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Full Length Research Paper

Hyperhomocysteinemia in a population of type 2 diabetics in Senegal

Niokhor Ndane Diouf[1]*, Maimouna Touré[2], Ousseynou Boye[3], Mame Ngoné Coly[1], Moustapha Djité[4], Najah Fatou Coly[5], IY Soumah[6], F Diédhiou[6], A Samba[6], Ibrahima Faye[6], Souleymane Thiam[6], Arame Ndiaye[6], Fatou Cissé[6], Fatou Diallo[6], Maguette Sylla-Niang [3,7] and Alassane Diatta[1]

[1]Department of Biology and Functional Explorations, Assane Seck University of Ziguinchor, Senegal.
[2] Laboratory of Human Physiology and Functional Explorations, Faculty of Medicine, Pharmacy and OdontoStomatology, Cheikh Anta Diop University of Dakar.
[3]Medical Biology Laboratory of the General Hospital Idrissa Pouye, Dakar, Senegal.
[4]Laboratory of Pharmaceutical Biochemistry, Faculty of Medicine and Pharmacy, Cheikh Anta Diop University, Dakar, Senegal.
[5]Biochemistry laboratory, Iba Der Thiam University of Thies, Senegal.
[6]Medical Biochemistry Laboratory, Faculty of Medicine, Cheikh Anta Diop University, Dakar, Senegal.
[7]Immunology Laboratory, Faculty of Medicine, Cheikh Anta Diop University, Dakar, Senegal.

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The objective of this study is to estimate the prevalence of hyperhomocysteinemia in a population of type 2 diabetics and to study the relationship between serum homocysteine levels and sociodemographic, clinical and biological characteristics in this population. This is a cross-sectional study involving 100 type 2 diabetic patients. Each patient underwent a routine biological assessment and a total homocysteinemia measurement. The overall prevalence of hyperhomocysteinemia is 27% (95% confidence interval : 18.6 to 36.8). The mean serum homocysteine value is 10.7±3.7 µmol/l and it is higher in men (11.5 ± 3.7 µmol/l) than in women (10.4 ± 3.7 µmol/l) with a non-significant difference (p=0.901). We found a positive significant correlation between homocysteinemia and creatinine (p = 0.03) and a negative significant correlation between homocysteinemia and serum HDL cholesterolemia (p=0.01). Mean serum homocysteine levels is significantly higher in hypertensive diabetics subjects than in non-hypertensive patients (p=0.006). The prevalence of hyperhomocysteinemia is relatively high in type 2 diabetics. This marker should be determined as part of the biological monitoring of these patients.

Key words: Hyperhomocysteinemia, risk factor, type 2 diabetes, Senegal.

INTRODUCTION

Homocysteine is a sulfur-containing amino acid produced from the breakdown of methionine, an essential amino acid (Sène and Cacoub, 2013). Hyperhomocysteinemia, characterized by elevated levels of homocysteine in the blood, is recognized as a predisposing risk factor for atherothrombotic pathologies, with established

Corresponding author. E-mail: nn.diouf@univ-zig.sn. Tel : +221 77 021 16 88.

associations to cardiovascular diseases (Muzurović et al., 2021). This condition can arise from genetic disorders affecting enzymes involved in homocysteine metabolism, such as methionine synthetase, cystathionine-β-synthase, and methylenetetrahydrofolate reductase, or from nutritional deficiencies in folate, vitamin B12, or vitamin B6 (Wijekoon et al., 2007; Trabetti, 2008). Cardiovascular diseases pose a significant threat to individuals with type 2 diabetes, contributing significantly to mortality and morbidity (Einarson et al., 2018). Hyperhomocysteinemia has been identified as a factor associated with an elevated risk of cardiovascular events (Hoogeveen et al., 2000), prompting interest in investigating its prevalence and potential correction in type 2 diabetic patients. The objective of this study is to assess the prevalence of hyperhomocysteinemia in a population with type 2 diabetes and examine the relationship between serum homocysteine levels and various sociodemographic, clinical, and biological characteristics within this population.

PATIENTS AND METHODS

Population and study setting

This prospective cross-sectional study was conducted over a six-month period and included 100 patients diagnosed with type 2 diabete subjects who presented to the Medical Biology Laboratory of the Idrissa Pouye General Hospital in Dakar, Senegal, for routine biological monitoring. All type 2 diabetic patients who visited the laboratory during the study period and provided voluntary and informed consent were eligible for inclusion in the study.

Type 1 diabetic subjects, pregnant women with diabetes, individuals with kidney failure, and patients with hypothyroidism or those taking medications known to affect homocysteine metabolism were excluded from the study.

Sociodemographic and clinical data

Data on age, sex, weight, height, smoking status, alcohol consumption, waist circumference, hip circumference, presence or absence of high blood pressure, engagement in physical activity, and duration of diabetes progression were collected for each participant.

Biochemical investigations

Venous blood samples were collected from all patients after a 12-h fasting period. The samples were drawn into EDTA tubes for the measurement of glycated hemoglobin (HbA1c) and into fluoride tubes without anticoagulant for the measurement of blood sugar, serum lipids, serum creatinine, and homocysteine levels. HbA1c was measured on the same day using the immunoturbidimetric method with a kit from Abbott Diagnostics (Sligo, Ireland). Serum samples intended for the determination of other biochemical parameters were centrifuged, and the resulting serum was collected and promptly frozen at -20°C until the time of assay. Fasting blood glucose (FBG) and lipids were measured using the enzymatic method with a kit from Abbott Diagnostics (Sligo, Ireland). Total serum homocysteine levels were determined by enzyme immunoassay using enzyme fluorescence polarization with a kit from Abbott Diagnostics (Sligo, Ireland).

Data analyzes

The data were entered into Excel 2013, and statistical analysis was conducted using R software version 4.3.1. Mean and standard deviation were calculated, and Student's T-test was employed to compare the observed results. A p-value less than 0.05 indicated a significant difference between two means. Multivariate analysis utilized unsupervised projection methods, including principal component analysis and focused principal component analysis. The Pearson correlation test was applied when a correlation between variables was identified during the analysis.

RESULTS

The study population is made up of 100 diabetic subjects including 31 men and 69 women, that is, a sex ratio equal to 0.45. Their average age is 55±8.9 years (range: 29 to 76 years). The overall prevalence of hyperhomocysteinemia is 27% (95% confidence interval : 18.6-36.8), it is 35.5% in men and 23.2% in women. The basic characteristics of the study population according to sex summarized in Figure 1 show that body mass index (BMI), waist circumference (WC), hip circumference (TC) and HDL cholesterol levels are significantly higher in women than in men; serum creatinine being higher in men than women with a statistically significant difference. There is no significant difference in the two sexes for the rest of the parameters. Table 1 shows the basic characteristics of the study population according to gender.

Serum homocysteine levels in smokers (7.67 µmol/L±0.31) are lower than the mean values obtained in non-smokers (10.81 µmol/L±3.71), the difference being not significant (p=0.14). The mean values of homocysteinemia were significantly higher (p=0.006) in hypertensives (11.93 µmol/L±1.27) than in non-hypertensives (10.81 µmol ±3.71).

Homocysteinemia is higher (p=0.39) in diabetic subjects practicing physical activity (11.06 µmol/L±5.56) than sedentary diabetic subjects (10.42 µmol/L±2.99). None of the diabetic patients consume alcohol.

Figure 1 indicates that the median serum homocysteine values of male subjects are higher than those of female subjects.

Serum homocysteine levels in the study population increased with age up to 60 years (Table 2). The average homocysteinemia of patients over 60 years old is slightly lower than that of subjects aged 51 to 60 years and is also higher in type 2 diabetic subjects found in other age groups.

The principal component analysis shown in Figure 2 only showed a correlation between fasting blood sugar and glycated hemoglobin. This correlation is positive with a Pearson correlation coefficient which is equal to 0.79; the 95% confidence interval varying between 0.70 and 0.85 with a p-value less than 0.001.

The principal component analysis focused on serum homocysteine indicated in Figure 3 shows that homocysteinemia is correlated positively with creatininemia and negatively with HDL cholesterolemia.

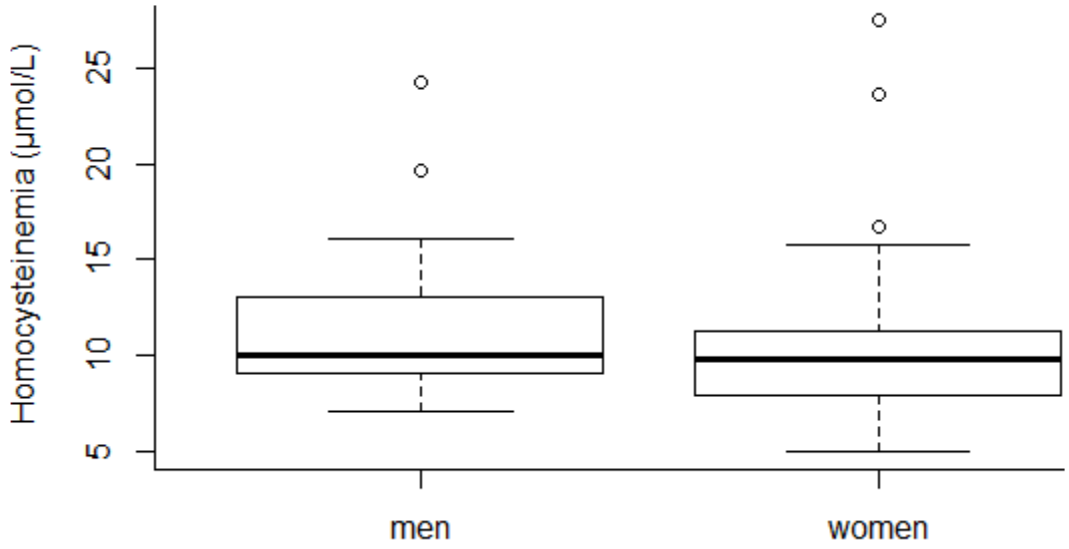

Figure 1. Variation in serum homocysteine concentrations according to sex.

Table 1. Basic characteristics of the study population according to gender.

Parameters	Total (n=100)	Men (n=31)	Women (n=69)	p-value
Age (years)	55±9.02	56.8±8.4	54.2±9.1	0.165
Duration of progression of diabetes (years)	6.7±6.7	6.4±5.8	6.8±7.1	0.763
Body mass index (kg/m^2)	26.6±4.8	24.2±3.3	27.7±4.9	<0.01
Waist circumference (cm)	97.4±10.7	93.5±8.7	99.0±11.3	0.008
Hip circumference (cm)	105.8±10.7	101.7±6.9	107.5±11.6	0.002
Waist/hip circumference ratio	0.92±0.06	0.92±0.06	0.92±0.06	0.801
Fasting blood sugar (g/l)	1.76±0.9	1.72±0.6	1.77±0.9	0.723
Glycated hemoglobin (%)	8.6±3.0	8.9±3.2	8.3±2.9	0.456
Homocysteinemia (µmol/l)	10.7±3.7	11.5±3.7	10.4±3.7	0.901
Total cholesterolemia (g/l)	2.11±0.47	2.14±0.56	2.09±0.43	0.684
HDL cholesterolemia (g/l)	0.49±0.14	0.43±0.12	0.52±0.14	0.003
LDL cholesterolemia (g/l)	1.08±0.46	1.09±0.43	1.08±0.48	0.901
Triglyceridemia (g/l)	0.91±0.45	0.98±0.55	0.88±0.40	0.345
Creatininemia (mg/l)	9.8±1.9	11±1.9	9±1.5	<0.01

However, there is no correlation between homocysteinemia and other quantitative variables studied.

DISCUSSION

Hyperhomocysteinemia is recognized as an independent risk factor for cardiovascular disease (Hoogeveen et al., 2000), and its association with myocardial infarction, stroke, and venous thromboembolism is well-established (Jaeger et al., 2010). Elevated homocysteine levels have been documented in patients with type 2 diabetes (Moraba et al., 2013). In our study, the prevalence of hyperhomocysteinemia among type 2 diabetic patients was found to be 27%. This prevalence varies across studies and countries. A Dutch study reported a similar prevalence of 25.8% (Hoogeveen et al., 2000), while slightly higher rates were observed in other studies: 31.1% in a Belgian study (Buysschaert et al., 2000), 32.4% in an Israeli study (Goldstein et al., 2004), and 36.3% in a Chinese study (Zhang et al., 2015). Another study conducted in Senegal by Cisse et al. (2015) reported a higher prevalence of 42.5% among type 2 diabetic patients. This disparity in prevalence could be attributed to differences in study population size and gender distribution. The high prevalence of elevated homocysteine levels in type 2 diabetic patients' rules out heterozygosity of homocystinuria, a rare disease, as the cause of

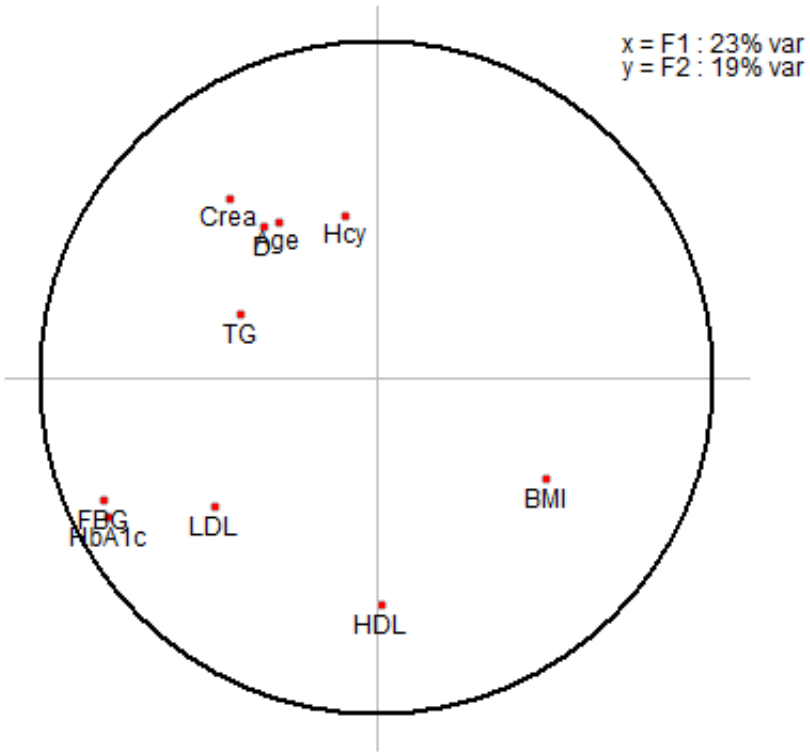

Figure 2. Correlation between the different quantitative variables. Crea=Creatininemia, D=Duration of diabetes, TG=Triglyceridemia, Hcy=Hyperhomocysteinemia

Table 2. Variation in serum homocysteine levels according to age groups.

Age groups (years) Range	Homocysteinemia (µmol/l) Means ± SD
< 30	7.26±0
[30-40]	10.14±2.57
[40-50]	10.52±4.74
[50-60]	10.89±3.60
> 60	10.82±3.64

these elevations (Reis, 2022). Variations in prevalence observed across studies may be influenced by factors such as age, sex, plasma concentrations of vitamins B6 and B12, smoking, coffee consumption, folate status, renal function, sedentary lifestyle, menopause, treatment with metformin, alcohol consumption, and genetic factors, including mutations in the gene responsible for cystathionine β-synthase synthesis (Guldener and Stehouwer, 2002; Trabetti, 2008; Mao et al., 2014; Rigaud et al., 1999). In our study, serum homocysteine levels showed a positive correlation with age up to 60 years, after which no significant correlation was observed. This finding aligns with previous research indicating an age-related increase in serum homocysteine levels (Zendjabil et al., 2017). The absence of correlation with age in patients over 60 years old could be attributed to better health education and healthier nutrition practices in this age group; this being in relation to the diabetes progression duration and it is the same observation of a Greek study which proved that the nutritional state greatly influences the values of serum homocysteine (Diakoumopoulou et al., 2005).

Additionally, our study revealed correlations between homocysteine levels and serum creatinine or HDL cholesterol. We also found associations between fasting blood glucose and HbA1c. However, no correlations were observed between homocysteine levels and other

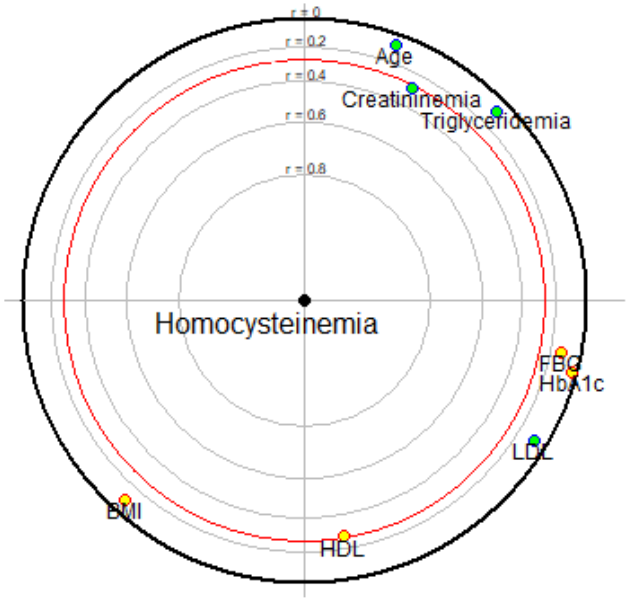

Figure 3. Correlation between homocysteinemia and other quantitative variables.

biological parameters such as fasting blood sugar, LDL cholesterol, triglycerides, duration of diabetes progression, or body mass index (BMI). In contrast, a Moroccan study reported associations between hyperhomocysteinemia and HbA1c and/or LDL cholesterol (Belkhair et al., 2019). Discrepancies in plasma homocysteine values may be attributed to genetic factors, particularly polymorphisms in the MTHFR gene, individual variability (e.g., dietary habits, lifestyle), and the use of metformin in diabetic subjects treatment (Schalinske, 2003; Xu et al., 2022; Diakoumopoulou et al., 2005; Sato et al., 2013; Kim et al., 2019).

Most authors agree on the influence of smoking, sedentary lifestyle, and high blood pressure on increasing serum homocysteine levels (Masaki et al., 2007; Jaegera et al., 2010; Belkhair et al., 2019). In our study, homocysteine levels were significantly higher in hypertensive individuals compared to non-hypertensive ones. Interestingly, smokers exhibited relatively lower homocysteine values than non-smokers, although this could be attributed to their low representation in our cohort, comprising only three subjects. Patients engaging in physical activity showed higher homocysteine levels compared to sedentary patients, a paradox possibly explained by the predominance of male participants in sports activities. Indeed, our results revealed higher average homocysteine levels in men than in women, a finding supported by previous studies (Rigaud, 1999; Reis, 2022). Rigaud (1999) suggested that lower homocysteine values in females are primarily linked to the protective effects of female sex hormones. Additionally, homocysteine levels were positively correlated with creatinine and muscle mass, which are typically higher in males. Furthermore, women tend to have higher levels of HDL cholesterol, which plays a protective role against atherosclerosis (Sabanayagam and Shankar, 2011). These findings confirm our observations, as serum homocysteine concentrations and serum creatinine were higher in men, while their HDL cholesterol levels were lower.

Conclusion

The prevalence of hyperhomocysteinemia is relatively high in type 2 diabetic subjects. Mean serum homocysteine levels are higher in male subjects and are correlated with creatinemia and HDL cholesterolemia. These results should lead us to adopt the homocysteine assay in the monitoring of type 2 diabetic patients, especially since this biochemical marker is adaptable to immunoanalysis machines and quickly achievable.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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