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Essential Hypertension and Risk Factors: Evaluation of Biochemical Parameters and Polymorphism of the *MMP*1 and *MMP*3 Genes

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Abstract

Background: Matrix metalloproteinases (*MMPs*) gene polymorphisms contribute to the risk of developing cardiovascular diseases. This study aimed to determine the possible association of two polymorphisms of two MMP genes (*MMP*1 and *MMP*3) with essential hypertension (EH) in a Burkinabè population. **Method**: The genomic DNA of 72 hypertensive patients and 73 normotensive patients was extracted from their blood samples by the Salting Out technique. The −1607 1G/2G *MMP*1, −1171 5A/6A *MMP*3 polymorphisms were detected by the allele-specific polymerase chain reaction technique. **Results**: The chi-squared test shows that an association exists between frequencies of alleles 1G (OR = 1.93; p = 0.012) and 5A (OR = 1.9; p = 0.013); genotypes 1G1G (p = 0.007) and 5A5A (p = 0.0001) and EH in the study population. So, the frequencies of the combined 1G1G/5A5A and 2G2G/6A6A genotypes were higher in cases (p = 0.0068). Multinomial logistic regression found that HDL cholesterol (OR = 38.27; p = 0.011), blood glucose (OR = 2. 46; p = 0.009), family history of hypertension (OR = 6.88; p = 0.03), lack of exercise (OR = 23.85; p = 0.008), were independent risk factors for developing essential hypertension in our general study population. **Conclusion**: Our study suggests that genetic polymorphism in *MMP*1 and *MMP*3 might be helpful in determining susceptibility to EH in Burkinabè patients. In addition, suscepti-

bility to EH might be related to *MMP*1 and *MMP*3 gene expression, which affect its plasma levels.

Keywords

Essential Hypertension, Risk Factors, *MMPs*, Polymorphism, Burkina Faso

1. Introduction

High blood pressure (HBP) is a chronic medical condition that causes a real public health problem. It affects, on average, 1 in 3 adults and is responsible for 13% of deaths worldwide [1]. In the world, the overall prevalence of HBP in adults from 39 to 79 years was around 33% [2]. It's higher among adults in low- and middle-income countries (LMICs) (31.5%) than in high-income countries (28.5%) [3] [4] and varies from one country to another and across residential areas [5]. The overall prevalence of hypertension in Burkina Faso was 18% in adults aged 25 to 65 years [6]. In several countries, HBP risk factors were well documented and comprise non-modifiable factors such as age, sex, and family history of HBP; behavioral risk factors such as salt intake, alcohol consumption, smoking, and physical inactivity; socio-demographic factors such as the place of residence, educational level, economic status; and metabolic factors such as diabetes, obesity, dyslipidemia. The family history as a risk factor suggests a genetic factor in HBP. However, in the almost HBP surveys in Sub-Saharan Africa as Burkina Faso, the genetic factors are least investigated. But, in 90% to 95% of hypertension, the cause is unknown; it's essential hypertension (EH) as opposed to secondary hypertension. Among these unknown causes genetic factors would be one of the main factors. Now, most of one hundred (100) human genes are suspected to be involved in hypertension variability. Overall, these genes are involved in the production of vasoactive metabolites which are very polymorphic. Among these metabolites, there are metalloproteinases (*MMPs*) which are a protein family involved in several biological processes such as extracellular matrix degradation [7] [8]. Because of their major significance in vascular remodeling, some studies have demonstrated that MMP gene polymorphism are associated with artery stiffness and high blood pressure [9] [10]. Increased expression and activity of MMP have been identified in the change of relative amounts of structural proteins and vascular remodeling, contributing to the developing arterial stiffness by vascular smooth muscle modification causing hyperplasia. In the *MMP*1 and *MMP*3 genes, some functional SNPs were found to correlate at the different levels of these genes' expression. Indeed, in the *MMP*1 gene, the SNP due to the additional insertion of a guanine (G) at position −1607/−1608 in the *MMP*1 promoter creates a binding site (5'-GGAA/T-3') for the transcription factors of the ETS family [11]. This SNP has been associated with up-regulation of *MMP*1 transcription and possibly increases the activity of this enzyme. The insertion of adenosine (A) into the promoter of the *MMP*3 gene, at position

−1612/−1617 upstream of the start of transcription, creates a polymonomeric series of six adenosines (allele 6A), while another variant has five adenosines (allele 5A). These activities of *MMPs* contribute to hypertension rising by a blood vessels constriction [12]. That explains the great interest in leading studies about these predisposing genes and their polymorphism to hypertension and cardiovascular diseases.

Studies about genetic factors associated with HBP risk and blood pressure regulation in populations of African ancestry were conducted [13]. However, to date, no study has explored the relationship between EH and metalloproteinase gene polymorphism. Given the genetic diversity of African populations, the available data cannot be extrapolated from one population to another. This study aims to determine the involvement of polymorphisms in the promoters of the *MMP*1 and *MMP*3 genes as genetic markers in the development of cardiovascular diseases, in particular EH, in Burkina Faso.

2. Methodology

2.1. Study Setting

It's a case control study which took place from December to February 2023 in Ouagadougou city, Burkina Faso. The sampling was performed at the Hôpital Saint Camille de Ouagadougou (HOSCO), Centre médical Schiphra, and Centre médical du Camp Sangoulé Lamizana. Biochemical and biomolecular analyzes were carried out respectively at Centre de Recherche biomoléculaire Pietro Annigoni (CERBA) and at Laboratoire de biologie moléculaire et de Génétique (LABIOGENE).

2.2. Study Population

Aged 20 years and older, the study population consisted of subjects of all genders and all social categories who came to consult in the health facilities mentioned above. In total, 145 subjects, including 72 patients suffering from EH (cases) and 73 normotensive subjects (controls), were included in this study. This relatively small sample size is explained by the limited means of hypertensive patients, who are generally elderly and choose to be native. Also, many people without vascular disease who should be control group refuse to participate in these studies because of certain cultural preoccupations, thus reducing the efficient recruitment of controls.

We considered the case of the black subject who had a systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg or who was under antihypertensive treatment. Secondary hypertensives or those on hormonal treatments (estrogen, thyroid, corticosteroids) and pregnant or breastfeeding women were not included in this study.

The control group was subjects whose blood pressure was less than 140/90 mmHg. Pregnant and breastfeeding (less than 6 months) women and anyone on antihypertensive or hormonal treatment or suffering from a cardiovascular condition were also not included in this group.

2.3. Biological Material and Data Collection

In each subject, about 4 mL of venous blood was taken in a tube with EDTA and one tube without anticoagulant. Serum from tubes without anticoagulants was used for biochemical analysis, and whole blood from EDTA tubes was used for molecular analysis.

We conducted face-to-face interviews with a structured questionnaire, including mainly participants' sociodemographic characteristics and family history for some noncommunicable diseases such as diabetes, HBP, and asthma.

2.4. Clinical, Anthropometric, and Biochemical Data

The clinical (*blood pressure*), anthropometric (*height*, *Weight*, *body mass index*, *and Waist circumference*), and biological (*Glycemia*, *Total Cholesterol*, *HDL-c*, *LDL-c*, *and Triglycerides*) parameters of patients were measured and collected on an individual sheet.

Height, Weight, and body mass index (BMI) were calculated by dividing the weight (kilograms) by the square of the height (meters). BMI was used to determine obesity when BMI $\geq$ 30 kg/m^2, overweight when BMI was between 25 and 30 kg/m^2, normal weight when BMI was between 20 and 25 kg/m^2, and underweight for a BMI less than 20 kg/m^2.

Waist circumference (WC) was determined by measuring the circumference of the abdomen when the subject had minimal breathing using a tape measure. Abdominal obesity was determined in men when the WC is greater than 102 cm and in women when it is greater than 88 cm.

Blood pressure was measured in both arms using a mercury sphygmomanometer in subjects after 20 minutes of rest, in a sitting or lying position, with the cuff placed on the plane of the heart. Two measurements were taken on each arm, 5 minutes apart during the same consultation, and the BP figure retained was the average of the readings in the arm where the BP was highest.

Biochemical analyses were conducted using the COBAS C311 automatic analyzer (Roche-Hitachi).

2.5. Characterization of *MMP*1 and *MMP*3 Genes Polymorphism

- *Purification of DNA*

The Salting Out technique described by Miller *et al.* [14] was used for DNA purification from whole blood. A Nanodrop spectrophotometer (TermoFisher Scientific Inc., Wilmington, DE, USA) was used to assess DNA purity and concentration before genotyping. DNA extracts with a good concentration and purity were stored at −20˚C until the next step.

- *Genotyping of genes MMP*1 *and MMP*3 *promoter polymorphisms*

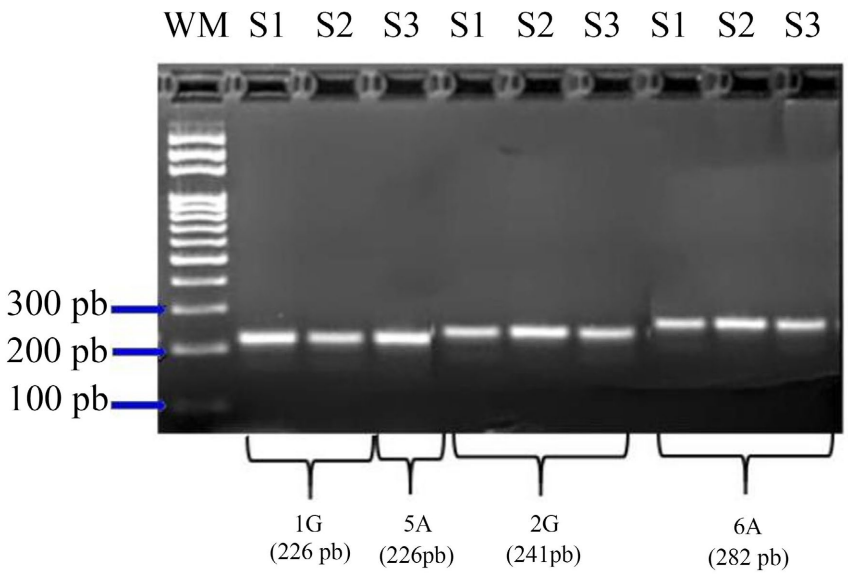
The polymorphism looked for was single nucleotide polymorphism (SNP) caused by an insertion (I) or a deletion (D) into the *MMP*1 and *MMP*3 genes' promoter. The amplification techniques used were described by Morosova *et al.* [15] which

consisted of amplification of each allele using specific primers (Table 1). The amplification was performed according to the following program: initial activation at 95˚C (5 min); 40 cycles of 94˚C (30 s), 55˚C (30 s), and 72˚C (30 s); and a final extension to 72˚C (7 min).

Table 1. The pairs of specific primers to the *MMP*1 and *MMP*3 alleles.

Alleles	Primers	Size (pb)	References
	***MMP*1^{-1607}**		
1G	**Forward**: gaa att gta gtt aaa taa tta gaa aga t **Reverse**: aaa aca tac agt gga gaa aca c	226	[15]
2G	**Forward**: aaa ttg tag tta aat aat tag aaa gga **Reverse**: tgg aag cat tta ttg aaa ac	241	
	***MMP*3^{-1171}**		
5A	**Forward**: ttg atg ggg gga aaa ac **Reverse**: act cca gag aaa att tac aaa gg	226	[15]
6A	**Forward**: ttg atg ggg gga aaa aa **Reverse**: aac ata tta tct atc agg ctt tcc t	282	

PCR products (*MMP*3 and *MMP*1) were evaluated after 45 min electrophoresis under 120 V and 450 mA in a 1.5% agarose gel under SYBR Green and visualized in an ultraviolet transilluminator (E-BOX Vilber) (Figure 1).



Legend: WM = weight marker (100 bp); S1: Samples 1; S2: Sample 2; S3: Sample 3.

Figure 1. Agarose gel picture showing *MMP*1 and *MMP*3 allele bands.

2.6. Statistical Analysis

The data were recorded in the Excel 2016 version, analyzed, and interpreted by the software STATA 14. The student test was used to compare means of quantitative

variables, and the Chi-square test was used to compare proportions between groups. The SNP analyses were performed using the SNPStat software online. By considering the hypertensive status as a dependent variable, we did a logistic regression to identify the risk factors associated with EH in this study. The results were considered statistically significant if the value of $p \leq 0.05$.

2.7. Ethical Approval and Informed Consent

This study obtained the agreement of the research internal ethics committee of CERBA/LABIOGENE. The confidentiality and anonymity of patients and the information concerning them are respected.

3. Results

3.1. Sociodemographic Features of Study Population

The overall features of the study population are summarized in Table 2. There are 145 subjects, including 72 hypertensives with 23 men and 49 women, and 73 normal-hypertensive with 32 men and 41 women. The gender distribution in the two groups (hypertensive and normotensive) was homogeneous. In the case group, the mean age (54,64 ± 2.58) was more than that of the control group (45.38 ± 2.06) ($p > 0.05$). Most biochemical parameters (SBP, DBP, Glucose, HDL-c, LDL-c, Total cholesterol, BMI) measured were significantly rising in the hypertensive group ($p < 0.05$), except for triglycerides ($p = 0.62$).

Table 2. Overall features of the study's population.

Variables		Total (% or IC, 95%)	Normotensive (control) (% or IC, 95%)	Hypertensive (Case) (% or IC, 95%)	p-value
Sex (n)	M	55 (0.44)	32 (0.38)	23 (0.32)	0,1415
	F	90 (0.56)	41 (0.62)	49 (0.68)	
Age (years)		49.98 (48.18 - 51.78)	45.38 (43.32 - 47.44)	54.64 (52.06 - 57.22)	**<0.0001***
SBP (mmHg)		127.69 (124.63 - 130.76)	115.25 (112.55 - 117.95)	140.31 (136.60 - 144.03)	**<0.0001***
DBP (mmHg)		78.24 (76.47 - 80.01)	73.52 (71.18 - 75.86)	83.03 (80.84 - 85.23)	**<0.0001***
Glucose (mM)		4.87 (4.56 - 5.18)	4.02 (3.71 - 4.33)	5.73 (1.97 - 5.27)	**<0.0001***
Triglyceride (mM)		1.13 (1.03 - 1.23)	1.10 (0.98 - 1.23)	1.15 (0.99 - 1.32)	0.6293
HDL-c (mM)		1.30 (1.19 - 1.40)	1.07 (0.99 - 1.16)	1.53 (1.35 - 1.71)	**<0.0001***
LDL-c (mM)		2.75 (2.6 - 2.89)	2.48 (2.29 - 2.67)	3.03 (2.85 - 3.20)	**<0.0001***
Total cholesterol (mM)		4.67 (4.48 - 4.85)	4.09 (3.84 - 4.35)	5.25 (5.07 - 5.43)	**<0.0001***
BMI (Kg/m^2)		26.86 (25.74 - 27.97)	24.70 (23.42 - 25.98)	29.04 (27.33 - 30.75)	**0.0001***

Values are reported as means ± standard deviation for continuous variables; Statistical analysis (Cases versus controls) by t-test or chi-square; *: significant difference between groups ($p < 0.05$); MD: Means difference, CI: Confidence interval, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HDL-c: High-density lipoprotein cholesterol, LDL-c: Low-density lipoprotein cholesterol, Mm: Millimolar, Mm/Micromolar, BMI: body mass index.

The sports practice was raising in the normotensive group than the hypertensive group (OR = 3.82, IC 95% = 1.81 − 8.06, $p < 0.0002$); there is no significant

difference in the alcohol consumption among the two groups (OR = 1.43, IC95% = 0.74 – 2.77, p = 0.28). Most subjects had previous own or family EH and diabetes type 2 in hypertensive groups (Table 3).

Table 3. Lifestyle and pathologic antecedents of the study population.

Parameters	Cases n (%)	Controls n (%)	OR (IC 95%)	P-value
Familial or personal history				
Fh-HTA	43 (0.60)	13 (0.18)	0.27 (0.11 - 0.62)	**0.0001**
Fh-Asthma	4 (0.06)	0 (0)	0.00 (ND)	0.06
Fh-DT2	8 (0.11)	2 (0.03)	0.36 (0.7 - 0.83)	**0.04**
Ph-Asthma	3 (0.04)	0 (0)	0.00 (ND)	0.07
Ph-DT2	7 (0.10)	2 (0.03)	0.42 (0.8 - 2.16)	**0.0314**
Sport practice and alcohol consumption				
Sport	32 (44.4)	55 (75.3)	3.82 (1.81 - 8.06)	**< 0.0001**
Alcohol	40 (55.5)	334 (46.6)	1.43 (0.74 - 2.77)	0.2811

Fh-HTA, Family history of HTA, *Fh-asthma*, Family history of Asthma, *Fh-DT2*, Family history of diabetes type 2, *Ph-asthma*, Personal history of asthma, *Ph-DT2*, Personal history of diabetes type 2.

3.2. Genetic Feature: Genotypic and Allelic

Table 4. Frequency distribution of haplotype *MMP*1 (−1607 2G/1G) and *MMP*3 (−1612 5A/6A) genotypes among case and control subjects.

SNPs			General pop n (%)	Case n (%)	Control n (%)	OR	P-value
***MMP*1**	Genotypes	1G1G	78 (0.54)	48 (0.67)	30 (0.41)	1 (ref groupe)	
		1G2G	51 (0.35)	17 (0.23)	34 (0.47)	0.31 (0.14 - 0.68)	**0.007**
		2G2G	16 (0.11)	7 (0.10)	9 (0.12)	0.48 (0.1 - 1.47)	
		HWE		p = 0.22	p = 0.36		
	Alleles	1G	0.71	0.78	0.64	1.93 (1.12 - 3.37)	0.012
		2G	0.29	0.22	0.36		
***MMP*3**	Genotypes	5A5A	68 (0.47)	47 (0.64)	21 (0.29)	1 (ref groupe)	
		5A6A	65 (0.45)	15 (0.21)	50 (0.68)	0.13 (0.05 - 0.32)	**<0.0001**
		6A6A	12 (0.08)	10 (0.15)	2 (0.3)	2.23 (0.44 - 11.33)	
		HWE		p = 0.24	p = 0.37		
	Alleles	5A	0.69	0.76	0.63	1.9 (1.10 - 3.27)	0.0132
		6A	0.31	0.24	0.37		

Genotypic and allelic frequencies generated by the two SNPs in each gene promoter (*MMP*1, *MMP*3*)* are summarized in Table 4. Both genes were in Hardy-Weinberg equilibrium (HWE) (p > 0.05). The two alleles looked for were found for each gene; there are 1G and 2G alleles for *MMP*1 and 5A and 6A alleles for the

*MMP*3 gene. The 1G allele was more frequent in hypertensive (0.78) than in the normotensive group (0.64). Similarly, the 5A allele was more frequent (0.76) than in the normotensive (0.63). Three genotypes were found for each gene (*MMP*1: 1G1G, 1G2G, 2G2G; *MMP*3: 5A5A, 5A6A, 6A6A), and among them, 1G1G was more frequent in the hypertensive group than the other two genotypes of the *MMP*1 gene (67% versus 41%, p = 0.007). Similarly, the 5A5A genotype was more frequent in the hypertensive group than the two other genotypes of the *MMP*3 gene (64% versus 29%, p = 0.0001).

To investigate the effect of gene-gene polymorphism interaction on the EH risk in case and control groups, haplotype and linkage disequilibrium were performed on two genes, *MMP*1 and *MMP*3. Four common haplotypes were found in both cases and the control. Haplotype 1G-5A being taken as a reference, any significant difference was found between the other free haplotypes in cases and controls (p > 0.05) (Table 5). In another part, there was no significant linkage disequilibrium (LD) D between both genes (D = 0.01; p = 0.52).

Table 5. Frequency distribution of haplotype *MMP*1 (−16072 G/1G) and *MMP*3 (−1612 5A/6A) genotypes among case and control subjects.

Haplotype	Frequency in the total population	Frequency in case	Frequency in control	OR (95% CI)	P-value
1G-5A	0.34	0.27	0.40	1.00 (ref)	
2G-5A	0.25	0.28	0.22	0.57 (0.27 - 1.20)	0.14
1G-6A	0.22	0.27	0.17	0.43 (0.18 - 1.03)	0.06
2G-6A	0.19	0.18	0.21	0.81 (0.39 - 1.68)	0.57
D		0.01			0.52

Table 6. Logistic regression for risk analysis of essential hypertension.

Factors	OR	IC95%	p-value
Age	1.04	0.96 - 1.13	0.336
Chol-HDL	38.27	2.33 - 627.98	**0.011**
Chol-Total	6.22	0.98 - 39.67	0.053
Glycemia	2.46	1.25 - 4.8	**0.009**
BMI	1.13	0.97 - 1.33	0.120
Fh-HTA	6.88	1.12 - 42.16	**0.037**
Alcohol	3.36	0.55 - 20.51	0.189
Sport	23.85	2.32 - 244.61	**0.008**

A logistic regression for the EH risks factor in the study population allowed us to show that the concentration rising of cholesterolemia HDL (OR = 38.27; IC 95% = 2.33 − 627.98; p = 0.011) and glycemia (OR = 2.46; IC 95% = 1.25 − 4.8; p = 0.009), familial EH previous history (OR = 6.88; IC 95% = 1.12 − 42.16; p < 0.001), and the sport practice lack (OR = 23.85; IC 95% = 2.32 − 244.61; p = 0.008),

was the independent risk factor associated to develop EH in our study population (Table 6).

4. Discussion

EH has become one of the frequent health issues both in developed and developing areas. EH raising is explained by the contribution of several factors, including genetics, which is estimated from 25% to 75% in different populations according to familial and twin studies [16]-[19]. Among these genetic factors, there are genes such as matrix metalloproteinase, which code for a specific enzyme group with biological activities such as the degradation of matrix extracellular (ECM) components [20] [21]. The imbalance between ECM synthesis and degradation caused by the modification of *MMPs* expression can lead to a decrease in the remodeling capacity of the vascular wall. It has been noticed that SNPs of *MMPs* genes are associated with EH and its complications in different populations such as Australian (rs3025058 *MMP*3), Polish (rs3025058 *MMP*3), American (rs652438 MMP12), Sweden (rs11568818 MMP7), Brazilian (rs243865 *MMP2*) and Serbian (rs11225395 et rs1320632 *MMP8*, rs1799750 *MMP*1) [22] [23]. This study aimed, on the one hand, to find features of *MMP*1 and *MMP*3 gene promoters in Burkina Faso and, on the other hand, to analyze a potential relationship between these genotypes and the risk of getting EH.

The study population consisted of 145 subjects with 55 men and 90 women. Similarly, the women are most raised in the hypertensive group (p = 0,1415). Overall, EH is less frequent in women than in men. This rising frequency in our study could be explained by two reasons: according to the national statistics, women represent 51.7% of the general population [24] and also women visit health facilities more than men in Burkina Faso [24]. Until then, no study has allowed explaining if this difference between men and women is related to the protective effect of endogenous estrogen on the EH risk, to genetic differences related to sex, or confounding variables such as salt and alcohol consumption, body mass index, psycho-socio-economic factors, and sedentary lifestyle.

The mean age in the study population was 45.38 ± 2.06 years in the normotensive group; in contrast, it was 54.64 ± 2.58 years in the hypertensive group ($p < 0.0001$). The average age in the hypertensive group was close to that (52 ± 9,82) reported in a study in Burkina Faso ten years ago [25]. Many studies have shown that advancing age increases the risk of hypertension, which is explained by arterial stiffness due to aging, and increasing pressure in the arteries [26]-[29].

Several biochemical parameters such as SBP (mmHg), DBP (mmHg), Glucose (mM), HDL-c (mM), LDL-c (mM), Total cholesterol (mM), and BMI (Kg/m^2) are significantly higher in hypertensives than in normotensives ($p < 0.001$). The BMI average in hypertensives was superior to that in normotensives (29.04 ± 1.70 versus 24.70 ± 1.28; $p < 0.001$). This BMI average supposes that most of the hypertensive subjects of our study were overweight, obesity being defined as BMI superior to or equal to 30 Kg/m^2 [30]. This significant difference in average BMI be-

tween the two groups means that obesity would be an EH risk factor. Similar studies have been carried out in Nigeria [31] and Burkina Faso [32] showed that obesity was the most prevalent risk factor associated with EH. In the hypertensive group, previous familial EH and diabetes type 2 were more frequent than in the normotensive group ($p < 0.001$). Many studies about subjects with parents' hypertension have shown an increasing risk of having hypertension, and that means heredity plays an essential part in the occurrence of hypertension occurring [33]-[35]. The elevation of HDL cholesterol in hypertensive patients compared to hypotensive patients can be explained by several pathophysiological mechanisms and associated risk factors. These include, for example, the use of antihypertensive medications that increase HDL levels; concomitant cardiovascular risk factors, such as diabetes, obesity, and dyslipidemia, which are associated with variations in HDL levels; and genetic variations influencing lipid metabolism, such as those affecting lipoprotein lipase (LPL), cholesterol exchange protein (CETP), or HDL receptors, may play a role in HDL concentration, independent of blood pressure status [36] [37].

MMPs are a family of enzymes encoded by a set of genes of the same name, which are involved in the degradation of the extracellular matrix (ECM). Among these genes, there are *MMP*1 and *MMP*3 genes, which are located on the same chromosome 11q21 - 22, and certain SNPs in these genes would be related to the level of expression of proteins coded by that [38]. In the hypertensive group *MMP*1, *MMP*2, *MMP*3, and *MMP*9 genes were the MMPs the most frequently expressed [21] [39].

Genotypic frequency analysis of each gene (*MMP*1, *MMP*3) has shown that the study population was in Hardy-Weinberg equilibrium ($p > 0.05$). We found three genotypes for each gene in our study population: *MMP*1 with genotypes 1G1G, 1G2G, 2G2G, and *MMP*3 with genotypes 5A5A, 5A6A, and 6A6A. Genotypes 1G1G and 5A5A were the most frequent in our study population, especially in the hypertensive group ($p = 0.007$, $p < 0.0001$ respectively). 1G1G genotype could be associated with EH, increasing the risk of developing the disease; in contrast, the 2G2G genotype, which is most frequent in control groups, could have a beneficial effect on EH. The first study about these SNPs, performed by Rutter *et al.*, described that the insertion of an additional guanine giving a 2G allele into the *MMP*1 gene promoter increases its expression, causing collagen and ECM degradation [11]. However, the 1G allele was associated with decreasing expression of the *MMP*1 gene [11], causing less degradation of collagen, leading to the accumulation of other ECM components in the arteries, which promotes fibrosis development in the arteries. These modulations raise the arterial stiffness and develop isolated systolic blood pressure [40]. The hybrid genotype 1G2G has shown a high frequency in the control group; that could mean normotensive subjects profit from the antagonist effect of these two alleles.

About the *MMP*3 gene, the 5A5A genotype was the most observed in the hypertensive subjects (0.64 vs 0.29; $p < 0.0001$). Also, the 5A6A genotype was more

frequent in the normotensive group than the hypertensive group (0.68 vs 0.21; $p < 0.0001$). As in several previous studies, 5A5A genotypes were related to EH. The adenine deletion in the *MMP*3 gene promoter at −1612/−1617 position creates a succession of five adenines instead of six, which is strongly recognized by transcription factors, causing a strong expression of *MMP*3 [20] [41].

In contrast, the 6A allele, creating a succession of six adenines, is strongly recognized by repression factors ZBP-89, which regulate down the *MMP*3 expression [20] [41]. That would explain that the heterozygous subjects 5A6A could be protected from EH due to the antagonist effect of these two alleles. Increasing MMP activities contribute to the development of arterial stiffness by vascular smooth muscle modification, causing hyperplasia [39]. That explains why the heterozygous 5A6A subjects are protected from EH due to the antagonist reactions of these two alleles.

Analysis of haplotypes and Linkage disequilibrium of two genes (*MMP*1 and *MMP*3) has not shown any significant results. Despite the lack of significant results about these parameters, probably due to the small size of the study population, this study gives the first doubt (data) in our community about the involvement of these genes and their polymorphism in the acquisition of EH.

5. Conclusion

The current study documented that EH is linked to biochemical parameters such as SBP, DBP, Glucose, HDL-c, LDL-c, Total cholesterol, BMI, and the genes *MMP*1 and *MMP*3 polymorphisms as 1G1G and 5A5A genotypes. Our results suggest that polymorphisms of the *MMP*1 and *MMP*3 genes may be linked with EH, and therefore, they can be considered as a potential marker of cardiovascular diseases. These findings need to be investigated in larger populations to better clarify this association, and further investigations are needed to explain the potential role of *MMP*1 and *MMP*3 in EH and cardiovascular diseases in the West African community.

Author Contribution Statement

This study was conceived and designed by Jacques SIMPORE, Florencia Wendkuuni DJIGMA, and Koudougou Jonas KOLOGO. Experiments performed, results analysis, and manuscript writing were done by Prosper BADO, Jean Marie KABORE, Herman Karim SOMBIE, and Lassina TRAORE. All authors have read and verified the underlying data and approved the final manuscript.

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Conflicts of Interest

The authors state no conflict of interest.

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