Demographics, socio-economic characteristics, and risk factor prevalence in patients with non-cardioembolic ischaemic stroke in low- and middle-income countries: the OPTIC registry

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Background **There is a paucity of data on patients with stroke/transient ischaemic attack in low- and middle-income countries. We sought to describe the characteristics and management of patients with an ischaemic stroke and recent transient ischaemic attack or minor ischaemic strokes in low- or middle-income countries.**

Methods **The Outcomes in Patients with TIA and Cerebrovascular disease registry is an international, prospective study. Patients ≥45 years who required secondary prevention of stroke (either following an acute transient ischaemic attack or minor ischaemic strokes (National Institutes of Health Stroke Scale <4) of <24 h duration, or recent (<6 months), stable, first-ever, non-disabling ischaemic stroke) were enrolled in 17 countries in Latin America, the Middle East, and Africa. The main measures of interest were risk factors, comorbidities, and socio-economic variables.**

Results **Between January 2007 and December 2008, 3635 patients were enrolled in Latin America ($n = 1543$), the Middle East ($n = 1041$), North Africa ($n = 834$), and South Africa ($n = 217$). Of these, 63% had a stable, first-ever ischaemic stroke (median delay from symptom onset to inclusion, 25 days interquartile range, 7–77); 37% had an acute transient ischaemic attack or minor ischaemic stroke (median delay, two-days; interquartile range, 0–6). Prevalence of diabetes was 46% in the Middle East, 29% in Latin America, 35% in South Africa, and 38% in North Africa; 72% had abdominal obesity (range, 65–78%; adjusted $P < 0{\cdot}001$); prevalence of metabolic syndrome was 78% (range, 72–84%, $P < 0{\cdot}001$). Abnormal ankle brachial index (<0·9) was present in 22%, peripheral artery disease in 7·6%, and coronary artery disease in 13%. Overall, 24% of patients had no health insurance and 27% had a low educational level.**

Interpretation **In this study, patients in low- and middle-income countries had a high burden of modifiable risk factors. High rates of low educational level and lack of health insurance in certain regions are potential obstacles to risk factor control.**

Funding **The Outcomes in Patients with TIA and Cerebrovascular disease registry is supported by Sanofi-Aventis, Paris, France.**

Key words: developing countries, epidemiology, prevention, risk factors, socio-economic factors, stroke

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Conflicts of interest: H. A. and J. L. reported none. A. A., A. B., P. G. L., A. M., M. M. C., P. G. S., B. I. Y., E. V., and P. A. received honorarium fees as members of the OPTIC steering committee.

Contributors: P. A. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. H. A., J. L., and P. A. drafted the manuscript. J. L. and E. V. did the statistical analyses. P. A., E. V., A. A., A. B., P. G. L., A. M., M. M. C., P. G. S., and B. I.Y. were responsible for the study concept, design and supervision. P. A., E. V., A. A., A. B., P. G. L., A. M., M. M. C., P. G. S., B. I. Y., J. L., and H. A. analysed and interpreted the data. All authors revised the manuscript for important intellectual content.

Role of the sponsor: Sanofi-Aventis was not involved in the design of the study, analysis and interpretation of the data, or preparation and review of the manuscript, but provided help in the conduct of the study, did the data managing, collection of data and gave its final approval for submission of the manuscript.

DOI: 10.1111/j.1747-4949.2012.00893.x

Introduction

Stroke is a rapidly growing health problem worldwide, due largely to a genuine epidemic of atherothrombosis in low- and middle-income countries, which offsets some of the progress made in the prevention and treatment of stroke/transient ischaemic attack (TIA) in affluent countries. Yet, few data are available in stroke/TIA patients in low- and middle-income countries regarding their demographics, clinical characteristics, risk factor profiles, including the involvement of several arterial beds (cerebral, coronary, and peripheral), and management. These characteristics will likely help to stratify patients at higher or lower risk of recurrence, as shown in 66 000 patients with coronary artery disease (CAD), cerebrovascular disease (CVD), or peripheral artery disease (PAD) included in the Reduction of Atherothrombosis for Continued Health (REACH) Registry (1). To the best of our knowledge, no large datasets have been reported in stroke/TIA patients regarding geographic differences and variations in socio-economic status and health insurance and social security coverage in low- and middle-income countries. Consequently, it is unclear whether these factors may explain the geographic disparity in stroke incidence and survival after stroke. The Outcomes in Patients with TIA and Cerebrovascular disease (OPTIC) registry was designed to address these issues.

OPTIC is a cross-sectional study in low- and middle-income countries with long-term follow-up of patients in the secondary prevention period following stroke, having either an acute TIA or minor ischaemic stroke [National Institutes of Health Stroke Scale (NIHSS) <4] (<24 h from symptom onset) or a recent (<6 months), stable, first-ever, non-disabling ischaemic stroke.

Methods

Study design and patient population

The OPTIC registry is an international, prospective, observational study performed in patients with a first-ever ischaemic stroke and recent TIA or rapidly reversible minor ischaemic strokes. OPTIC was designed to collect information on demographic data, socio-economic status, clinical characteristics, and management of patients with stroke/TIA in low- and middle-income countries, and to evaluate the long-term risk of recurrent atherothrombotic events. The registry enrolled patients in 17 countries in Latin America (Brazil, Chile, Colombia, Dominican Republic, Ecuador, Mexico, Peru, Venezuela), the Middle East (Egypt, Iran, Jordan, Lebanon, Saudi Arabia), North Africa (Algeria, Morocco, Tunisia), and South Africa (2). Enrolment occurred between January 2007 and December 2008. Investigators were general practitioners or specialists (cardiologists, neurologists, endocrinologists, and internists) selected according to preference by country. Physician selection was based on the best available sources concerning epidemiology and medical care data at the country level. Investigators participating in the study were selected randomly from a list of centres that represented the country as fully as possible, and included public, private, and teaching hospitals, hospitals in different locations, hospitals admitting patients with public and/or private health insurance, and hospitals with all or only some of the services listed in the site questionnaire. Recruiting physicians received an expense allowance for each patient enrolled.

Inclusion and exclusion criteria

The OPTIC registry enrolled the whole spectrum of patients with an ischaemic stroke in the secondary prevention period: patients aged ≥45 years with one of the following three criteria: TIA within the previous two-weeks; minor ischaemic stroke (NIHSS ≤3) of <24 h duration; or first-ever ischaemic stroke (modified Rankin ≤4) within the previous six-months, confirmed by imaging. The aim of these criteria was to obtain the whole spectrum of ischaemic non-cardioembolic strokes within the previous six-months.

Patient management was neither delayed nor altered by inclusion in the registry.

The major exclusion criteria included patients with any stroke defined as category 3 in the Trial of Org 10172 in Acute Stroke Treatment classification (stroke associated with cardiac source of embolism). Categories 1, 2 (atherosclerosis), and 5, 6 (lacunar) were included (3). Patients were also excluded from the study if they were currently enrolled in another clinical trial, did not grant informed consent, or were expected to be unable to comply with the scheduled follow-up visits.

Evaluations

Patient demographics (gender, age, race-ethnicity), physical examination findings (weight, height, waist circumference, current blood pressure reading), medical history (medical treatments, influenza vaccination, atherothrombotic and cardiac history), socio-economic profile (housing, employment status, health insurance cover, education level), and laboratory measurements [serum creatinine, fasting blood glucose, total cholesterol, low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), triglycerides, haemoglobin A1c] were recorded at baseline and at follow-up on standardized international case report forms and entered into a central database.

Risk factors included hypertension, diabetes mellitus (type 1 or 2), dyslipidaemia, smoking habits (current smoking was defined as consuming ≥5 cigarettes/day on average in the three-months before entering the study; former smoking was defined as ≥5 cigarettes/day on average ≥1 month before entering the study), current physical activity (moderate exercise–walking, cycling, or gardening; or strenuous exercise

for ≥30 mins twice/week), and alcohol consumption. Hypertension, diabetes, and dyslipidaemia were defined as the use of medications for these conditions at hospital discharge or at the time of study enrolment.

Abdominal obesity was defined as elevated waist circumference (≥94 cm in men and ≥80 cm in women), and body mass index (BMI) was calculated by dividing weight by height squared (4). Obesity was defined as a BMI ≥30 kg/m^2. Fasting hyperglycaemia was defined as a glucose concentration ≥7 mmol/l (126 mg/dl). Elevated blood pressure was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mm Hg.

For the diagnosis of the metabolic syndrome, three or more of the following parameters were taken into account: (1) elevated blood pressure (systolic ≥130 mmHg and/or diastolic ≥85 mmHg or taking antihypertensive drugs); (2) elevated triglycerides (≥150 mg/dl); (3) reduced HDL-C (<50 mg/dl in women, <40 mg/dl in men); (4) elevated fasting glucose (≥110 mg/dl or taking antidiabetic drug); (5) elevated waist circumference (4).

The ankle-brachial index (ABI) was determined at the baseline visit in all patients after five-minutes of rest in the supine position. For calculation of the ABI, the systolic blood pressure in each leg was divided by the highest systolic pressure measured in both arms. This provided two ABI measurements (one from each leg), the lower of which was used in the analysis. A detailed instruction on ABI measurement was included in the case report form and all participating centres received an Omron automatic blood pressure monitor (Kyoto, Japan). Abnormal ABI was defined as <0·9 in the left or the right side.

Follow-up assessments

Clinical events or hospitalizations that occurred were recorded every 6 ± 1 month during the two-year follow-up period. Patients' treatments and any change in employment status were recorded at each follow-up visit. The primary study endpoint was the time from inclusion into the study to non-fatal stroke recurrence, first non-fatal myocardial infarction, or cardiovascular death.

There was one prespecified secondary composite outcome defined as the first occurrence of non-fatal stroke, non-fatal myocardial infarction, hospitalization for peripheral vascular intervention (angioplasty/stenting, artery bypass graft, amputation affecting lower limbs), hospitalization for atherothrombotic event (PAD, worsening of claudication related to PAD, or unstable angina), and cardiovascular death.

Written informed consent was obtained from all patients and the study was conducted according to the principles of the Declaration of Helsinki (Edinburgh Amendment, 2000). As a quality assurance measure, data quality control was performed in 10% of the active sites (that enrolled ≥1 patient), chosen at random in each country. In these sites, all patient data forms were checked for completeness and plausibility. If specific issues were identified in some sites or countries, the percentages of quality control in the concerned site/country were increased and corrective actions were implemented.

Sample size determination

The sample size for the OPTIC registry was estimated using a poll technique. Assuming a normal distribution centred on the mean for an estimated risk of primary study end-point of 8% with a precision of 1%, a lost to follow-up rate of 30%, and an alpha risk of 5%, 3600 patients would be included.

Statistical analysis

Continuous variables are expressed as mean (standard deviation) or median (interquartile range) and categorical variables as frequencies and percentages. Baseline characteristics, medication use, and socio-economic characteristics were compared, first between the type of qualifying event for enrolment into the registry (first-ever ischaemic stroke vs. TIA or rapidly reversible minor ischaemic stroke), and second between the four geographic regions (Latin America, Middle-East, North Africa, and South Africa). All comparisons were adjusted for age and gender. An additional adjustment for geographic region was made for analyses stratified by qualifying events, and an additional adjustment on qualifying events was made for analyses stratified by geographic region. Between-group comparisons for continuous variables were performed using analysis of covariance; between-group comparisons for binary variables were performed using logistic regression models. Statistical testing was done at the two-tailed alpha level of 0·05. Data were analysed with the SAS software package, version 9·1 (SAS Institute, Cary, NC, USA).

Results

Between January 2007 and December 2008, 3635 patients aged ≥45 years in the secondary prevention period of an ischaemic stroke were enrolled in the OPTIC registry from 245 sites in 17 countries in the following regions: Latin America (1543 patients), the Middle East (1041 patients), North Africa (834 patients), and South Africa (217 patients). The study sample included 63% of patients with a stable, first-ever ischaemic stroke (median delay from symptom onset to study inclusion, 25 days; interquartile range, 7–77 days), ranging from 42% in Egypt to 88% in Brazil; the remaining 37% of patients had an acute TIA or minor ischaemic stroke (median delay from symptom onset to study inclusion, two-days; interquartile range, zero- to six-days) (Fig. 1). The main baseline characteristics of the study population are described in Table 1.

The mean age was 65 ± 11 years and 57% were men, with statistically significant differences across geographic regions (Table 1). Regardless of the qualifying event, the prevalence of treated diabetes, hypertension, and dyslipidaemia was high,

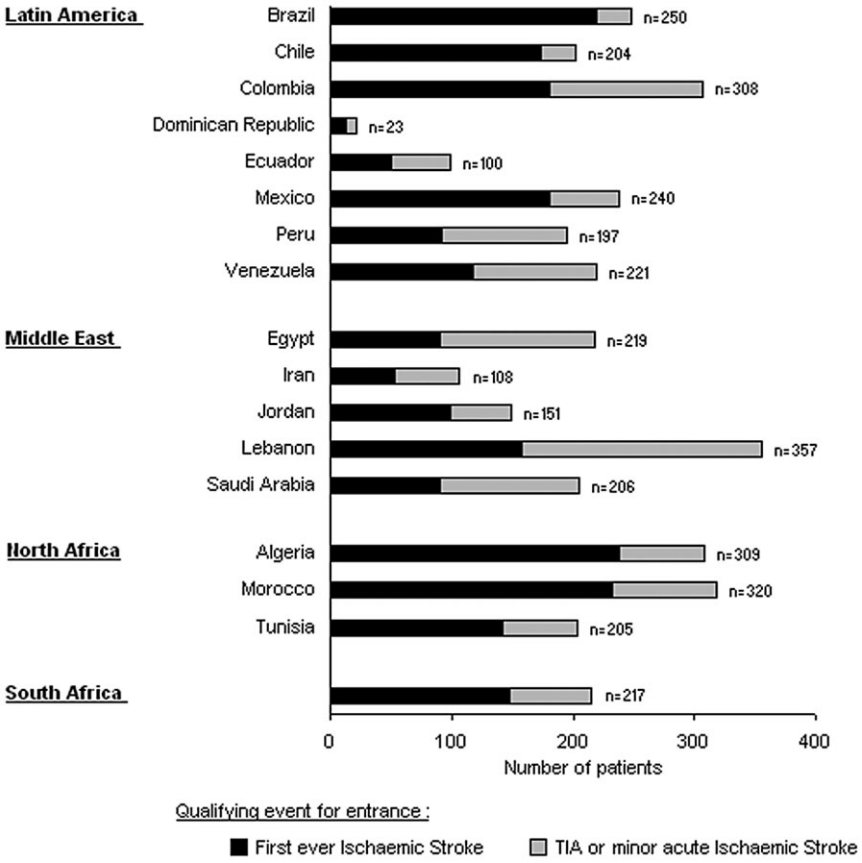

Fig. 1 Patient enrolment by country and qualifying event for the OPTIC registry.

and highest among patients with stroke compared with TIA. Likewise, geographic variations were seen in the prevalence of diabetes, which was present in 46% of patients from the Middle East vs. 29% in Latin America, 35% in South Africa, and 38% in North Africa. Fasting glucose concentration, documented at the baseline visit in a substantial number of patients ($n = 2763$), was higher in the Middle East (median 6·7 mmol/l) than in the three other regions (adjusted *P*-value for geographic difference <0·001). Of the patients without known diabetes, 11% had fasting hyperglycaemia (16% in North Africa, 11% in the Middle East, 10% in Latin America, and 8% in South Africa). Elevated blood pressure at baseline visit was found in 60% of patients, ranging from 50% in South Africa to 65% in the Middle East (adjusted $P < 0{\cdot}001$). Among patients without known hypertension, baseline blood pressure was elevated in 38% (44% in the Middle East, 43% in North Africa, 32% in Latin America, and 19% in South Africa). Lipid profile concentrations documented at baseline visit in 2514 patients varied between geographic regions and qualifying event; overall, 51% had elevated LDL-C (using the Adult Treatment Panel III LDL-C goals) (5), ranging from 44% in Latin America to 64% in South Africa (adjusted $P < 0{\cdot}001$). Prevalence of current smoking was 22% in the overall study sample, decreasing to 14% in patients in Latin America (adjusted $P < 0{\cdot}001$). There were no significant differences in BMI and the type of qualifying event, but a higher mean BMI was found in patients enrolled in the Middle East. The prevalence of obesity was 25% overall, ranging from 19% in Latin America to 35% in the Middle East (adjusted $P < 0{\cdot}001$). Using the recommended waist circumference threshold for abdominal obesity, 72% of patients were classified as abdominally obese (ranging from 65% in North Africa to 78% in South Africa; adjusted $P < 0{\cdot}001$). On the basis of a subgroup of patients with no missing criteria for a clinical diagnosis of metabolic syndrome, the prevalence of metabolic syndrome was 78% (Fig. 2), ranging from 72% in North Africa to 84% in the Middle East ($P < 0{\cdot}001$).

The overall prevalence of abnormal ABI was 22%, ranging from 19% in South Africa to 23% in North Africa (adjusted $P = 0{\cdot}16$). Of the total sample, 13% had a history of CAD (angina, 8·6%; myocardial infarction, 5·8%; coronary stenting, 2·2%; coronary artery bypass surgery, 2·0%; coronary angioplasty, 1·5%) and 7·6% had a history of PAD, giving an overall prevalence of polyvascular disease of 18% (ranging from 12% in North Africa to 25% in the Middle East; adjusted $P < 0{\cdot}001$). As shown in Fig. 3, the prevalence of the main vascular risk factors tended to increase with the number of arterial beds clinically involved in disease.

Table 1 Baseline characteristics in the optic registry, overall, by qualifying event, and by geographic region

Characteristics	Overall (*n* = 3635)	Qualifying event		Geographic region			
		TIA or minor AIS (*n* = 1356)	First-ever ischaemic stroke (*n* = 2279)	Latin America (*n* = 1543)	Middle East (*n* = 1041)	North Africa (*n* = 834)	South Africa (*n* = 217)
Demographics							
Age, mean (SD), y	65·2 (10·9)	64·8 (11·1)	65·3 (10·8)	66·4 (11·3)	63·1 (10·4)	65·2 (10·3)	65·3 (11·3)*
Men	56·8%	54·7%	58·0%**	50·9%	62·3%	60·3%	58·5%*
Medical history							
Hypertension†	82·4%	79·0%	84·4%*	83·6%	80·7%	80·7%	88·0%
Diabetes†	36·1%	33·0%	37·9%*	28·5%	45·9%	38·3%	35·0%*
Dyslipidaemia†	72·9%	71·1%	74·0%*	76·5%	78·0%	57·9%	81·1%*
Current smoking	21·5%	24·0%	20·0%	14·3%	32·1%	20·6%	25·5%*
Coronary artery disease	12·7%	15·0%	11·3%	9·6%	20·4%	8·0%	15·7%*
Peripheral artery disease	7·6%	8·1%	7·3%	9·2%	7·1%	5·0%	7·9%**
TIA	22·8%	38·7%	13·4%*	20·0%	33·9%	14·5%	20·9%*
Congestive heart failure	3·4%	3·8%	3·2%	2·8%	5·2%	2·5%	2·3%*
Aortic valve stenosis	0·9%	0·8%	1·0%	0·7%	1·4%	0·7%	0·5%
Abdominal aortic aneurysm	0·5%	0·9%	0·2%**	0·6%	0·5%	0·1%	0·5%
Examination findings							
BMI, kg/m^2, mean (SD)	27·4 (4·9)	27·6 (4·8)	27·2 (4·9)	26·7 (4·4)	28·9 (5·3)	26·7 (4·6)	27·1 (5·0)*
Systolic BP, mean (SD), mmHg	144 (25)	145 (25)	144 (25)	142 (24)	146 (24)	148 (26)	140 (23)*
Diastolic BP, mean (SD), mmHg	85 (13)	85 (13)	84 (13)	84 (13)	87 (13)	84 (14)	83 (13)*
Total cholesterol, mean (SD), mmol/l	5·1 (1·4)	5·4 (1·5)	5·0 (1·3)*	5·0 (1·3)	5·4 (1·5)	4·9 (1·3)	5·5 (1·2)*
LDL-cholesterol, mean (SD), mmol/l	3·2 (1·1)	3·3 (1·1)	3·0 (1·0)*	3·0 (1·1)	3·3 (1·1)	3·0 (1·1)	3·6 (1·1)*
HDL-cholesterol, mean (SD), mmol/l	1·2 (0·4)	1·2 (0·5)	1·1 (0·4)	1·1 (0·4)	1·2 (0·5)	1·2 (0·5)	1·2 (0·4)
Triglycerides, median (IQR), mmol/L‡	1·6 (1·1)	1·7 (1·2)	1·5 (1·0)*	1·6 (1·0)	1·8 (1·3)	1·4 (0·8)	1·5 (1·2)*
Creatinine, median (IQR), mmol/L‡	86·0 (35·4)	88·4 (35·4)	84·0 (35·4)	79·6 (26·5)	88·4 (35·4)	88·4 (35·4)	88·0 (35·0)*
Glucose, median (IQR), mmol/L‡	6·1 (3·4)	6·1 (3·4)	6·1 (3·3)	5·7 (2·0)	6·7 (4·5)	5·4 (3·8)	5·9 (2·4)*
Haemoglobin A1c >7%§	53·2%	52·4%	53·7%	53·1%	55·4%	45·7%	69·4%**
Left or right ABI <0·9	22·4%	21·6%	22·9%	22·1%	22·7%	23·4%	18·8%

*$P < 0·001$.

**$P < 0·05$ for comparison between qualifying events or geographic regions.

†Patients treated at hospital discharge or at the time of study enrolment.

‡Analysis using the logarithmic values.

§Based on 934 patients with available measure of haemoglobin A1c.

Values are percentage of population unless otherwise indicated.

ABI, ankle-brachial index; AIS, acute ischaemic stroke; AVS, aortic valve stenosis; BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; SD, standard deviation; TIA, transient ischaemic attack.

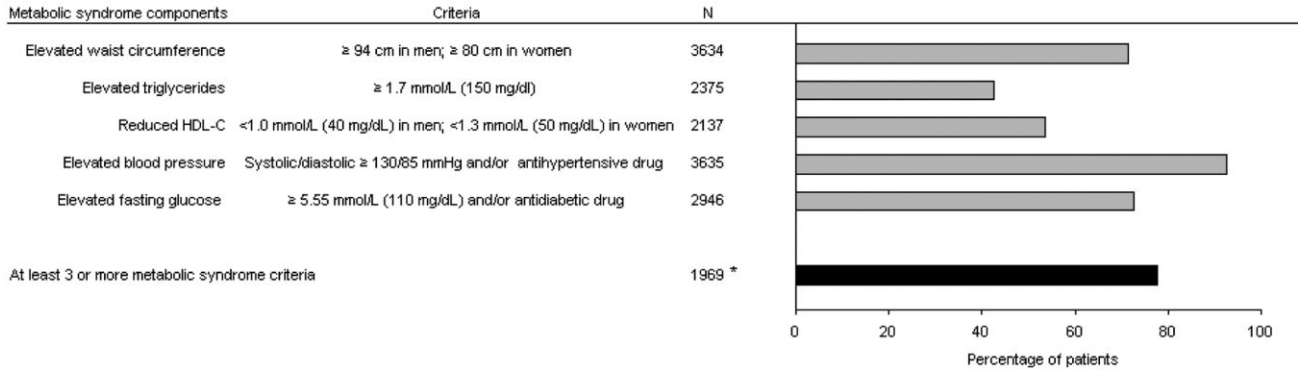

Fig. 2 Prevalence of metabolic syndrome and its components in the OPTIC registry. *Sample of patients with no missing criteria for clinical diagnosis of metabolic syndrome.

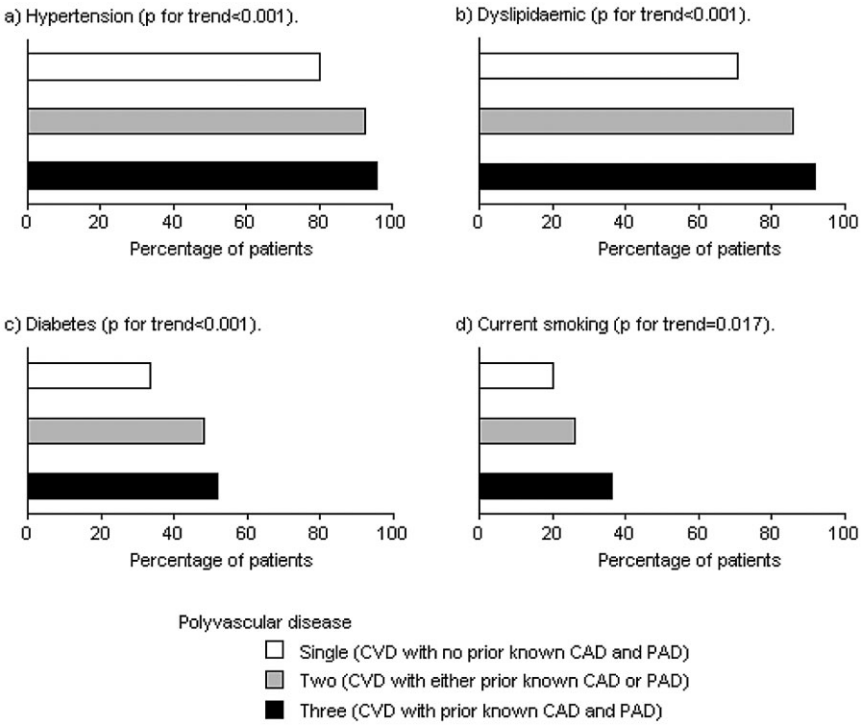

Fig. 3 Prevalence of main vascular risk factors as a function of polyvascular disease. *P*-values for trend are reported, adjusted for age, gender, geographic regions, and qualifying event.

Medications used at the time of hospital discharge are listed in Table 2. Overall, 96% of patients received an antiplatelet agent (33% were treated with ≥2 agents), 7·1% received anticoagulant therapy, 79% received blood pressure-lowering therapy (51% were treated with ≥2 agents), 72% received lipid-lowering therapy (mainly statins, in 97% of cases), and 34% received antidiabetic therapy (mainly oral agents, in 77% of cases). There was substantial variation in medication use depending on qualifying events and geographic region. For example, adenosine diphosphate (ADP)-receptor antagonists were more often prescribed in patients with a TIA or minor ischaemic stroke than in patients with a first-ever ischaemic stroke, and in patients from the Middle East vs. those in the other regions.

Patients' socio-economic characteristics at enrolment into the OPTIC registry are described in Table 3. Regional differences were apparent in health insurance cover, employment status, and educational level of participants. Overall, 24% of patients had no health insurance. The proportion of patients with no insurance was higher in North Africa (42%) than in Latin America (15%), South Africa (20%), and the Middle East (23%) (adjusted $P < 0{\cdot}001$). Among 2770 patients with

Table 2 Medication use at hospital discharge in the optic registry, overall, by qualifying event, and by geographic region

Treatments	Overall (*n* = 3635)	Qualifying event		Geographic region			
		TIA or minor AIS (*n* = 1356)	First-ever ischaemic stroke (*n* = 2279)	Latin America (*n* = 1543)	Middle East (*n* = 1041)	North Africa (*n* = 834)	South Africa (*n* = 217)
≥1 antiplatelet agent	3470 (95·5%)	1287 (94·9%)	2183 (95·8%)	1464 (94·9%)	1003 (96·4%)	800 (95·9%)	203 (93·6%)
Acetylsalicylic acid	81·9%	75·8%	85·5%*	76·8%	80·5%	90·8%	90·6%*
ADP-receptor antagonist	38·9%	49·8%	32·5%*	37·2%	64·6%	13·0%	26·6%*
Other agent	13·3%	13·0%	13·4%	9·3%	12·2%	23·6%	6·4%*
Oral anticoagulant therapy	7·1%	9·0%	6·0%	4·0%	13·6%	4·9%	6·0%*
≥1 blood pressure-lowering agent	2868 (78·9%)	1010 (74·5%)	1858 (81·5%)*	1211 (78·5%)	821 (78·9%)	645 (77·3%)	191 (88·0%)**
ACE inhibitor	52·7%	46·5%	56·1%*	53·5%	46·5%	55·0%	66·5%*
Calcium channel blocker	34·8%	36·9%	33·7%	36·8%	34·7%	31·3%	35·1%
Diuretic	32·1%	34·6%	30·7%	31·5%	32·6%	27·8%	48·2%*
Beta-blocker	25·7%	28·1%	24·3%	20·8%	36·5%	20·9%	25·7%*
Angiotensin II receptor blocker	19·5%	21·7%	18·3%	22·9%	21·1%	13·2%	12·0%*
Other agent	7·6%	7·4%	7·7%	7·1%	9·6%	5·4%	9·4%**
≥1 Lipid-lowering agent	2599 (71·5%)	947 (69·8%)	1652 (72·5%)*	1153 (74·7%)	803 (77·1%)	467 (56·0%)	176 (81·1%)*
Statin	97·0%	96·3%	97·3%	98·1%	96·8%	93·8%	98·9%*
Other agent	8·0%	11·5%	6·1%*	8·2%	9·6%	6·9%	3·4%
≥1 Diabetic agent	1232 (33·9%)	421 (31·1%)	811 (35·6%)*	395 (25·6%)	455 (43·7%)	307 (36·8%)	75 (34·6%)*
Insulin	34·1%	30·6%	35·9%	28·1%	33·4%	43·7%	30·7%*
Oral agent	77·1%	79·6%	75·8%	81·5%	78·9%	65·2%	92·0%*
Non-steroidal anti-inflammatory drug	4·7%	6·6%	3·6%**	4·3%	7·6%	1·6%	5·1%*
Nitrates and other anti-angina agent	6·7%	8·3%	5·7%	3·5%	11·8%	6·1%	6·5%*
Anti-arrhythmic agent	3·2%	4·4%	2·5%**	2·2%	5·4%	2·8%	1·4%*
Inotropic agent	2·1%	2·7%	1·8%	2·1%	2·8%	1·8%	0·5%
Peripheral artery claudication agent	3·2%	4·6%	2·4%**	2·0%	6·4%	1·8%	1·8%*

*$P < 0{\cdot}001$. **$P < 0{\cdot}05$ for comparison between qualifying events or geographic regions. Values are percentage of population. ACE, angiotensin-converting enzyme; ADP, adenosine diphosphate; AIS, acute ischaemic stroke; TIA, transient ischaemic attack.

Table 3 Patient's socio-economic characteristics in the optic registry, overall, by qualifying event, and by geographic region

		Qualifying event		Geographic region			
Characteristics	Overall (n = 3635)	TIA or minor AIS (n = 1356)	First-ever ischaemic stroke (n = 2279)	Latin America (n = 1543)	Middle East (n = 1041)	North Africa (n = 834)	South Africa (n = 217)
Lives alone	8·5%	7·8%	8·9%	10·2%	7·4%	5·3%	13·5%*
Lives in a rural area	13·2%	15·4%	11·9%**	7·8%	18·6%	18·0%	7·9%*
Lives in a house or flat	92·4%	90·9%	93·3%**	93·9%	93·1%	88·0%	95·4%*
Hospital distance from home ≥30-min drive	44·3%	40·1%	46·7%*	44·2%	44·6%	49·2%	24·2%*
Unemployed†	31·4%	32·4%	30·8%	27·5%	37·1%	36·4%	12·9%*
No health insurance cover	23·6%	24·5%	23·1%	14·7%	23·3%	41·5%	19·9%*
Education level‡							
Low	26·6%	23·3%	28·6%**	11·5%	26·1%	62·1%	2·3%*
High	45·1%	48·3%	43·2%	46·5%	52·1%	21·8%	89·9%*

*P < 0·001. **P < 0·05 for comparison between qualifying events or geographic regions. †Excluding social pensioner on disability grant and old age pensioner. ‡Low defined as <2 years of schooling and high as >6 years. Values are percentage of population. AIS, acute ischaemic stroke; TIA transient ischaemic attack.

health insurance, 35% had private health insurance. Sixty-seven per cent of the study sample was unemployed (31% were unemployed through choice and 36% had a chronic disability or were pensioners). Patients who were in employment were categorized into three groups according to their employment level: upper-management/professional (e.g. professional, upper-management position, commercial farmer) in 36% of cases; intermediate (e.g. middle management, manual foreman, skilled artisan, clerical and semiskilled positions) in 44%; and unskilled (e.g. subsistence farmer, unskilled worker, informal sector trader) in 20% of patients. Overall, 27% of patients had a low educational level, ranging from 62% in North Africa to 12% in Latin America, 26% in the Middle East, and 2·3% in South Africa (P < 0·001).

Discussion

In the OPTIC registry, we assessed patients in the secondary prevention period following a TIA or non-disabling, non-cardioembolic ischaemic stroke in geographic regions from which data are scarce. Low- and middle-income countries have a high rate of stroke death, which is expected to rise steeply in the near future (6,7). We evaluated cardiovascular risk factors, clinical data, and management of patients in this unique registry in order to identify a profile that is likely to confer a higher risk for subsequent vascular events.

The OPTIC registry also provides an opportunity to evaluate the role of socio-economic factors and health insurance cover in stroke management, particularly the control of risk factors.

Our study included acute and chronic ischaemic stroke populations that are typical targets for secondary prevention of new vascular events, i.e. patients with TIA or minor ischaemic strokes (NIHSS <4) of <24 h from symptom onset, and patients with stable disease with a first-ever ischaemic stroke during the previous six-months.

The prevalence of diabetes showed significant geographic variation, ranging from 29% in Latin America to 46% in the Middle East. If a fasting serum glucose concentration ≥7 mmol/l is considered to be a marker of diabetes in patients not treated for this condition, then the prevalence of diabetes would range from 34% in Latin America to 50% in the Middle East. Although these prevalence rates are similar to those reported in the CVD patients included in the REACH Registry or the Middle East, they are two- to threefold higher than the frequency reported in Europe and Australia (8). Similar results were observed in the OPTIC registry for obesity, with a prevalence ranging from 19% in Latin America to 35% in the Middle East. However, the prevalence of abdominal obesity ranged from 65% in North Africa to 78% in South Africa. Overall, the prevalence of hyperlipidaemia, smoking, and hypertension was similar to that in western European populations (8), but the main cardiovascular risk factors were slightly more prevalent in patients from the Middle East. Epidemiological transition probably explains the increase in risk

factor prevalence (9). As populations age and progress economically, the nature of the diseases shifts from those of poverty (infection, malnutrition, perinatal disease) to non-communicable disease including stroke.

As observed in the REACH Registry, the prevalence of hypertension, diabetes, hyperlipidaemia, and smoking tended to increase with the number of vascular beds involved (stroke; stroke and CAD or PAD; stroke and CAD and PAD). Polyvascular disease was found in 18% of cases and was significantly more frequent in the Middle Eastern population. While PAD was observed in only 8% of patients, an abnormal ABI was found in 22% of patients and CAD in 13% of cases. Prevalence of ABI was similar to that observed in other populations such as Asian patients (10).

On discharge from hospital, 96% of patients received antiplatelet agents, 79% received antihypertensive medication, 72% received lipid-lowering therapy, and 34% were treated with an antidiabetic agent. Forty-two per cent of patients not treated for hypertension on discharge had an elevated baseline blood pressure. Despite a prevalence of 49% for diabetes, only 36% of patients were treated with oral hypoglycaemic agents following discharge.

Given the high burden of risk factors that would require treatment with expensive drugs, it is noteworthy that 24% of patients had no health insurance or social security cover and could probably not afford long-term treatment for secondary prevention of stroke. Patients in North African countries not only had the worst risk factor profile overall, but 42% of patients from this region were not covered by health insurance or social security. These countries had the lowest use of ADP-receptor antagonists (13%) compared with Middle Eastern countries (65%). Not surprisingly, low income and high cost of certain drugs play an important role in prescription practices in countries where health insurance is not available. Significant disparities were noted in educational levels among the different regions. The highest rate of low-level education was noted in North Africa (62% of patients), while patients from South Africa showed the highest rate of high-level education (90%), which is unlikely to be reflective of the general population of South Africa. The impact of socio-economic factors on outcome and event recurrence is expected to be high (11,12).

One of the limitations of this registry is that it is a hospital-based rather than a population-based study, and the patients enrolled reflect the catchment areas of participating hospitals. Patients who did not seek medical attention (e.g. patients with milder or very severe strokes, poor patients, or those with TIA or minor strokes who were less informed about risk or concerned with their health) were unlikely to be included, and the underrepresentation of poor peoples has likely impacted our results towards an overestimation of provision of care in these countries. The overwhelming majority of South African patients were from urban areas, and stroke patients from poorer rural areas in the country are under-represented, so our results are unlikely to be generalizable to the entire region. Another limitation of this study is that only interested physicians participated and patients were more likely to be enrolled if they were able to return for follow-up visits, which overestimates access to care and underestimates the proportion of patients in the population with no health insurance or social security cover. Patients without health insurance may be treated in hospitals within the public healthcare system when seeking medical attention in the acute phase, but may be less likely to buy and take long-term medication if they have to bear the cost themselves. The follow-up part of our study will show the long-term (two-year) uptake of secondary prevention medication. In low- and middle-income countries with a tax-funded public healthcare system, the choice of drugs available in the public sector depends on health-economic issues based on a simple, cost-effective decision-making process (e.g. only aspirin or generic simvastatin may be available for secondary stroke prevention, having taken into account the cost and the 'numbers needed to treat for benefit' with an ADP-receptor antagonist vs. aspirin or a more recent, potent statin vs. simvastatin). By design, we have excluded patients who had a stroke deemed by investigators to be secondary to cardiac source of embolism. OPTIC registry cohort was therefore formed by atherothrombotic stroke patients. Cardioembolic strokes are likely more frequent in OPTIC registry countries than in western countries given the higher prevalence of valvular disease. Despite these limitations, the OPTIC registry provides useful information on low- and middle-income countries, which are usually not well represented or included in international registries. In the REACH Registry, only Israel, Lebanon, United Arab Emirates, and Saudi Arabia were included in the Middle East sample; in Latin America, only Brazil, Argentina, Mexico, Venezuela, and Chile were included; and no countries from North Africa were included. In the INTERSTROKE study (13), North Africa and most of Middle Eastern countries were not included.

In conclusion, the burden of modifying risk factors, particularly metabolic risk factors, was unusually high in the patients enrolled in the OPTIC registry. Targeted interventions that aim at lowering blood pressure, decreasing serum LDL-C concentrations, discontinuing smoking, and controlling diabetes may help reduce the burden of stroke and polyvascular disease recurrence. However, limited access to primary health care, particularly in rural areas, a high prevalence of low educational level, and the number of patients without health insurance or social security in some regions may significantly hamper such efforts. These issues will need to be addressed in order to reduce the burden of stroke in low- and middle-income countries.

Acknowledgements

Sophie Rushton-Smith, PhD, provided editorial assistance on the final version of this manuscript, including editing, checking content and language, and formatting, and received compensation from Sanofi-Aventis.

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