Effects of lifestyle on plasma levels of the IGF system and the antioxidants coenzyme Q10 and vitamin E in Kenyan rural and urban populations

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1. Introduction

Infections and nutritional deficiency related disorders predominate in populations of the developing countries. In the middle income countries, however, as nutritional situation improves and sedentary life style becomes more common, the infectious diseases are reduced and cardiovascular diseases are increasing. According to The World Health Organization Report 1999, non-communicable diseases and cardiovascular diseases are increasing in the middle income countries [1]. The high incidences of cardiovascular diseases, obesity, diabetes, dyslipidaemia and hypertension in the developing countries are linked by common lifestyle determinants such as diet, physical activity, as well as alcohol and tobacco consumptions [1]. The IGF system plays a significant role in normal growth and development as well as in several major diseases and pathologic states such as diabetes and cancer [2,3]. IGF-I is an insulin-like growth factor hormone mainly produced in the liver and its activity is regulated by IGFBP-1. IGFBP-1 facilitates the transport of IGF-I from plasma to tissues thus increasing the bioavailability and activity of IGF-I in the target tissues, but it may also have independent effects through interactions with cell surface molecules [4]. IGFBP-1 is an important determinant of IGF-I activity. IGFBP-1s highly depend on insulin concentrations and is found in higher concentrations in the serum during fasting and early mornings [5]. High levels of insulin are associated with low IGFBP-1 concentrations, and low levels of circulating IGFBP-1 are associated with the typical characteristics of metabolic syndromes such as insulin resistance, obesity and the development of cardiovascular diseases [2,6]. Serum levels of IGFBP-1 vary considerably in healthy individuals, 64% of which is attributed to non-genetic factors such as dietary and other environmental factors. On the other hand, IGF-I variations in healthy individuals could be ascribed to non-genetic factors by 35% [7].
Genetic and environmental factors independently determine the levels of coenzyme Q10 (CoQ), while the other major lipid soluble antioxidant, vitamin E originates from the diet. We have previously analyzed these substances in healthy females from three European countries with different nutritional habits. Significant differences in the IGF and antioxidant contents between the populations were observed [8]. CoQ and vitamin E are the main lipid-soluble antioxidants in the body involved in the protective mechanisms of neutralizing free radicals and reactive oxygen species that are present in the cells in abundance, not only as a result of toxic reagents from our environment, but also as a product of catabolic reactions under normal conditions [9]. Vitamin E is also important in a number of other metabolic functions such as stimulating the immune response, modulating protein kinase C and countering the conversion of nitrates to nitrosamines [10,11]. CoQ is a member of the mitochondrial respiratory chain, modulates the function of uncoupling proteins, regulates the mitochondrial permeability transition pool and activates the immune response of the monocytes [9].

The aim of this study was to explore and establish the association of the IGF-system and lipid-soluble antioxidants to the lifestyle of different ethnic groups and populations in the Southern hemisphere in order to find connections to the increasing number of pathological conditions such as the metabolic syndrome and cardiovascular diseases.

2. Materials and methods

2.1. Study populations

The population in this study was composed of 143 healthy individuals 30-60 years of age from two different regions in Kenya, an urban population from Nairobi and a semi-nomadic rural population from the district of Samburu in north central Kenya. The cohorts were composed of sixty nine individuals from Samburu (42 females and 27 males) and sixty seven from Nairobi (30 females and 37 males). The participants were healthy (self-reported) and not taking any medications. The protocol was approved by the ethical committee of the country. Age, weight and height were recorded for every participant and blood samples, 10 ml from each were collected in appropriate tubes after an overnight fasting. The samples were subsequently centrifuged at 2000 rpm for 5 min. The isolated plasma was immediately frozen at −20 °C and later shipped on dry ice for analysis.

2.2. Inclusion and exclusion criteria

Subjects were eligible if they were between the ages of 30 to 60 years. Presentation of an identity card or passport was used to determine the age of subjects. Since among the Samburu, many were illiterate and did not know their age, the local authorities were used to verify their age. Age, weight and height were recorded for every participant and blood samples, 10 ml from each were collected in appropriate tubes after an overnight fasting. The samples were subsequently centrifuged at 2000 rpm for 5 min. The isolated plasma was immediately frozen at −20 °C and later shipped on dry ice for analysis.

2.3. IGF-I and IGFBP-1 analysis

IGF-I was analyzed by an in-house RIA after separating IGFs from IGFBPs by acid ethanol extraction and Crayon-precipitation. To minimize interference of remaining IGFBPs, des (1-3) IGF-I tracer was used as radio-ligand [12]. The intra-and inter-assay coefficients of variation were 4% and 11%, respectively. Since serum levels of IGF-I are age dependent, and decrease with age, the IGF-I values were expressed as SD scores calculated from the age adjusted regression of the values of Swedish subjects with a total of 122 individuals between 20 and 60 years old, the gender distribution was 58 men and 64 women [13].
showed an SDS distribution of +1 to −2 which is significantly higher (P<0.0001) than the Samburu cohorts and considered closer to the normal distribution values (0 SDS) as compared to the samples from Samburu. In the Samburu population, the IGFBP-1 values exhibited a broad range of distribution mainly from 10−110 μg/ml but some individuals had values exceeding 120 μg/l (Fig. 2C) for both male and female groups. Most of the Nairobi cohorts have low IGFBP-1 concentrations ranging from 10 to 50 μg/l (Fig. 2D). IGF-I mean values were lower (P<0.0001) in the Samburu populations of both genders than the Nairobi cohorts. However, IGFBP-1 mean values were higher (P<0.0001) than that of the Nairobi cohorts (Table 2).

3.2. CoQ and vitamin E

The CoQ values were extremely high in the Samburu population ranging from 2 to 9 nmol/ml (Fig. 3A), while those of the urban population from Nairobi (1−2 nmol/ml) (Fig. 3B) are comparable to that published previously in a European population, with around 1−2 nmol/ml [8]. It should be noted that the two populations had relatively similar age distribution, as CoQ values are known to decrease during aging.

The rural population of Samburu, both female and male shows very low vitamin E levels ranging from 1 to 10 nmol/ml (Fig. 3C), while the Nairobi cohorts show higher levels (10−20 nmol/ml, P<0.0001) (Fig. 3D) but significantly lower (P<0.0001) compared to the values observed in previous measurements of European populations, ranging between 20 and 40 nmol/ml. The Nairobi cohorts had lower mean values of CoQ and higher vitamin E mean values than the Samburu population, (Table 2).

3.3. LDL and HDL

The HDL values of both populations were in the range of 1−2 mmol/l (Fig. 4A). There was a significant difference in HDL amount between the Samburu and Nairobi populations with the Nairobi cohorts having lower amounts (P<0.0005) (Table 1). LDL concentrations were between 1.5 and 3.5 mmol/l in the Samburu population and between 1.5−4.5 mmol/l in the Nairobi groups (Fig. 4B). A significant difference is shown between the two populations, with the Samburu having lower levels compared to that of the Nairobi cohorts (P<0.0068) (Table 1). The percentage distribution of LDL values higher than 3 mmol/l was 30% and 39% (P<0.0001) for the females and 7% (P<0.05) and 32% (P<0.0001) for the males, from the Samburu and Nairobi groups respectively (not shown). We also calculated the LDL/HDL ratio (Fig. 4C and Table 1) as this is a predictor of coronary plaque formation and cardiovascular diseases. In the Samburu cohorts, the values were spread between ratios 1 and 3 for both the male and female groups. The ratios for the Nairobi groups varied from 1 to 4.5, while the Samburu values for LDL/HDL ratio were significantly lower, (P<0.0001). Only 3% (P<0.05) of the Samburu population had LDL/HDL ratio above 3, while in the Nairobi population, 23% (P<0.0001) had LDL/HDL ratio exceeding 3 (not shown).

3.4. Apo A and Apo B

The ApoA levels were in the range of 1.5−3 g/l for all population groups without gender preferences (Fig. 5A). However, the mean values were significantly higher in the Samburu population (P<0.0001). Likewise the ApoB values (Fig. 5B) were between 1 and 1.5 g/l in all groups.
with significant differences between Samburu and Nairobi with the latter having higher values ($p<0.0022$). The ApoB/ApoA ratio has been known to be associated with metabolic syndrome and insulin resistance and was therefore calculated (Fig. 5C and Table 1). The majority of the Samburu and Nairobi populations, both males and females had a distribution ratio of 0.5–0.75 with some ($p<0.0001$) of the Nairobi females reaching up to ratio 1. Calculated in percent, 27% ($p<0.0001$) of the males and 15% ($p<0.0001$) of the females in Samburu had ratios exceeding 0.5. Ratios exceeding 0.5 are considered as indicators of insulin resistance. In the Nairobi group, 31% ($p<0.0001$) of the females and 60% ($p<0.0001$) of the males had ApoB/ApoA ratio exceeding 0.5 (not shown). The ApoB/ApoA ratio correlation to IGFBP-1 concentrations is shown in (Fig. 5D), $r=−0.34$ and $p<0.0001$.

3.5. Age, height, weight and BMI

Both population groups had a similar age pattern with the rural female group from Samburu (43.9±9.51, years) being slightly ($p<0.041$)
Table 1
Clinical characteristics and physical features of the two populations, both females and males. Results are expressed as mean values ± SD; ns = not significant; P(S) and P(N) = P-values when comparing females against males for both (S) Samburu and (N) Nairobi cohorts respectively; All(S) and All(N) = mean value of all participants in the (S) Samburu and (N) Nairobi groups respectively; P(All) = P-values comparing the Samburu with the Nairobi groups.

<table>
<thead>
<tr>
<th></th>
<th>Samburu Female</th>
<th>Samburu Male</th>
<th>P(S)</th>
<th>All(S)</th>
<th>Nairobi Female</th>
<th>Nairobi Male</th>
<th>P(N)</th>
<th>All(N)</th>
<th>P(All)</th>
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<tr>
<td>N</td>
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<td>27</td>
<td>69</td>
<td>30</td>
<td>37</td>
<td>67</td>
<td></td>
<td></td>
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<tr>
<td>Age (years)</td>
<td>43.9±9.5</td>
<td>42.0±9.6</td>
<td>Ns</td>
<td>43.2±9.5</td>
<td>41.7±7.0</td>
<td>38.5±6.7</td>
<td>Ns</td>
<td>39.9±7.0</td>
<td>Ns</td>
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<tr>
<td>Height (m)</td>
<td>1.63±0.05</td>
<td>1.77±0.08</td>
<td>&lt;0.0001</td>
<td>1.68±0.10</td>
<td>1.60±0.06</td>
<td>1.74±0.09</td>
<td>&lt;0.0001</td>
<td>1.68±0.10</td>
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<td>Weight (Kg)</td>
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<td>Ns</td>
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<td>73.9±12.5</td>
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<td>BMI</td>
<td>19.9±4.6</td>
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<td>&lt;0.03</td>
<td>18.9±4.60</td>
<td>26.2±4.6</td>
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<td>HDL (mmol/l)</td>
<td>1.30±0.38</td>
<td>1.37±0.49</td>
<td>Ns</td>
<td>1.34±0.40</td>
<td>1.25±0.34</td>
<td>1.10±0.31</td>
<td>&lt;0.005</td>
<td>1.12±0.34</td>
<td>&lt;0.0002</td>
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<tr>
<td>LDL (mmol/l)</td>
<td>2.59±0.82</td>
<td>2.21±0.58</td>
<td>&lt;0.04</td>
<td>2.44±0.75</td>
<td>2.95±0.75</td>
<td>2.79±1.0</td>
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<td>HDL/HDL</td>
<td>1.98±0.61</td>
<td>1.77±0.67</td>
<td>Ns</td>
<td>1.89±0.64</td>
<td>2.35±0.68</td>
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<td>ns</td>
<td>2.56±0.88</td>
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<tr>
<td>ApoA/ApoB</td>
<td>1.29±0.71</td>
<td>1.22±0.61</td>
<td>Ns</td>
<td>1.26±0.67</td>
<td>1.56±1.21</td>
<td>2.17±1.15</td>
<td>&lt;0.04</td>
<td>1.90±1.20</td>
<td>&lt;0.0002</td>
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<tr>
<td>ApoB/ApoA</td>
<td>0.49±0.15</td>
<td>0.39±0.14</td>
<td>&lt;0.01</td>
<td>0.45±0.16</td>
<td>0.51±0.19</td>
<td>0.62±0.19</td>
<td>&lt;0.03</td>
<td>0.57±0.20</td>
<td>&lt;0.0002</td>
</tr>
<tr>
<td>Cholesterol (mmol/l)</td>
<td>4.38±1.13</td>
<td>4.13±0.82</td>
<td>Ns</td>
<td>4.28±1.02</td>
<td>4.79±0.98</td>
<td>4.65±1.20</td>
<td>ns</td>
<td>4.71±1.10</td>
<td>&lt;0.0219</td>
</tr>
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</table>

Table 2, hormone and antioxidant levels of both Kenyan cohorts are shown, and for comparison the Swedish values as representative for the European population, are also included.

3.6. Total cholesterol and triglycerides

Total cholesterol levels in the majority of the individuals were between 4 and 5 mmol/l (Table 1). This value is considered to be the upper limit in a European population. A significant amount of the females, 27% of the Samburu and 37% of the Nairobi had cholesterol concentrations exceeding 5 mmol/l (P<0.0001), while for the male population it was lower, 7% (not significant) and 22% (P<0.0001) respectively. The triglyceride levels of the Samburu female and male cohorts were significantly lower (P<0.0002) than their Nairobi counterparts. Overall, the Samburu groups had values ranging between 1 and 2 mmol/l while those of the Nairobi had values between 1 and 3 mmol/l (Table 1). In the Samburu population the percentage of older than those of Nairobi males (38.5±6.74, years) (Fig. 6A, B and Table 1). The height of the Samburu females (1.63±0.05, m) was similar to that of the Nairobi females (1.61±0.05, m) while that of the Samburu males (1.77±0.08 m) was similar to their counterparts in the Nairobi male group (1.74±0.09 m) (Fig. 6C, D and Table 1). There was a significant difference of weight between the Nairobi (73.3±11.5, kg) and Samburu (53.8±13.5 kg) (P<0.0001) populations both in males and females reflecting the standard of living of the groups (Fig. 7A and Table 1). Based on the height and weight parameters, the BMI (kg/m²) for each group was calculated and there was a significant difference between the Nairobi (26.1±3.9 kg/m²) and Samburu (18.7±4.4 kg/m²) groups both in males and females (P<0.0001) (Fig. 7B and Table 1). A log-transformed scatter plot correlation between body weight and IGFBP-1 (Fig. 7C) (r = -0.73, p = 0.001) and BMI and IGFBP-1 (Fig. 7D) (r = -0.75, p = 0.0001) was made showing inverse correlation. In Table 2, hormone and antioxidant levels of both Kenyan cohorts are shown for comparison the Swedish values as representative for the European population, are also included.

Fig. 5. ApoA (A), ApoB (B) concentrations (g/l), ApoB/ApoA ratio (C) and ApoB/ApoA ratio correlation to log IGFBP-1 (D) measured in the two Kenyan populations. Values are grouped in intervals of 0.5 for ApoA and ApoB and 0.25 for ApoB/ApoA ratio. S = Samburu and N = Nairobi.
males and females with triglyceride levels exceeding 1.8 mmol/l was 11% and 12% respectively (P < 0.0001). The percentage was considerably higher for both Nairobi groups reaching as high as 21% for females and 51% for the males (P < 0.0001).

4. Discussion

Both genetic and environmental factors are important determinants of the levels of circulating IGF-I and IGFBP-1 as well as of the antioxidant
Table 2
Hormone and antioxidant levels in blood plasma values of the Samburu and Nairobi population are shown, and for comparison the Swedish values as representative for the European population, are also included. Results are expressed as mean values ± SD. n = number of participants.

<table>
<thead>
<tr>
<th></th>
<th>Samburu</th>
<th>Nairobi</th>
<th>P</th>
<th>Sweden</th>
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<tbody>
<tr>
<td>N</td>
<td>69</td>
<td>67</td>
<td></td>
<td>122</td>
</tr>
<tr>
<td>IGF-I (μg/ml)</td>
<td>−1.82±1.46</td>
<td>−0.62±0.87</td>
<td>&lt;0.0001</td>
<td>0.07±1.02</td>
</tr>
<tr>
<td>IGFBP-1 (μg/ml)</td>
<td>68.8±48.3</td>
<td>20.7±15.5</td>
<td>&lt;0.0001</td>
<td>27±22.0</td>
</tr>
<tr>
<td>CoQ (nmol/ml)</td>
<td>3.79±1.61</td>
<td>1.14±0.81</td>
<td>&lt;0.0001</td>
<td>0.98±0.30</td>
</tr>
<tr>
<td>Vitamin E (nmol/ml)</td>
<td>5.76±3.63</td>
<td>11.79±7.60</td>
<td>&lt;0.0001</td>
<td>23±12.1</td>
</tr>
</tbody>
</table>

CoQ, while plasma levels of the lipid soluble antioxidant vitamin E are dependent on the nutritional status of the individual. We have previously analyzed these lipids in three European countries with different economic and nutritional habits where a significant difference in the IGF and antioxidant distribution between the populations was observed reflecting on how lifestyle and environmental factors affect these components. In this study we have investigated healthy female and male cohorts from two different regions of Kenya: an urban population from Nairobi and a rural population from the district of Samburu in northern central Kenya. In the urban population of Nairobi, most of both genders have low amounts of IGFBP-1 indicating higher risk of developing insulin resistance and type 2 diabetes mellitus [4,11]. In addition these cohorts also have high cholesterol, triglycerides and LDL serum levels which are indicators of the risk of cardiovascular diseases and insulin resistance. In a recent study conducted on Asian Indian population, circulating IGFBP-1 amount was significantly lower in subjects who had insulin resistance compared to those without insulin resistance [21]. Subjects with diabetes mellitus had significantly lower IGFBP-1 levels when compared to those with normal glucose tolerance but with insulin resistance. The same study also shows that circulating IGFBP-1 levels decreased with increasing number of metabolic abnormalities which also seems to be the case in our study. However, a positive correlation between circulating IGFBP-1 levels and atherogenicity was observed [32].

Conflict of interest
The authors have nothing to declare.

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References


