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Original article

Dyslipidemias in Stroke

Dyslipidémies dans les accidents vasculaires cérébraux

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Résumé

La prévalence des facteurs de risque vasculaire majeurs est en constante augmentation, influencée par de nouveaux modes de vie de la population générale, notamment les habitudes alimentaires malsaines telles que les repas riches en graisses. L'objectif était d'évaluer le profil lipidique des patients hospitalisés pour accident vasculaire cérébral (AVC) en identifiant ceux présentant des dyslipidémies.

L'étude a porté sur les résultats du bilan lipidique de 609 patients. Toutes les variables ont été incluses dans le modèle a priori sans aucune sélection, avec les variables lipidiques et anthropométriques (âge, sexe). Les moyennes et écarts-types des fractions lipidiques analysées étaient respectivement : CT (1,89 ; 0,55) ; HDL (0,49 ; 0,24) ; LDL (1,24 ; 0,50) et TG (0,90 ; 0,41). Après ajustement des facteurs de confusion par analyse bivariée, les résultats obtenus pour les dyslipidémies pures ont montré que le HDL était significativement associé en premier lieu à l'AVC [OR 1,77 ; IC 95 % 1,15-2,72 ; p = 0,002], suivi par le LDL [OR 2,00 ; IC 95 % 1,04-3,87 ; p = 0,03]. La fréquence observée des AVC était de 72 % pour la forme ischémique et de 28 % pour la forme hémorragique. Celle-ci augmentait avec l'âge, quel que soit le type. Les âges extrêmes des patients étaient de 17 et 95 ans, avec une moyenne de 62,8 ans. Les hommes représentaient 53 % des cas et les femmes 47 % des cas. Le taux de mortalité globale était de 25 %. Parmi les patients décédés présentant une dyslipidémie, la majorité avait une diminution significative du taux de HDL-cholestérol.

Mots-clés : Accident vasculaire cérébral, Dyslipidémie pure, Facteurs de risque vasculaire.

Abstract

The prevalence of major vascular risk factors is steadily increasing, influenced by new lifestyles in the general population including unhealthy eating habits such as high-fat meals. The objective was to assess

the lipid profile of patients hospitalized for stroke by identifying those presenting with dyslipidemias. The study focused on lipid profile results from 609 patients. All variables were included in the a priori model without any selection, with lipid and anthropometric variables (age, sex).

The means and standard deviations of the analyzed lipid fractions were respectively: TC (1.89; 0.55); HDL (0.49; 0.24); LDL (1.24; 0.50) and TG (0.90; 0.41). After controlling for confounding factors by bivariate analysis, the results obtained for pure dyslipidemias showed that HDL was significantly associated primarily with stroke [OR 1.77; 95% CI 1.15-2.72; p=0.002] followed by LDL [OR 2.00; 95% CI 1.04-3.87; p=0.03]. The observed frequency of stroke was 72% for the ischemic form and 28% for the hemorrhagic form. It increased with age regardless of type. The extreme ages of patients were 17 and 95 years with a mean of 62.8 years. Men represented 53% of cases and women 47% of cases. The overall mortality rate was 25%.

Among deceased patients presenting with dyslipidemia, the majority had a significant decrease in HDL-cholesterol levels.

Keywords: Stroke, Pure dyslipidemia, Vascular risk factors.

Introduction

Abnormalities in plasma lipid levels are among the ten major vascular risk factors that favor the occurrence of Stroke [12;14;4;6]. The prevalence of major vascular risk factors is constantly increasing, such as unhealthy high-fat meals. It would be influenced by the emergence of new lifestyles attributable to rapid demographic changes observed not only in so-called developed countries but also in low- or middle-income countries [8;13]. In the USA, dyslipidemia affects approximately 53% (105.3 million) of American adults (13). Several associated lipid abnormalities have been observed in stroke patients. Therefore, the recommendations of the Third Report of the National Cholesterol Education Program; Adult Treatment Panel-III (NCEP_ATP-III) have proposed for the effective management of dyslipidemia, a more flexible and appropriate classification for large-scale epidemiological and interventional actions [5]. Indeed, few studies have compared both stroke forms associated with the lipid profile of patients suffering from this condition [7]. The objective of the study was to analyze the lipid profile of patients hospitalized for stroke (Ischemic or Hemorrhagic) by identifying among them those who presented with pure dyslipidemias.

Methodology

The study conducted in Senegal, at the Fann National and University Hospital, in the neurology department during the period from January 1, 2013 to December 31, 2014, focused on lipid profile results of 609 patients among the 776 hospitalized during this period for a constituted stroke (Ischemic, Hemorrhagic) [Fig.1]. Each lipid fraction was studied at two levels relative to NCEP_ATP-III reference values, namely: LDL-cholesterol < 1.6g/l ≥, Total Cholesterol (TC) < 2.4g/l ≥, triglycerides (TG) < 1.5g/l ≥, HDL-cholesterol < 0.4g/l ≥. Other variables were taken into account, mainly anthropometric: age group in four ranges (16 to 35 years, 36 to 55 years, 56 to 75 years, 76 to 95 years), sex (female and male). Also, the mortality rate in this studied population. Data processing and statistical analysis were performed using IBM SPSS Statistics version 23 software. All variables were included in the a priori model without any selection, first with lipid variables, then secondarily age and sex. Univariate and bivariate analyses were performed to calculate frequencies, means, standard deviation, and study the association between lipid fractions as a dependent variable of stroke. The error risk was estimated at 5%. The overall mortality rate in this studied population was calculated.

Study limitations: This study was monocentric. The multivariate analysis adjusted by logistic regression to confirm the independent association of lipids with

stroke relative to other vascular risk factors involved in its occurrence (HTN, diabetes, smoking, alcohol, hyperuricemia, pill use and others) constituted a selection bias of the study. Data on hypolipidemic drugs were concealed.

Results

- *Epidemiological and clinical characteristics of patients*

The observed population consisted of 53% men and 47% women. The sex ratio was 0.88 (F/M). The extreme ages of patients were 17 and 95 years with a mean of 62.8 (±14.2) years. 72% of patients presented with Ischemic Stroke and 28% with Hemorrhagic Stroke. The prevalence of stroke had increased with age regardless of type. The majority of these victims were aged between 56 and 75 years [Fig.2].

- *Table I: Lipid profiles associated with stroke type*

These results indicate that the majority of patients in the cohort had a normal lipid profile. Among those who presented with abnormal lipid profile in both stroke forms, the high number of cases was observed with the HDL-cholesterol fraction, namely 363(60%).

- *Table I: Prevalence of pure dyslipidemias by age and sex*

These results suggest that pure HDL-cholesterol dyslipidemia was the dominant form in men while other forms were predominantly observed in women, particularly in the 56-75 years age range.

- *Table III: Pure dyslipidemias after bivariate analysis*

The means, standard deviations and P-Values of the observed lipid fractions were respectively for: TC [1.89; 0.55; 0.17]; HDL [0.49; 0.24; 0.002]; LDL [1.24; 0.50; 0.03] and TG [0.90; 0.41; 0.59]. Among all observed cases, except for HDL-Cholesterol, the values of normal lipid fractions were higher than abnormal ones. These results further indicate that there is a statistically significant difference in HDL-cholesterol and LDL-cholesterol levels.

- *Table IV: Stroke mortality rates by lipid profiles*

In the recruited population, 25% (154 cases) of patients were deceased. Except for abnormal HDL-cholesterol, the majority of deceased patients presented with a normal lipid profile. Ischemic stroke was much more fatal than hemorrhagic stroke.

Table I: Lipid profiles associated with stroke types

Extreme lipid values (g/l)		Number\ n609(%)	Stroke		Mean	Standard deviation	P-value
			Hemorrhagic\ n171(28%)	Ischemic\ n438(72%)			
TC	[0.35-2.39[\ nVS\n[2.40-3.49[	510(84)\ n99(16)	147(24)\n24(4)	363(60)\n75(12)	1.89	0.55	0.45
HDL	[0.04-0.39[\ nVS\n[0.40-2.45[	363(60)\ n246(40)	43(7)\n128(21)	320(53)\n118(19)	0.49	0.24	0.002
LDL	[0.16-1.59[\ nVS\n[1.60-3.02[	484(79)\ n125(21)	142(23)\n29(5)	342(56)\n96(16)	1.24	0.50	0.17
TG	[0.06-1.49[\ nVS\n[1.5-3.01[	554(91)\ n55(9)	159(26)\n12(2)	395(65)\n43(7)	0.90	0.41	0.27

Legend: TC=Total Cholesterol; HDL=High Density Lipoprotein; LDL=Low Density Lipoprotein; TG=Triglycerides.

Table II: Prevalence of pure dyslipidemias by age and sex

Risk Factors		Frequency (%) of pure dyslipidemias [g/l]			
		TC≥[2.4] 99(16)	HDL<[0.4] 363(60)	LDL≥[1.6] 125(21)	TG≥[1.5] 55(9)
Sex	Male	43(7)	195(32)	56(9)	23(4)
	Female	56(9)	168(28)	69(12)	32(5)
Age	[16-35[	2(N/A)	50(8)	2(N/A)	1(N/A)
	[36-55[	25(4)	90(15)	31(5)	13(2)
	[56-75[	48(8)	140(23)	63(10)	20(3)

Legend: TC=Total Cholesterol; HDL=High Density Lipoprotein; LDL=Low Density Lipoprotein; TG=Triglycerides; N/A=Non-Applicable (Value not significant to be applied).

Table III: Pure dyslipidemias after multivariate analysis

Lipid fractions (g/l)	Mean	Standard deviation	OR	95% CI	P-value
TC≥2.4 vs <2.4	1.89	0.55	0.71	0.44 - 1.16	0.17
HDL<0.4 vs ≥0.4	0.49	0.24	1.77	1.15 - 2.72	0.002
LDL≥1.6 vs <1.6	1.24	0.50	2.00	1.04 - 3.87	0.03
TG≥1.5 vs <1.5	0.90	0.41	1.20	0.60 - 2.63	0.59

Legend: TC=Total Cholesterol; HDL=High Density Lipoprotein; LDL=Low Density Lipoprotein; TG=Triglycerides; OR=Odds Ratio; CI=Confidence Interval.

Table IV: Stroke mortality rates by lipid profiles

Lipid fractions (g/l)	Stroke cases deceased (%)		Death rate (%)\ n154(25)
	Hemorrhagic\n30(5)	Ischemic\n124(20)	
TC			
≥ 2.4	7(1)	17(3)	24(4)
< 2.4	23(4)	107(17)	130(21)
HDL			
≥ 0.4	8(1)	50(8)	58(9)
< 0.4	22(4)	74(12)	96(16)
LDL			
≥ 1.6	6(1)	21(3)	27(4)
< 1.6	24(4)	103(17)	127(21)
TG			
≥ 1.5	3(N/A)	17(3)	20(3)
< 1.5	27(4)	107(17)	134(22)

Legend: N/A=Non-Applicable (Value not significant to be applied); TC=Total Cholesterol; HDL=High Density Lipoprotein; LDL=Low Density Lipoprotein; TG=Triglycerides; OR=Odds Ratio; CI=Confidence Interval.

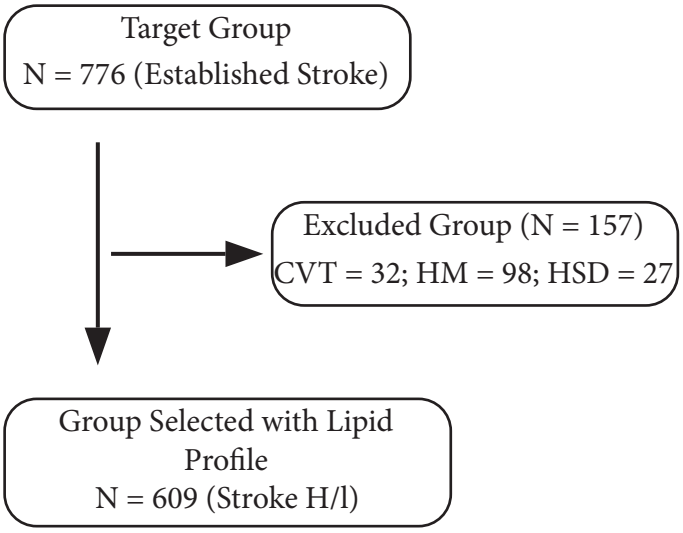

Figure 1: Flow Diagram of Recruited Patients

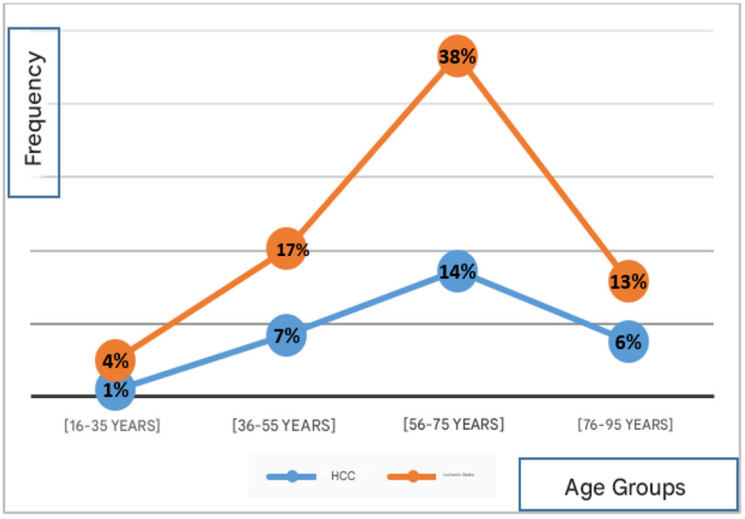

Figure 2: Frenquency of Stroke typess under study by age group

Discussion

- *Epidemiological and clinical characteristics of patients*

The present study reports a prevalence of IS of 72% and HS of 28%. This prevalence had increased linearly with age regardless of forms, peaking from 56 years before declining towards 76 years [Fig.2]. In China, data collected from the China National Stroke Screening Survey (CNSSS) registries between 2013 and 2014 in 31 provinces of China, the authors reported an adjusted prevalence of 2.06% of stroke (31,188 cases), namely 74.3% ischemic stroke (23,169 cases); 9.4% hemorrhagic stroke (2,921 cases) and 16.3% non-specific (5,098 cases). The reported annual temporal incidence of first stroke had increased from 189/100,000 in 2002 to 379/100,000 in 2013, representing an overall annual increase of 8.3% [11]. In Togo, the prevalence of dyslipidemia among 301 stroke patients was estimated for LDL-cholesterol at 51.36% (n=75/146) for IS and 41.33% (n=31/75) for HS while the decrease in HDL-cholesterol level was associated with 56.71% (n=38/67) for IS and 25% (n=8/32) for HS. This series had reported that 60.11% (n=181) of patients presented with IS versus 30.89% (n=120) with HS [1]. In Dakar, a study conducted in 2016 on the lipid profile of IS victims had reported that the 235 patients were aged between 10 to 99 years with a mean of 67.06 years. The standard deviation was 13.89. The most representative age ranges were those between 65 to 74 years and those between 75 to 84 years, respectively at 28.94% and 28.51%. The sex ratio was 0.74 in favor of women (57.45%) [3].

- *Lipid profiles associated with stroke type*

The majority of patients in the cohort had a normal lipid profile, respectively 84% for TC (24% HS; 60% IS), 40% for HDL (19%; 21%), 79% for LDL (23%; 56%) and 91% for TG (26%; 65%). Patients who had an abnormal lipid profile represented respectively for TC 16% (4% HS; 12% IS); HDL 60% (7% HS; 53% IS); LDL 21% (5% HS; 16% IS) and TG 9% (2% HS; 7% IS). The 2016 study conducted in Dakar had noted that the lipid profile of IS victims relative to total cholesterol (TC) levels was elevated in 52.34% of patients while the low HDL-cholesterol level was observed in 34.47% of patients. For LDL-cholesterol, the elevated level was observed in 12.76%. TG-cholesterol elevation had only been observed in 3% of patients. This study had only taken into account the ischemic form [3].

- *Prevalence of pure dyslipidemias by age and sex*

The pure dyslipidemias observed in this cohort were predominantly HDL 363(60%), namely 7% for HS and 53% for IS and LDL 125(21), namely 5% for HS

and 16% for IS [Tab.1]. A study conducted in 2016 in Dakar had focused on the lipid profile during IS in 235 patients. The patients were aged 10 to 99 years with a mean of 67.06 years. The standard deviation was 13.89. The most representative age ranges were those between 65 to 74 years and those between 75 to 84 years, respectively at 28.94% and 28.51%. The sex ratio was 0.74 in favor of women (57.45%). In this series, the total cholesterol (TC) level was elevated in 52.34% of patients while the low HDL-cholesterol level was observed in 34.47% of patients. For LDL-cholesterol, the elevated level was observed in 12.76%. TG-cholesterol elevation had only been observed in 3% of patients [3]. In Togo, a study had focused on the prevalence of dyslipidemia in 301 stroke patients. The team had indicated that the mean age of patients was 58.22 years. The most represented age range was that of 70 years. The latter had presented mainly with IS while that of 45-49 years had presented mainly with HS. The study population consisted of 163 men for 138 women with a sex ratio (F/M) of 0.85. This series had reported that 60.11% (n=181) of patients presented with IS versus 30.89% (n=120) with HS. The authors reported that the observed elevation of LDL-cholesterol level was 51.36% (n=75/146) for IS and 41.33% (n=31/75) for HS while the decrease in HDL-cholesterol level was associated with 56.71% (n=38/67) for IS and 25% (n=8/32) for HS [1]. The results of the present study had indicated that the most representative age ranges were those of 56 to 75 years and those of 36 to 55 years with respective frequencies of 52% and 24% of cases. The results had further indicated that men (53%) were more affected than women. Among the patients, 38% presented with the ischemic form compared to the hemorrhagic form which was 15%. Pure HDL fraction dyslipidemias concerned men much more 195(32%) than women 160(28%). Conversely, those with LDL fraction concerned mainly women 69(12%) than men 56(9%). The rate was identical in women and men for the TC fraction [Tab.2].

- *Pure dyslipidemias after bivariate analysis*

The mean values, standard deviations and P-values of the different observed lipid fractions were respectively for TC [1.89; 0.55; 0.17]; HDL [0.49; 0.24; 0.002]; LDL [1.24; 0.50; 0.03] and TG [0.90; 0.41; 0.27]. After bivariate analysis, the results of this cohort on the association between stroke and abnormal lipid profile had shown that low HDL-cholesterol level was significantly associated with stroke (OR, 1.77 95% CI 1.15-2.72, p=0.002) as well as elevated LDL-cholesterol level (OR, 2.00 95% CI 1.04-3.87, p=0.03). No significant association could be demonstrated between TC and TG levels in the two studied stroke forms [Tab.3]. The proportion of stroke risk attributable to dyslipidemia in the cohort was estimated at 2.77 on average. The Multiple Risk Factor Intervention (MRFIT) study conducted in the USA had demonstrated a significant relationship between pure hypercholesterolemia (TC) and the risk of IS, unlike HS [10]. A prospective cross-sectional case-control study conducted in India had included 127 patients aged 20 to 85 years, including 102 individuals with stroke and 25 individuals without stroke. It had proposed to study the incidence and correlation of dyslipidemia during stroke. The authors reported that 45.09% of stroke patients were aged between 61-85 years followed by 44% of patients aged between 41-60 years. In the group of stroke patients, the majority were male (61.76%) while among individuals without stroke, the majority were female (84%). The prevalence of dyslipidemia was more significant (P=0.009) in stroke patients (56.86%) compared to individuals without stroke (28%). For stroke patients, 41/65 patients (63.07%) had dyslipidemia in the ischemic form compared to 17/37 patients (45.94%) who presented with the hemorrhagic form. The decrease in HDL cholesterol level was 74% (43 cases) in the group of patients with stroke versus 100% (7 cases) in the group of individuals without stroke [9]. A mixed study was conducted in China which had focused on a sample of 1,292,010 between 2002 and 2013 to estimate the prevalence, temporal incidence and contribution of stroke risk factors in adults aged over 40 years from the China National Stroke Screening Survey (CNSSS)

registries. Data were collected between 2013 and 2014 in 31 provinces of China. The authors reported an adjusted prevalence of 2.06% of stroke (31,188 cases), namely 74.3% ischemic stroke (23,169 cases); 9.4% hemorrhagic stroke (2,921 cases) and 16.3% non-specific (5,098 cases). Dyslipidemia was present in 17.6% of cases [OR 1.65; 95% CI 1.61-1.70]. The annual temporal incidence of first stroke had increased from 189/100,000 in 2002 to 379/100,000 in 2013, representing an overall annual increase of 8.3% [11].

- *Stroke mortality rates by lipid profiles*

The overall mortality rate in the present cohort was 25% (154 cases) [Tab.4]. The 56 to 75 years age range was predominantly concerned, namely 13% (78 cases). This rate was very high in patients who had presented with ischemic stroke, 20% (124 cases). The majority of deceased patients had a normal lipid profile. Among patients who had an abnormal lipid profile, the mortality rate was in descending order 16% (96 cases) with low HDL (<0.4 g/l), with elevated LDL (≥1.6g/l) at 4% (27 cases), with elevated TC (≥2.4 g/l) at 4% (24 cases) and with elevated TG (≥1.5 g/l) at 3% (20 cases). In a case-control series, the observed death rate was 13.72% (14 cases) among the 102 notified stroke cases. The team had emphasized that among the deceased, 71.42% (10 cases) had dyslipidemia. This team had further indicated that the decrease in HDL-cholesterol would be the main culprit in the occurrence of fatal vascular events in the series [10]. These two results suggest that abnormal decrease in HDL-cholesterol level would probably favor the occurrence of fatal stroke. In the USA, a team had conducted a meta-analysis on 352 full-text articles on the interest of screening or treatment of asymptomatic dyslipidemia in young adults aged 21 to 39 years, evaluating the risk of mortality, cardiovascular disease, morbidity or stroke-related mortality. This study had revealed the difficulties in assessing information on the situation regarding dyslipidemias. It had suggested that long-term studies or trials will be necessary in people with very high lipid levels regardless of the type of dyslipidemia to increase the statistical power of the data [2]. These different results suggest that there is great variability in the reported findings. This fact may be attributable on the one hand to the objectives assigned to each study and on the other hand to the judgment criteria used by the different methods.

Conclusion

The information provided by this study reports that pure or mixed dyslipidemia was progressing in these stroke victims and increases with age. Among deceased patients presenting with dyslipidemia, the majority had a significant decrease in HDL-cholesterol levels. Large-cohort multicenter African studies that will include specific dietary habits of each region or locality will be able to better assess the harmful impact of certain dietary habits. The results of these studies will help constitute a reliable database at the African scale allowing the formulation of recommendations on this underdiagnosed problem with high impact on public health.

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Conflict of interest : None

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