high in men compared to women (11.9% vs 6.3%) in our study in which individuals aged 17–68 years were included; this emphasizes a higher risk of cardiovascular disease in men through the sixth decade of life. However, it is also important to note that, even for individuals with SBP of 120–139 mmHg and/or DBP of 80–89 mmHg, there may be a 3.5-fold and 1.7-fold risk of myocardial infarction and of ischaemic heart disease, respectively, compared to individuals with lower blood pressure levels (Qureshi et al., 2005) and a reduction of 2 mmHg in SBP has been shown to reduce stroke and ischaemic heart disease mortality by 10% and 7%, respectively (Lewington et al., 2002).

Our results clearly indicate higher plasma cholesterol levels (all sub-types except for HDL-C) with increasing age in both men and women and higher absolute values in men compared to women. The higher level of total cholesterol:HDL-C ratio with increasing age indicates higher CVD risk, as this ratio may have the highest predictive value of ischaemic heart disease (Lemieux et al., 2001). It is of note that almost nine in 10 individuals with dyslipidaemia had isolated low levels of HDL-C, while isolated high TG levels or in combination with a low HDL-C level were much less common. This lack of increase in TG independent of age—even in insulin resistant individuals—or low TG levels in obese black Africans has been shown in previous studies in SSA, concomitantly with low levels of HDL-C, regardless of insulin resistance status or whether normal weight or obese, respectively (Jennings et al., 2009; Goedecke et al., 2010). It is possible that isolated low HDL-C levels may be a major factor contributing to CVD in black Africans. Alternatively, it has been proposed that a high activity of lipoprotein lipase which clears TG-rich lipid particles from the circulation could be a key mechanism for explaining the normal levels of TG in insulin-resistant black Africans (Despres et al., 2000).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP (mmHg)</td>
<td>1.63 (0.77;2.49)</td>
<td>1.08 (0.25:1.91)</td>
<td>0.90 (0.03:1.77)</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>1.00 (0.45:1.56)</td>
<td>0.74 (0.20:1.28)</td>
<td>0.34 (−0.21:0.89)</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>0.71 (0.11:1.31)</td>
<td>0.50 (−0.10:1.10)</td>
<td>0.59 (−0.03:1.22)</td>
</tr>
<tr>
<td>Sitting pulse rate (beats/min)</td>
<td>2.51 (−3.3;−1.73)</td>
<td>2.56 (−3.35;−1.77)</td>
<td>2.94 (−3.73;−2.16)</td>
</tr>
<tr>
<td>Triglycerides (% difference)</td>
<td>9.5 (7.1:12.0)</td>
<td>8.2 (5.9:10.6)</td>
<td>6.9 (4.4:9.3)</td>
</tr>
<tr>
<td>HDL-cholesterol (mmol/L)</td>
<td>0.02 (0.00:0.04)</td>
<td>0.02 (0.00:0.04)</td>
<td>0.03 (0.01:0.05)</td>
</tr>
<tr>
<td>LDL-cholesterol (mmol/L)</td>
<td>0.18 (0.14:0.23)</td>
<td>0.16 (0.11:0.20)</td>
<td>0.15 (0.11:0.20)</td>
</tr>
<tr>
<td>VLDL-cholesterol (% difference)</td>
<td>10.5 (8.1:13.0)</td>
<td>9.0 (6.6:11.4)</td>
<td>7.5 (5.1:10.0)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>0.24 (0.19:0.30)</td>
<td>0.21 (0.16:0.26)</td>
<td>0.21 (0.16:0.26)</td>
</tr>
<tr>
<td>Total:HDL cholesterol (% difference)</td>
<td>4.5 (2.5:6.5)</td>
<td>3.4 (1.5:5.4)</td>
<td>2.4 (0.5:4.4)</td>
</tr>
</tbody>
</table>
As mentioned, a rural protective factor in Africa has been proposed in connection with low prevalence of cardiovascular risk factors and disease (Steyn & Damasceno, 2006) including hypertension, which has been shown in several studies going back almost a century (Donnison, 1929; Mugambi & Little, 1983; Williams, 1969). Prevalence of dyslipidaemia is not as well-documented and, even within rural populations, substantial differences have been found depending on lifestyle differences, for example when comparing mean triglyceride levels of fish consumers (male Njemps of Kenya 1 mmol/L, serum) and milk and meat consumers (male Maasai of Tanzania = 2.1 mmol/L, plasma) (Njelekela et al., 2002; Robinson & Day, 1986), even though these differences may not have any clinical significance and could depend on seasonal differences in fat consumption, especially in the Maasai.

Low prevalence of, for example, hypertension or dyslipidaemia per se or rural–urban differences may independently suggest whether or not rural residency and lifestyle protect against cardiovascular risk and disease. The prevalence of hypertension in our study was relatively low, but a study in rural Maasai in Tanzania showed an increase from 7% to 25% and from 5% to 19% in men and women, respectively, without a correspondingly high increase in obesity over the course of a decade between 1987–1998 (Njelekela et al., 2001). Furthermore, the Kenyan Luo Migration Study—which resulted in a series of publications between 1980–1990—investigated a rise in blood pressure following rural–urban migration and showed associations with higher body weight, dietary energy intake and reduced potassium intake (Poulter et al., 1984, 1985, 1990). However, as sitting PR was also higher, increased autonomic nervous system activity may have contributed to the higher blood pressure levels as well. Our results on sitting PR showed no change with each 10 years of increasing age for men, while sitting PR was significantly lower (−3.0 beats/min) in women for the same time interval. The inverse association between sitting PR and age for the women may suggest a generational decline in fitness or higher prevalence of anaemia, but could also be explained by high mental stress and lack of sleep in young women within the sexually reproductive age; longitudinal data are required to further elucidate these phenomena.

The Luo, Kamba and Maasai, who participated in this study, differ when it comes to dietary intake, especially energy intake, absolute and relative fat intake and carbohydrate intake (Hansen et al., 2011). They also differ in physical activity energy expenditure (Christensen et al., 2012), insulin resistance and action (Christensen et al., 2014) and

---

Figure 1. Estimated regressions lines for a hypothetical non-smoking Luo with a BMI of 21 (kg/m²), average daily PAEE of 69 (kJ/day/kg), with no alcohol intake, haemoglobin level of 8.4 (mmol/L) and an energy intake of 6.9 MJ for systolic BP (A), diastolic BP (B), pulse pressure (C) and sitting pulse rate (D) from age 17–68 years. Dashed lines are 95% confidence limits. Black: men and women together; Blue: men; Red: women.
anthropometric measurements, especially abdominal fat accumulation (Christensen et al., 2008), with the Maasai group deviating most from the two other ethnic groups in all of these modifiable lifestyle factors. It is, therefore, surprising that—in spite of these differences—ethnicity did not modify the age associations in any of the blood pressure or cholesterol parameters measured. As for blood pressure, not only lifestyle parameters such as diet and physical activity influence the results, but so does mental stress. The latter factor may not differ amongst these ethnic populations in rural Kenya, while high physical activity level in the Maasai may nullify the potentially adverse effects of the higher fat intake as compared to the other two ethnic populations. The lack of age-related ethnic differences in dyslipidaemia may also be explained by these factors.

In our statistical analyses, we have used multiple imputation (MICE) to handle the large number of missing data in this study instead of complete case analysis. Several

Figure 2. Estimated regressions lines for a hypothetical non-smoking Luo with a BMI of 21 (kg/m²), average daily PAEE of 69 (kJ/day/kg), with no alcohol intake and an energy intake of 6.9 (MJ) for triglycerides (A), HDL cholesterol (B), LDL cholesterol (C), VLDL cholesterol (D), total cholesterol (E) and ratio of total:HDL cholesterol (F) from age 17–68 years. Dashed lines are 95% confidence limits. Blue: men; Red: women.
simulation studies have shown that complete case analysis generally leads to biased estimates (Janssen et al., 2010) and the MICE method is currently the state-of-the-art-method for dealing with data missing at random (Sterne et al., 2009). Furthermore, since our results are based on cross-sectional data, the age-related associations presented in this report may be due to residual variation in lifestyles of participants of different ages and not necessarily an age trend; had the elderly lived a more traditional lifestyle, we would not have expected age-related increases in blood pressure and cholesterol due to the possible rural protection factor. It is important to emphasise that, although the populations in the current study are considered rural, they consisted of a mixture of rural and semi-urban individuals. All resided in rural villages, but some commuted regularly to the nearest town for business and were, thus, exposed to urban life.

Study strengths were a large sample size from three different ethnic populations with three distinct lifestyles, which made it potentially possible to examine ethnic differences in age-related blood pressure and lipid profile whilst controlling for lifestyle factors. Furthermore, the study was carried out under standardised conditions, despite challenges in field lab facilities. Limitations of the study include the fact that we studied a sample which cannot be considered random, with an unknown number of Maasai not showing up for the study, despite an invitation to participate. However, the majority of the Luo and Kamba participants were randomly selected through public village meetings and, therefore, most likely representative of the general population. The study is based on collection of observational, cross-sectional data and, thus, inference on causality is limited. Finally, even though all study participants were rural residents, we noticed that a large segment of the study participants worked in nearby urban settings. However, we did not collect detailed information on this aspect, for which reason we cannot distinguish between individuals working in an urban setting and those who did not. This may offer part of the explanation for differences in cardiovascular risk factor outcomes and should be assessed in future studies.

In conclusion, blood pressure and plasma cholesterol parameters were higher in older age in both men and women and the majority of the cardiovascular risk factors were higher in men compared to women. Age associations were not different across ethnic groups, after adjustment for differences in lifestyle. This study suggests that rural residency and life conditions do not protect the Kenyan Luo, Kamba and Maasai from elevation of CVD risk factors.

Acknowledgements

We are grateful to all participants, the local chiefs and sub-chiefs, the local elder councils and district politicians. We are also indebted to the late Benedict Omondi (KEMRI), Tobias Oketch (CVBCR and KEMRI), Arthur J. Ukumu (DVBD), Odero Sabiano (DVBD) and Saidi Kisiwa (KEMRI) for their skilful collection and analysis of blood samples in the field. We sincerely thank Philista Singore for excellent clinical health assessment of the study participants and we are thankful to all local assistants for their effort in excellent social mobilization and collection of data. We acknowledge the permission by the Director of KEMRI to publish this manuscript. The study was supported by DANIDA (J. no. 104.DAN.8-871, RUF project no. 91202), Cluster of International Health (University of Copenhagen), Steno Diabetes Center, Beckett Foundation, Dagmar Marshall Foundation, Dr Thorvald Madsen’s Grant, Kong Christian den Tiende’s Foundation, Brdr Hartmann Foundation and the Novo Nordisk Foundation (Grant no. 29847).

Declaration of interest

The authors report no conflicts of interest. The funding bodies (see under Acknowledgement for details) had no role in the study design, data collection, data analysis, data interpretation or decision to publish the findings.

References


---

Supplementary material available online

Supplementary Table S1.