Stroke in Young Black Patients at Dr George Mukhari Hospital: A Retrospective Analysis

MMED (NEUROL)

M.R. MOKABANE
2012
Stroke in Young Black Patients at
Dr George Mukhari Hospital: A Retrospective Analysis

By

Mikateko Rosemond Mokabane

(MINI-) DISSERTATION
Submitted in (partial) fulfillment of the requirements for the degree of

Master of Medicine
in
Neurology

in the

FACULTY OF HEALTH SCIENCES
(School of Medicine)

at the

UNIVERSITY OF LIMPOPO
(MEDUNSA Campus)

Prof. DS Magazi

2012
DEDICATION

I dedicate this piece of work to my late father, Reverend Simon Hanyani Nkwinika; and my spiritual overseer, the late Reverend Nicholas Bhengu, founder of the Back to God Crusade of the Assemblies of God Church; and the Almighty God, Father of my Lord and Saviour, Jesus Christ.
DECLARATION

I declare that the mini-dissertation hereby submitted to the University of Limpopo, for the degree of Master of Medicine (Neurology) has not been previously submitted by me for a degree at this or any other university; that it is my work in design and in execution, and that all material contained herein has been duly acknowledged.

Mokabane, M.R. (Dr)                                          Date:
ACKNOWLEDGEMENTS

To my family, I wish to extend gratitude for the support you me gave throughout my studies. You always gave me an ear when I was down and lifted me up to finish the race.

I wish to express my heartfelt gratitude and thanks to Prof. Dali Magazi, the Head of Department of Neurology, University of Limpopo, for his mentorship, supervision, encouragement and support; and further for granting me an opportunity in the registrar training programme. Further I acknowledge Drs Moagi, Manyane and Iqbal for support and encouragement.

I also acknowledge the Medi-Clinic Group for sponsorship of my postgraduate studies.

I also wish to extend thanks to Ms Dinah Nkoana for administrative support, Ms Lydia Mantwa and Ms Tshidi Motau for assistance with retrieval of patients files for this study and to everyone else who made a direct and indirect contribution.
# Table of Contents

ABSTRACT .................................................................................................................. 7

CHAPTER 1 ................................................................................................................. 8
  INTRODUCTION AND BACKGROUND .................................................................. 8
  Problem statement ................................................................................................. 12
  Aim and Objectives ............................................................................................... 12

CHAPTER 2 ................................................................................................................. 14
  LITERATURE REVIEW ......................................................................................... 14
  Overview of Stroke ............................................................................................... 14
  Risk factors for stroke .......................................................................................... 14
    Non-modifiable risk factors for stroke ............................................................... 15
    Modifiable Risk Factors .................................................................................... 16

CHAPTER 3 ................................................................................................................. 22
  METHODOLOGY .................................................................................................... 22
  Study Design ......................................................................................................... 22
  Study Population ................................................................................................. 22
  Sample Size .......................................................................................................... 22
  Inclusion Criteria .................................................................................................. 22
  Exclusion Criteria ................................................................................................. 22
  Materials and Apparatus ...................................................................................... 23
  Data Collection ...................................................................................................... 23
  Data Analysis ........................................................................................................ 24
  Reliability .............................................................................................................. 24
  Validity ................................................................................................................... 24
  Bias ......................................................................................................................... 24
  Ethical Considerations ........................................................................................... 25
List of Tables

Table 1: Overview of studies on stroke in South Africa.................................................. 11
Table 2: Frequencies, percentages and cumulative frequencies of young stroke patients........ 26
Table 3: Age category and gender of young stroke patients............................................. 27
Table 4: Risk Factors for stroke among young black patients.......................................... 30
Table 5: Risk factor for stroke among young black stroke patients according to stroke subtype ................................................................................................................................. 31
Table 6: Stroke occurrence over the five year period......................................................... 31
Table 7: Type of radiological investigation........................................................................ 33
Table 8: Type of biochemical analytical investigation....................................................... 33

List of Figures

Figure 1: Distribution of patients over a five year period according to age. ....................... 26
Figure 2: Gender distribution of young stroke patients over a five year period................. 27
Figure 3: Geographic location of stroke patients............................................................... 28
Figure 4: Radiological findings and anatomical sites of haemorrhagic stroke.................. 32
Figure 5: Month of stroke occurrence in a total of 228 patients..................................... 34
ABSTRACT

Background and purpose: Stroke is the second most common cause of death worldwide. In South Africa, the true burden of stroke in the black population in general is unknown. Stroke is the third most common neurological condition seen in the Department of Neurology at Dr. George Mukhari hospital. Empirical evidence suggests an increase in recent years of the occurrence of strokes in young patients.

Aim and Objectives: The aim of the study was to investigate the demographics, risk factors and radiological patterns of stroke among the young black patients presenting at Dr. George Mukhari Hospital, Gauteng province, South Africa.

Methods: Medical records of 15 to 54 year old patients with strokes from the period 2005 to 2009 were retrospectively reviewed. Two hundred and twenty eight out of seven hundred and seven patients met inclusion criteria. Excluded were patients above the age of 54, and any patient without a CT scan done. Also excluded were patients with subarachnoid haemorrhage. Data was captured and analysed using the STATA version 11. Statistical significance was set at $P \leq 0.05$ with a 95% confidence interval.

Results: The male to female ratio of stroke occurrence was 1:1.33. Hypertension, hyperlipidemia and cardiac disease were major risk factors, 32.89%, 26.75% and 22.37%, respectively. There was a statistically significant gender difference in smoking ($P = 0.0000$) and alcohol usage ($P = 0.0000$) between males and females. Computed tomography revealed cerebral infarction in 92.98% of young black stroke patients. In patients with cerebral haemorrhage, hypertension was the most frequent (75%) risk factor. Of the 109 (47.81) patients tested for HIV, 73.39% ($n=80$) tested positive. The mean CD4 count was 178.95 cells/ul.

Conclusion: Hypertension remains an important risk factor even in young black stroke patients at Dr. George Mukhari. Hyperlipidemia is an important risk factor in our patient population which could be a finding peculiar to the urbanised black South African.

Recommendation: High blood pressure awareness of programmes are important as a preventative measure against strokes.
CHAPTER 1

INTRODUCTION AND BACKGROUND

The brain has no capacity for anaerobic respiration and has no energy storage system. This makes it particularly vulnerable to any interruption to the blood supply, the effects of which are immediate and this is what constitutes a stroke.

Strokes continue to be a common cause of morbidity and mortality. There is a paucity of stroke epidemiological data in Africa. Empirical evidence shows that strokes among the young are on the increase in recent years. At the Dr. George Mukhari hospital, the majority of our patients are black Africans thus affording us an opportunity to interrogate stroke in this relatively homogenous population. This is a tertiary hospital with a capacity of 1550 beds located approximately 35 km, north-west of Pretoria, the capital city of South Africa. It serves the North Western townships of Pretoria, including GaRankuwa, Soshanguve, Mabopane, Winterveld and others.

Epidemiology

Epidemiology of strokes in industrialised countries
In 1997, Murray and Lopez found stroke to be the second most common cause of death worldwide (Murray and Lopez, 1997). In 2002, stroke was the third leading cause of death and a major cause of disability in the western countries (Kochanek et al, 2004). In 2008, it was the fourth leading cause of disability and death in western countries (Minino et al, 2010). This decline is attributable to preventive measures and modification or control of modifiable risk factors (Roger et al, 2012; McCarron et al, 2006). The decline has however, not been observed among African Americans (Kleindorfer et al, 2010).

The availability of CT scans has made epidemiological studies on strokes more accurate. This further helps to identify the different stroke subtypes, viz., cerebral infarction, intracerebral haemorrhage and subarachnoid haemorrhage. The Manhattan study looked at incidence of strokes among blacks, whites and Hispanics, and found the overall incidence of stroke to be 23 per 100 000 population (Jacobs et al, 2002). The relative risk of any stroke in
the young was greater in blacks and significantly greater in Hispanics. On the other hand, young African Americans have two to three fold greater risk of ischaemic stroke than the Caucasian population of the same group. Higher incidence of stroke was reported among blacks than in Hispanics and whites (White et al, 2005). The incidence of ischaemic stroke per 100,000 was 191 for blacks, 149 for Hispanics and 88 for whites, respectively. Similar findings were reported by Kissela et al (2004) in a hospital-based biracial prospective study conducted in the greater Cincinnati metropolitan region between January 1993 and June 1994. The incidence rates per 100,000 for ever first stroke was 278 in blacks and 153 in whites (Kissella et al, 2004).

In the United Kingdom (UK) the incidence of stroke fell by 30% from 1.48 per 1000 population in 1999 to 1.04 per 1000 population in 2008. Crude mortality decreased from 21% in 1999 to 12% in 2008 (Lee et al, 2011). Martin et al (1997) estimated the annual incidence of young stroke in the UK to be approximately 10 per 100,000 with a male to female ratio of 1.6:1 in a prospective community based study. In Auckland, New Zealand, Carter et al (2006) also found a significant decrease in stroke incidence between 1981 and 2003 among whites but the rates remained high or increased in other ethnic groups.

Stroke was also reported the second leading cause of death for all ages in Taiwan since 1983. The 1994 National Health Survey (NHIS-1994) conducted by the Institute of Public Health of National Taiwan University revealed a crude prevalence for stroke of 5.95 per 1000 for all ages in Taiwan (Huang et al, 1997).

**Epidemiology of strokes in developing countries outside Africa**

Stroke is not limited to the western or high income countries. It is a global epidemic to the extent that about 85% of all stroke deaths occurred in developing countries (Murray & Lopez, 1997; Connor et al, 2007)). Epidemiological studies in developing countries, although small in number, provide evidence that stroke mortality rates tend to be higher than coronary heart disease rates (Zhai and McGarvey, 1992).

In India, the annual stroke incidence in a population-based study was reported to be 89 per 100,000 population (Gupta et al, 2008). According to Kaul et al (2009), the average annual incidence rate of stroke in India is 145 per 100,000 population, which is higher than the in western nation.
Epidemiology of stroke in sub-Saharan Africa

Stroke mortality in sub-Saharan Africa is as high, and even higher than in high-income regions with a lower prevalence, but disabling stroke is as prevalent (Connor et al., 2007). There is evidence that the incidence rates in developing countries have increased by more than 100 per cent during the last four decades, while they have decreased by 42 per cent in developed countries over the same period (Feigin et al., 2010). Two thirds of stroke deaths occurred in the developing regions of the world, such as Sub-Saharan Africa (Murray and Lopez, 1997; Connor et al., 2007).

A study conducted in Harare, Zimbabwe, by Matenga et al. (1986) found a stroke mortality rate of 35% one month after the stroke. In Tanzania, a population-based study was carried out to look at the mortality rate of stroke and 5.5 % of deaths were attributed to cerebrovascular disease (Walker et al., 2000). In a community-based study in rural and urban Tanzania, the overall crude yearly stroke incidence rates were 94.5 per 100 000 population in Hai and 107.9 per 100 000 population in Dar-es-Salaam (Walker et al., 2010).

A retrospective study in Nigeria looked at stroke data over a 10 year period, ie., 1993 to 2003, and the study revealed that stroke is a common entity in African Nigerians and remains a significant cause of mortality at all times. Intracerebral haemorrhage constituted 45% of the total strokes and cerebral infarction, 49% (Ogun et al., 2005). The age ranged from 27 to 96 years of age.

Epidemiology of stroke in South Africa

Studies on stroke incidence and prevalence rates in South Africa are few. A hospital-based prospective study conducted at Kalafong hospital between 1984 and 1985, found the incidence rate to be 1.01 per 1000 population per year. High incidences were also observed with increasing age and males in the ages 65 to 74 years. The mortality rate was 33.6% for the whole group, 22.4% for cerebral infarctions and 57.9% for cerebral haemorrhage (Rosman, 1986). Later, Joubert (1991) reported a mortality rate of 33% in a study conducted at the then GaRankuwa hospital (now Dr. George Mukhari hospital).
### Table 1: Overview of studies on stroke in South Africa

<table>
<thead>
<tr>
<th>Author</th>
<th>No. Patients</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosman, 1986</td>
<td>220 black patients at Kalafong hospital (prospective study)</td>
<td>Stroke incidence&lt;br&gt;Death rate of 33.6%&lt;br&gt;Hypertension – most common risk factor&lt;br&gt;Smoking and alcohol - less frequent</td>
</tr>
<tr>
<td>Joubert, 1991</td>
<td>304 black patients at GaRankuwa hospital (retrospective study)</td>
<td>Hypertension – most common risk factor&lt;br&gt;Mortality rate of 33%</td>
</tr>
<tr>
<td>Hoffman, 2000</td>
<td>320 (173 white, 100 black, 32 Asian Indian)</td>
<td>Infection may be an important factor in young black stroke including HIV, TB, neurocysticercosis and syphilis</td>
</tr>
<tr>
<td>Hoffman et al, 2000</td>
<td>172 patients at Durban metropolitan acute stroke unit (prospective study)</td>
<td>the cryptogenic stroke was more common in the HIV-infected population. HIV increased the risk of stroke.</td>
</tr>
<tr>
<td>Mochan et al, 2003</td>
<td>35 black patients (prospective study)</td>
<td>Most common coagulopathy – Protein S&lt;br&gt;Significant association between HIV and protein S deficiency</td>
</tr>
<tr>
<td>Connor et al, 2004</td>
<td>103, black patients</td>
<td>Hypertension most prevalent&lt;br&gt;Females &gt; males</td>
</tr>
<tr>
<td>Mochan et al, 2005</td>
<td>33 black patients</td>
<td>Presence of protein S deficiency in HIV + patients with stroke is an epiphenomenon in HIV infection</td>
</tr>
<tr>
<td>Patel et al, 2005</td>
<td>293 black patients</td>
<td>Chances of stroke higher in HIV + patients &lt;br&gt;HIV + status should not halt search for alternative aetiology</td>
</tr>
<tr>
<td>Tipping et al, 2007</td>
<td>67 HIV + patients, prospective study</td>
<td>A thorough investigation even in patients who are HIV positive is necessary to identify cause</td>
</tr>
<tr>
<td>Connor et al, 2009</td>
<td>308 black, 76 white</td>
<td>Cerebral haemorrhages, blacks &gt; whites&lt;br&gt;Hypertension, blacks = whites&lt;br&gt;Ischaemic heart disease uncommon in blacks</td>
</tr>
</tbody>
</table>

Connor *et al* (2004) conducted the first community-based study, the South African Stroke Prevention Initiative (SASPI) at Agincourt, Limpopo province. They found the crude prevalence for stroke to be 300/100 000 (95% CI, 250 to 375). Stroke prevalence was higher in females than males at 348 and 246, respectively.

A prospective study in Natal found a difference in risk factors between black and white subjects. White people had more traditional risk factors of hypertension, hyperlipidaemia and
alcohol abuse whereas in blacks infections like HIV, tuberculosis, neurocysticercosis and syphilis are common (Hoffman, 2000).

The paucity of epidemiological studies on stroke in South Africa is partly as a result of a scarcity of resources like the CT scan and/or MRI which are important for the definitive diagnosis.

**Problem statement**
Stroke is the third commonest condition that diagnosed and treated by the Department of Neurology at Dr. George Mukhari Hospital. Previous studies showed that age is the major risk factor for stroke (Martin *et al*, 1997 & Murray *et al*, 1997). In the past few years however, we have been seeing an increase in young strokes presenting at the Dr. George Mukhari hospital. It is in this light that we conducted this study.

**Aim and Objectives**
The aim of the study was to investigate the demographics, risk factors and radiological patterns of stroke among the young black patients presenting at Dr. George Mukhari Hospital, Gauteng province, South Africa.

**Objective of the study**
The objectives of the study were to determine:

- the prevalence of stroke in young black patients presenting at Dr. George Mukhari hospital
- the demography of stroke patients at Dr. George Mukhari hospital
- the occurrence of strokes over the years (2005 January to 2009 December) at Dr. George Mukhari hospital
- radiological patterns
- risk factors
- whether there is seasonal preference in occurrence of strokes

**Research Questions**

- Is there gender bias among the young stroke patients?
- How common is stroke in young patients and is it on the increase?
• What are the risk factors in young black patients with strokes?
• What are the radiological patterns?
• Is there any seasonality in occurrence?
CHAPTER 2

LITERATURE REVIEW

Overview of Stroke
Stroke is a condition made up of three pathological types, viz., cerebral infarction, cerebral haemorrhage and subarachnoid haemorrhage. Cerebral infarction occurs when an artery to the brain or in the brain gets narrowed or blocked, causing severely reduced blood flow (ischaemia). Diminished blood supply or lack of blood flow deprives the brain of oxygen and nutrients resulting in cell death. Cerebral haemorrhage on the other hand results when a blood vessel in the brain ruptures, usually the penetrating vessels. The majority of strokes, more than 85% are ischaemic and the remainder are haemorrhagic. Many factors can increase a person’s risk for stroke. Stroke risk factors are divided into modifiable and non-modifiable risk factors. Non-modifiable risk factors include age, male gender, genetic factors, family and previous history of stroke. Modifiable risk factors include hypertension, diabetes mellitus, cardiac disease, cigarette smoking, alcohol consumption, hyperlipidaemia, and others.

Three decades ago, strokes in young adults were uncommon and accounted for about 3% in those aged 15 and 45 years of age (Bevan et al, 1990 & Hart and Miller, 1983). Degenerative atherosclerotic disease and cardioembolism account for most ischaemic strokes in the elderly, whereas in the younger age groups cerebral infarction in younger age groups may be the presenting feature of a diverse range of local and systemic diseases (Martin et al, 1997). The young stroke patient requires extensive investigation in order to identify the underlying cause, many of which are treatable (Neto et al, 1996).

Risk factors for stroke
There are two categories of risk factors, viz., modifiable and non-modifiable. Modifiable risk factors are further divided into two categories, viz., lifestyle and medical factors. Among the modifiable risk factors are hypertension, hyperlipidaemia, cardiac causes, diabetes, smoking and obesity. Non-modifiable factors include age, gender, race, family history and a previous stroke.
Non-modifiable risk factors for stroke

Age is the single most important non-modifiable risk factor for stroke in both developing and non-developing countries. For each successive 10 years after age 55, the stroke rate more than doubles in both men and women (Brown et al, 1996 & Wolf et al 1992). Stroke incidence rates are 1.25 times greater in men, but because women tend to live longer than men, more women than men die of stroke each year (Sacco et al, 1997).

While stroke is common among the elderly, a lot of people under 65 also have stroke. The rate of stroke in African Americans is almost double that of Caucasians (Kissela et al, 2004 & Kleindorfer et al, 2010), and stroke tends to occur earlier in African Americans than Caucasians (Kleindorfer et al, 2010). Even though age is the most single important risk factor for stroke, of note is that 12 per cent of first stroke occur in patients younger than 45 years of age (Martin et al, 1997). In India, 10% to 15% of strokes occur in people aged below 40 years (Kaul et al, 2009). In blacks, stroke tends to occur at a younger age compared to whites (Stewart et al, 1999).

Strokes occur more frequently in male and yet mortality of strokes was higher in women. According to Reeves et al (2008) women and men share the same traditional risk factors for stroke. A number of studies however have shown that at the onset of stroke hypertension and atrial fibrillation are more prevalent in women. In men, peripheral vascular disease, diabetes mellitus, alcohol consumption and smoking are more prevalent. In the younger age group the female to male ratio seems to be higher. In the SASPI study, stroke prevalence was higher in females than in males (Connor et al, 2004).

According to Martin et al (1997) heredity plays a minor role in the pathogenesis of cerebral infarction. However, increased risk is seen in family history of stroke among first degree relatives. Accelerated atherosclerosis has been shown to occur with hereditary dyslipoproteinemias. A number of inherited diseases are non-atherosclerotic in nature, viz, Ehlers-Danlos syndrome (especially type IV), Marfans syndrome, osteogenesis imperfecta, Rendu-Osler-Weber syndrome, cerebral autosomal dominant arteriopathy with subcortical infarcts with leucoencephalopathy (CADASIL), mitochondrial cytopathies like mitochondrial encephalopathy, lactic acidosis and stroke-like episodes (MELAS), etc.
**Modifiable Risk Factors**

**Hypertension**

Hypertension is the single most important risk factor for ischaemic stroke. All stroke studies in South Africa and abroad list hypertension as the most prevalent risk factor. The most extensive epidemiological study on stroke in South Africa to date by Rosman (1986) was conducted at Kalafong Hospital in Pretoria. The focus of the study was on stroke in the black urban population of Mamelodi and Atteridgeville. The study found hypertension to be the single highest risk factor with the prevalence of 69.8%. A study conducted at GaRankuwa by Joubert (1991) also found hypertension to be the most prevalent risk factor for stroke at 42.4%.

Other studies in Africa and the USA among the African black population show similar prevalence of hypertension in black stroke patients (Abraham et al, 1971; Rosman, 1986; Joubert, 1991 & Qureshi et al, 1995). A meta-analysis on stroke studies from 1990 to 2009 conducted by the University of Nigeria, Department of Clinical Pharmacology, found the prevalence of hypertension to be from 12.4% to 34.8% in the general Nigerian population (Ekwunife and Aguwa, 2011).

Sacco et al (1997) however, found that hypertension is more prevalent in blacks than whites. Qureshi et al (1995) also found hypertension was frequently associated with stroke in young black patients than in non-white patients. Racial differences in renal physiology and environmental influences such as socio-economic status seem to be likely candidates for important contributions to blood pressure differences (Gillium, 1979). Opie and Seedat (2005) found environmental factors to be more important than the genetic in explaining higher incidence of severe hypertension in black subjects. From the available data focusing on black groups, hypertension seems more common with increasing urbanisation, leaving behind a group of truly rural dwellers who still seem relatively protected (Opie and Seedat, 2005). According to Ergul (2000), hypertension in blacks is characterised by an abnormal hemodynamic reactivity and increased salt sensitivity and both normotensive and hypertensive black individuals are known to be more salt sensitive than white Americans.

Aggressive treatment of hypertension can reduce incidence of stroke. A study conducted in rural north-eastern Japan in 1965 where 3219 people were assigned to a full intervention
community programme, and 1468 to a minimal intervention community programme showed an overall decline in incidence of stroke for men, 75% in the full intervention community and 29% in the minimal intervention community, however, stroke occurrence in women was less affected. Stroke incidence declined significantly in the former group than in the latter group (Iso et al, 1998).

Reduction of hypertension directly leads to lowering of cardiovascular disease and all stroke prevention measures should start at treatment of hypertension.

**Hyperlipidemia**
A study conducted in Washington DC found the prevalence of hyperlipidemia to be the same for whites and African Americans (Prisant et al, 2000 & Song et al, 2012). Unlike hypertension and diabetes, hyperlipidemia is not an obvious noticeable ailment. Studies conducted in South Africa showed that black Africans have lower total cholesterol and lower density lipoproteins and higher levels of the protective high density lipoproteins (Maritz, 2006). Connor et al (2009) also found low levels of cholesterol in black South Africans. It is worth noting that in the light of the HIV/AIDS pandemic is the association of hyperlipidaemia with protease inhibitors which results in high total cholesterol to low high density lipoproteins (Tsiodras et al, 2000).

**Diabetes Mellitus**
Diabetes mellitus is an important risk factor for stroke. Patients with diabetes mellitus are at increased risk for both stroke and hypertension (Barret-connor and Khaw, 1988). According to Bevan et al (1990), the increased risk of stroke in patients with hypertension may be attributable to glucose abnormality and not necessarily related to blood pressure. A prospective study conducted in a Finish population found that blood pressure levels in diabetic subjects were much higher than in non-diabetic subjects. The study further showed that diabetes is a strong and independent risk factor for death from stroke among both men and women (Tuomilehto et al, 1996). Diabetes was found to be a risk factor in 14% of black patients in a study conducted at Johannesburg hospital, South Africa (Connor et al, 2009).

Duration of diabetes is independently associated with ischemic stroke, and the risk increases by 3% each year, and triples with diabetes ≥10 years (Banerjee et al, 2012).
Smoking

Smoking is an independent risk factor for stroke in men and women of all age groups and race groups. Smoking causes more death and disability in the UK than any other avoidable stroke risk factor (Lewis et al, 2005). Smoking also nearly doubles the risk of ischemic stroke (Shinton and Beevers, 1989). A prospective cohort study of 6780 men and women with stroke in an adult population in China found that there was a positive and dose-response relationship between cigarette smoking and risk of stroke (Kelly et al, 2008).

Statistic SA (1999) between 1990 and 1998 showed that cigarette consumption in South Africa decreased by approximately 40 per cent. The government taxes on cigarettes made smoking too expensive for poor people. According to Peer et al (2009) smoking rates in South Africa decreased rapidly between 1992 and 1998, dropping from 52% to 42% in men, and continued declining from 1998 to 2003. The coloured people have the highest smoking prevalence of all South Africans at 49%, followed by whites and Indians at 37% and 28%, respectively. Blacks are the lowest at 22.7%. The study also indicates that the prevalence is high among males than females. Black men and women smoked significantly less than other population groups.

Alcohol

Light to moderate consumption of alcohol has been shown to be protective against stroke but heavy alcohol consumption is associated with increased risk (Hansagi et al, 1995). In the Physicians’ Health Study, the benefit was observed among physicians who had only one alcoholic drink per week, and the magnitude of this protective effect did not increase with increased alcohol consumption (Berger et al, 1999). Alcohol consumption may have a distinct dose-response relationship within each stroke subtype; linear in subarachnoid haemorrhage, U-shaped in intracerebral haemorrhage, and J-shaped in cerebral infarction, but further studies are warranted (Leppälä et al, 1999).

Heavy drinking (>60 g/d) is related to increased risk of both haemorrhagic and ischemic stroke (Donahue et al, 1986 & Gill et al, 1991). The Honolulu Heart Programme which is based on longer follow-up (12 years) study on alcohol and haemorrhagic stroke, found that the risk of intracranial haemorrhage increases monotonically with increased alcohol intake to the extent that heavy drinkers have three times the risk of stroke than non-drinkers (Donahue et al, 1986).
Obesity
Obesity has been shown in a number of studies to be associated with an increased risk of stroke (Kurth et al, 2002). High body mass index (BMI) may increase the risk of total stroke, especially ischaemic stroke. A prospective study of 22,071 males in the US aged 40 to 84 years found that an increasing BMI was associated with a steady increase in the risk of total, ischaemic and haemorrhagic stroke (Kurth et al, 2002). Although high body mass index (BMI) is regarded as a risk factor for stroke, a population-based case control study of 576 ischaemic stroke cases and 1142 controls found that increased waist-to-hip ratio (WHR) was associated with a greater risk of stroke in men and women in all race-ethnic groups (Suk et al, 2003).

Cardiogenic embolism
A cardiac source of emboli is found in 20-30 % of young stroke patients. In a study conducted in Atlanta among young black patients with stroke, most ischaemic strokes were attributable to small vessel occlusion, which differed from results of other studies where ischaemic strokes were due largely to cardioembolism and dissection of large vessels (Qureshi et al, 1995). The most common lesions are prosthetic heart valves, rheumatic to valve disease, bacterial endocarditis, dilated cardiomyopathy, ischaemic dyskinetic segments, atrial septal aneurysm, patent foramen ovale, and mitral valve prolapsed. Carotid dissection accounts for 10-25% of stroke in the 15-45 year age (Martin et al, 1997).

According to Adams et al (1986), when the causes of stroke in the young are broken down by age, atherosclerosis becomes increasingly prominent from the 15-30 year age group (2%) to the 30-45 year group (30-35%). In addition to the usual risk factors (hypertension, cigarette smoking, hyperlipidaemia and diabetes mellitus), premature atherosclerosis has less widely recognised associations. Blunt arterial trauma is recognised as an important additional cause of cerebral infarction among young adults (Adams et al, 1986)

Coagulopathies
Coagulopathies are an important risk factor for stroke amongst young people. A retrospective case control study in a large inner city hospital in the US, found the frequency of cerebral infarctions associated with protein S deficiency to be higher in HIV-infected patients than in seronegative patients (Qureshi et al, 1997). Mochan et al, in a case control
study in Baragwanath hospital also found that proteins S deficiency occurred more frequently in HIV positive than in HIV negative patients (Mochan et al, 2005).

**Other Risk Factors**

Vasculitis can affect the central nervous system (CNS) as an isolated phenomenon (isolated angiitis of the CNS) or as part of a systemic necrotising vasculitis (e.g., Wegener's, polyarteritis nodosa). Other categories of arteritis include autoimmune disorders (rheumatoid arthritis, systemic lupus erythematosus, scleroderma, etc.), infections like herpes zoster, cytomegalovirus, human immunodeficiency virus (HIV) and tuberculosis (Martin et al, 1996).

A study conducted at Groote Schuur hospital, Cape Town, showed that in 20% of HIV positive patients who presented with stroke, there was radiological evidence of intracranial (9%) or extracranial (11%) vasculopathy for which no other cause could be determined (Tipping et al, 2007). A Johannesburg based study found the risk factors for stroke in young HIV positive black South Africans to be similar to the HIV negative group (Mochan et al, 2003). A study in KwaZulu-Natal (KZN) found that a positive HIV test does not provide causal information (Patel et al, 2005).

**Oral contraceptives**

High dose oestrogen oral contraceptives, particularly with coexisting hypertension, cigarette smoking, migraine and increasing age are associated with an increased risk of stroke (Bousser and Kittner, 2000). The newer oral contraceptives with lower oestrogen levels however, do not seem to pose a significant independent risk for strokes (Petitti et al, 1996)

**Seasonal variation of stroke**

A seasonal variation in the incidence of stroke events in both men and women and in younger and older age groups has been described. Turin et al (2008) found stroke incidence to be higher in the spring, followed closely by the winter season. A similar pattern seasonal pattern of stroke was observed for both cerebral infarction and haemorrhage and that this pattern seemed to hold regardless of the presence or absence of a history of risk factors such as hypertension, diabetes mellitus, cigarette smoking and alcohol consumption. Blood pressure, shows marked seasonal variation, being higher in winter (colder) months and that is a strong
risk factor for both stroke and acute myocardial infarction and venous thromboembolism (Dobson, 2004)
CHAPTER 3

METHODOLOGY

Study Design
This was a descriptive retrospective study conducted at Dr George Mukhari Hospital.

Study Population
The Department of Neurology diagnose and treats stroke patients from the age of 13 to 60 years, whereas the Department of Internal Medicine diagnose and treats stroke patient above the age of 60 years. The study population comprised of 707 stroke patients from the age of 15 years seen at Neurology outpatients’ clinic and admitted stroke patients admitted to the medical wards by the Departments of Neurology and Internal Medicine over a five year period, January 2005 to December 2009.

Sample Size
All young stroke patients (n=228) formed part of the study out of the 707 patients from the Data Base from the period January 2005 to December 2009. Young stroke refers to stroke below the age of 55. Patients were divided into four categories, viz., 15-24, 25-34, 35-44 and 45-54 years of age.

Inclusion Criteria
Hospital records of patients admitted with stroke in the medical wards and those seen at Neurology outpatients from the age of 15 years to 54 years between 2005 January to 2009 December were included. All patients should fit the WHO definition of stroke “Neurological deficit of cerebrovascular cause that persists beyond 24 hours or interrupted by death in 24 hours” (WHO, 1997).

Exclusion Criteria
- Neurological deficit not of vascular origin, e.g., brain tumour.
- Stroke due to subarachnoid haemorrhage.
Materials and Apparatus
There was primary data collected from January 2005 to December 2009 that was used for the study. Secondary data was collected from Hospital records of patients including discharge summaries; laboratory results; pharmacy scripts; electrocardiogram (ECG), echocardiogram (cardiac echo), Carotid Doppler and brain CT scan reports and information from the Data Bank of the Department of Neurology.

Data Collection
All new patients seen at Neurology outpatients’ clinic and those admitted to the wards are seen by the registrar in attendance. On consultation by the registrar, he/she follows a prescribed protocol (Annexure A) to record information from the patient and then examines the patient. The patient is then presented to the consultant. Subsequently, a typed report (summary) is compiled and assessed by the Head of Department before it is filed into the Department’s Data Bank.

Data was collected from the aforementioned stroke data bank from the Department of Neurology and hospital records in the hospital patient files at Dr George Mukhari hospital. The following data was collected:

- Age, gender, geographic location and risk factors.
- RPR, TPHA, autoimmune screen, Protein S and C, antiphospholipid antibodies, lipid profile and HBA1c.
- Where relevant CSF results
- Results from previous laboratory tests.
- Imaging and reports – Brain CT scan (infarction or haemorrhage).
- Cardiac evaluation - ECG, Cardiac Echo, Carotid Doppler.

Information was presumed absent if clear documentation was not found, e.g., ECG records, Cardiac Echo, Carotid Doppler, CT scan brain reports and biochemical results. If such information is not available, it should at least be documented in the patient’s notes.
Data Analysis
Data was captured and analysed using STATA version 11. Statistical significance was set at $P \leq 0.05$ with 95% confidence interval. Chi-Square test to compare stroke patients will also be conducted, as well as ANOVA tests.

Reliability
All the patients were consulted and treated by a registrar supervised by a Neurologist or Physician. All the scans were reported by the Department of Radiology and confirmed by a Neurologist or Physician. This highly enhanced the sensitivity and specificity of the diagnostic tool.

Validity
Stroke is diagnosed based on history, clinical assessment and supportive radiological findings on CT scan brain. The CT scan brain is a gold standard imaging modality for patient with stroke and thus reliable.

Bias

Selection bias
This is a retrospective descriptive study and hospital based. Thus, stroke patients that demised before reaching the hospital and those that do not seek medical attention would have been missed.

Diagnostic bias
A standardised form (Annexure A) and data collection sheet (Annexure B) were used and the same researcher has gone through the documentation. All the patients were have been seen by a Registrar, Neurologist or Physician. Correlation of clinical findings and radiological findings will be made, thus minimising this type of bias. Brain CT scans done within 24 hours of onset of stroke might have possibly missed early infarcts.
Ethical Considerations
Permission to conduct the study was obtained from the School Research Ethics Committee (SREC) and MEDUNSA Research Ethics Committee (MREC), and the Dr. George Mukhari Hospital administration. The study commenced after permission was granted by the SREC and MREC.

Information from patients’ records was treated with the highest confidentiality. No names and personal details of patients were published.
CHAPTER 4

RESULTS

Young stroke patients (15-54) comprised almost a third of patients seen at Dr. George Mukhari hospital (228:707, 32.25%). There were 30 (13.16%) young stroke patients in 2005, 26 (11.04%) in 2006, 31 (13.60%) in 2007, 64 (28.07%) in 2008 and 77 (33.77%) in 2009 (Table 2). The highest number of patients was in 2009 and the least in 2005 (Figure 1). The patient’s demographic information, risk factors, radiological findings as well as biochemical results, and seasonality of strokes are reported below.

Table 2: Frequencies, percentages and cumulative frequencies of young stroke patients

<table>
<thead>
<tr>
<th>Year</th>
<th>Freq.</th>
<th>Percentage</th>
<th>Cum.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>30</td>
<td>13.16</td>
<td>13.16</td>
</tr>
<tr>
<td>2006</td>
<td>26</td>
<td>11.40</td>
<td>24.56</td>
</tr>
<tr>
<td>2007</td>
<td>31</td>
<td>13.60</td>
<td>38.16</td>
</tr>
<tr>
<td>2008</td>
<td>64</td>
<td>28.07</td>
<td>66.23</td>
</tr>
<tr>
<td>2009</td>
<td>77</td>
<td>33.77</td>
<td>100.00</td>
</tr>
<tr>
<td>Total</td>
<td>228</td>
<td>100.00</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1: Distribution of patients over a five year period according to age.
Age and Gender

From the four age categories as indicated in Table 3, the age category 45-54 showed the highest number of stroke patients, 50 males and 37 females. The age category 35-44 was the second highest with a predominance of females, 44 (63.77%) and 25 (36.23%) males. The age category 15-24 had the least number of patients with a predominance of females, 5 (21.74%) males and 18 (78.26%) females. From the year 2007 there are steep increase in the number of males. There were 130 (57.02%) female and 98 (42.98%) male patients (mean, 36.94 and 41.92, respectively), with a female to male ratio of 1.33:1.

Table 3: Age category and gender of young stroke patients

<table>
<thead>
<tr>
<th>Age category</th>
<th>Gender</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female (%)</td>
<td>Male (%)</td>
</tr>
<tr>
<td>15-24</td>
<td>18 (78.26)</td>
<td>5 (21.74)</td>
</tr>
<tr>
<td>25-34</td>
<td>31 (63.27)</td>
<td>18 (36.73)</td>
</tr>
<tr>
<td>35-44</td>
<td>44 (63.77)</td>
<td>25 (36.23)</td>
</tr>
<tr>
<td>45-54</td>
<td>37 (42.53)</td>
<td>50 (57.47)</td>
</tr>
<tr>
<td>Total</td>
<td>130</td>
<td>98</td>
</tr>
</tbody>
</table>

Figure 2: Gender distribution of young stroke patients over a five year period
Geographic Location
Hundred and one patients (44.3%) came from Soshanguve; 16.23% \((n=37)\), Brits; 10.53% \((n=24)\), Mabopane; 10.1% \((n=23)\), Garankuwa; 6.58% \((n=15)\), Hammanskraal; 4.39% \((n=10)\), Pretoria North; 3.51% \((n=8)\), Limpopo Province; 1.32% \((3)\), North West Province and other provinces, respectively. No address was furnished in 3 patients 1.32% \((n=3)\).

![Figure 3: Geographic location of stroke patients](image)

Risk Factors for Stroke
The frequency of risk factors among young black patients is shown in Tables 4 and 5. Hypertension was the highest frequent risk factor among young black patient and was more in females than males \((P = 0.636)\). It was predominant in patients with both cerebral infarction and hypertension.

Hyperlipidemia was the second frequent risk factor (26.75%). Of the 61 patients, 11 (18.03%) patients had hypercholesterolemia with a mean cholesterol of 5.5 mmol/L, 8 (13.11%) patients had hypertriglyceridemia with a triglyceride mean of 1.96 mmol/L, 21 (34.42%) patients had low HDL with an HDL mean of 0.69 mmol/L; and 18(29.51%)
patients had high LDL with an LDL mean of 3.20 mmol/L. The gender difference for hyperlipidaemia was statistically insignificant (P=0.590).

Cardiac disease was the third frequent a risk factor in 23.25% (n=53). Cardiac risk factors ranged from vulvular pathology (n=17), enlarged chambers (n=16), dysrhythmias (n=6), cardiomyopathy (n=4), infective endocarditis (n=4) and ischaemic heart disease (n=1). Of the 4 patient with a cardiomyopathy one had a dilated cardiomyopathy. There was no statistical gender difference (P = 0.378).

The least common risk factors were family history of stroke; trauma (n=4), herpes ophthalmicus (n=2), atrial fibrillation (n=2), oral contraceptive (n=1) and migraine (n=1), and statistically they were non-significant. The patient on oral contraceptives had hypercholesterolemia and high LDL. Both patients with atrial fibrillation were females and in the age group 25-34 and 45-54 years of age. Migraine was the likely cause in one patient with no additional risk factors.

The risk factors were unknown in 43 patients. Cigarette smoking and alcohol consumption were predominant in males than females. The gender difference was statistically significant (P = 0.0000), respectively).
Table 4: Risk Factors for stroke among young black patients

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>No of patients (%)</th>
<th>Females (n)</th>
<th>Males (n)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>76 (33.33)</td>
<td>44</td>
<td>32</td>
<td>0.636</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>61 (26.75)</td>
<td>33</td>
<td>28</td>
<td>0.590</td>
</tr>
<tr>
<td>Cardiac cause</td>
<td>53 (23.25)</td>
<td>29</td>
<td>24</td>
<td>0.378</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>31 (13.6)</td>
<td>6</td>
<td>25</td>
<td>0.0000</td>
</tr>
<tr>
<td>Neurosyphilis</td>
<td>28 (12.28)</td>
<td>14</td>
<td>14</td>
<td>0.423</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>21 (9.21)</td>
<td>11</td>
<td>10</td>
<td>0.936</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>18 (7.89)</td>
<td>3</td>
<td>15</td>
<td>0.0000</td>
</tr>
<tr>
<td>Previous CVA</td>
<td>14 (6.14)</td>
<td>8</td>
<td>6</td>
<td>0.992</td>
</tr>
<tr>
<td>Meningitis</td>
<td>14 (6.14)</td>
<td>6</td>
<td>8</td>
<td>0.269</td>
</tr>
<tr>
<td>Puerperium</td>
<td>12 (4.26)</td>
<td>12</td>
<td>N/A</td>
<td>0.002</td>
</tr>
<tr>
<td>Autoimmune conditions</td>
<td>12 (4.26)</td>
<td>7</td>
<td>5</td>
<td>0.488</td>
</tr>
<tr>
<td>Obesity</td>
<td>6 (2.63)</td>
<td>4</td>
<td>2</td>
<td>0.268</td>
</tr>
<tr>
<td>Trauma</td>
<td>4 (1.75)</td>
<td>2</td>
<td>2</td>
<td>0.775</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>2 (0.88)</td>
<td></td>
<td>2</td>
<td>0.217</td>
</tr>
<tr>
<td>Family history</td>
<td>2 (0.88)</td>
<td>1</td>
<td>1</td>
<td>0.840</td>
</tr>
<tr>
<td>Herpes ophthalmicus</td>
<td>2 (0.88)</td>
<td>1</td>
<td>1</td>
<td>0.840</td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>1 (0.44)</td>
<td>1</td>
<td>N/A</td>
<td>0.384</td>
</tr>
<tr>
<td>Migraine</td>
<td>1 (0.44)</td>
<td>1</td>
<td>0</td>
<td>0.384</td>
</tr>
<tr>
<td>Unknown</td>
<td>43 (18.86)</td>
<td>24</td>
<td>19</td>
<td></td>
</tr>
</tbody>
</table>

*Patients may have more than one risk factor.
Table 5: Risk factor for stroke among young black stroke patients according to stroke subtype

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Infarcts (n=212)</th>
<th>Haemorrhages (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No of patients</td>
<td>(%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>64 (30.19%)</td>
<td>12 (75%)</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>58 (27.36%)</td>
<td>3 (18.75%)</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>49 (23.11%)</td>
<td>4 (25%)</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>24 (11.32%)</td>
<td>4 (25%)</td>
</tr>
<tr>
<td>Neurosyphilis</td>
<td>26 (12.26%)</td>
<td>2 (12.5%)</td>
</tr>
<tr>
<td>Meningitis</td>
<td>14 (6.60%)</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>18 (8.49%)</td>
<td>1 (6.25%)</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>17 (8.02%)</td>
<td>1 (6.25%)</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>13 (6.13%)</td>
<td>1 (6.25%)</td>
</tr>
<tr>
<td>Autoimmune</td>
<td>12 (5.66%)</td>
<td>0</td>
</tr>
<tr>
<td>Puerperium</td>
<td>11 (5.19%)</td>
<td>1 (6.25%)</td>
</tr>
<tr>
<td>Autoimmune diseases</td>
<td>12 (5.66%)</td>
<td>0</td>
</tr>
<tr>
<td>Obesity</td>
<td>5 (2.36%)</td>
<td>1 (6.25%)</td>
</tr>
<tr>
<td>Trauma</td>
<td>4 (1.89%)</td>
<td>0</td>
</tr>
</tbody>
</table>

*Patients may have more than one risk factor

Table 6: Stroke occurrence over the five year period

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of patients (%)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hypertension</td>
<td>Hyperlipidaemia</td>
<td>Cardiac disease</td>
<td>HIV Infection</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>4 (5.26%)</td>
<td>6 (9.84%)</td>
<td>5 (9.43%)</td>
<td>11 (13.75%)</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>10 (13.16%)</td>
<td>4 (6.56%)</td>
<td>8 (15.09%)</td>
<td>14 (17.50%)</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>13 (17.11%)</td>
<td>12 (19.67%)</td>
<td>9 (16.98%)</td>
<td>10 (12.50%)</td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>19 (25%)</td>
<td>11 (18.03%)</td>
<td>17 (32.08%)</td>
<td>22 (27.50%)</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>30 (39.47%)</td>
<td>28 (45.9%)</td>
<td>14 (26.42%)</td>
<td>23 (28.75%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>76</td>
<td>61</td>
<td>53</td>
<td>80</td>
<td></td>
</tr>
</tbody>
</table>
Investigations

Radiological Findings
Computed tomography (CT scan) of the head was performed on all 228 patients. The scan revealed cerebral infarction in 92.98% (n=212) patients, intracerebral haemorrhage in 16 (7.02%) (Figure 4). Of the 16 bleeds, 43.75% were putaminal; 18%, brainstem; 12.5%, hemispheric and thalamic, respectively; 6.25%, cerebellar and non-specified in another 6.25% (Figure 5).

![CT Scans and Haemorrhages Diagram]

Figure 4: Radiological findings and anatomical sites of haemorrhagic stroke

Electrocardiography was done in 47 patients (20.61%) and was normal in 17 patients (36.17%) and abnormal in 30 patients (63.83%). Echocardiography was done on 47 patients (20.61%) and was normal in 13 patients (28.26%) and abnormal in 33 patients (71.73%). Carotid Doppler studies were done on 16 patients (7.08%) and were normal in 11 (68.75%) and abnormal in 5 (31.25%). The abnormal Carotid Doppler showed a plaque in the right carotid artery in 2 cases; right carotid stenosis in 1 case and right internal carotid artery stenosis in another patient, a huge thrombus in the left carotid artery in 1 patient.
Table 7: Type of radiological investigation

<table>
<thead>
<tr>
<th>Radiological study</th>
<th>No. of patients n=228</th>
<th>Normal</th>
<th>Abnormal</th>
<th>Not done n=228</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG</td>
<td>47 (20.61%)</td>
<td>17 (n=47; 36.17%)</td>
<td>30 (n=47; 63.83%)</td>
<td>181 (79.39%)</td>
</tr>
<tr>
<td>Echo</td>
<td>48 (21.05%)</td>
<td>12 (n=48; 25%)</td>
<td>36 (n=48; 75%)</td>
<td>180 (78.95%)</td>
</tr>
<tr>
<td>CD</td>
<td>16 (7.02%)</td>
<td>11 (n=16; 68.75%)</td>
<td>5 (n=16; 31.25%)</td>
<td>212 (92.98%)</td>
</tr>
</tbody>
</table>

Table 8: Type of biochemical analytical investigation

<table>
<thead>
<tr>
<th>Biochemical analysis</th>
<th>No. of patients n=228</th>
<th>Abnormal</th>
<th>Normal</th>
<th>Not done n=228</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>109 (47.81%)</td>
<td>80 (73.39%)</td>
<td>29 (26.61)</td>
<td>119 (52.19%)</td>
</tr>
<tr>
<td>RPR</td>
<td>150 (65.79%)</td>
<td>15</td>
<td>135</td>
<td>78 (34.21%)</td>
</tr>
<tr>
<td>TPHA</td>
<td>77 (33.77%)</td>
<td>26</td>
<td>51</td>
<td>151 (66.23%)</td>
</tr>
<tr>
<td>Lipogram</td>
<td>91 (39.91%)</td>
<td>55</td>
<td>36</td>
<td>137 (60.09%)</td>
</tr>
<tr>
<td>HBA1c</td>
<td>29 (12.72%)</td>
<td>12</td>
<td>15</td>
<td>199 (87.28%)</td>
</tr>
<tr>
<td>ANA</td>
<td>61 (26.75%)</td>
<td>12</td>
<td>49</td>
<td>167 (73.25%)</td>
</tr>
<tr>
<td>Platelets</td>
<td>211 (92.54%)</td>
<td>28</td>
<td>183</td>
<td>17 (7.46%)</td>
</tr>
<tr>
<td>CSF</td>
<td>18 (7.89%)</td>
<td>16</td>
<td>2</td>
<td>108 (92.11%)</td>
</tr>
<tr>
<td>Antiphospholipid</td>
<td>13 (5.70%)</td>
<td>2</td>
<td>11</td>
<td>215 (94.30%)</td>
</tr>
<tr>
<td>antibodies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein S</td>
<td>15 (6.58%)</td>
<td>2</td>
<td>13</td>
<td>213 (93.42%)</td>
</tr>
<tr>
<td>Protein C</td>
<td>16 (7.02%)</td>
<td>2</td>
<td>14</td>
<td>212 (92.98%)</td>
</tr>
</tbody>
</table>

* The CD4 count of 57 HIV positive patients was below 200 and in 23 patients was above 200 cells/ul. The mean CD4 count of HIV positive patients was 178.95 cells/ul. Of those who tested positive, 53.83% (n=35) were women and 46.15% (n=30), men. CSF VDRL was positive in 2 patients. Fourteen patients had thrombocytopenia and another 14 had thrombocytosis.
Seasonality of Strokes
Twenty eight per cent (n=65) of the strokes occurred in summer, 27.19% (n=62), 18.86% (n=43) and 22.37% (n=51). Thirty five (15.36%) of the strokes occurred in the month of January; 22 (9.6%) in February; 20 (8.77%) in March, April and October, respectively; 17 (7.46%) in September; 16 (7.14%) in July, 15 (6.58%) in November and December, respectively; 14 (6.14%) in June and August, respectively; 13 (5.7%) in May.

Figure 5: Month of stroke occurrence in a total of 228 patients
CHAPTER 5

Discussion
The study shows that age is an important risk factor for stroke. There is an increase in the occurrence of stroke with increasing age. In the age group 15-24, there were 10.09% (n=23) patients, followed by 21.05% (n=48), 31.58% (n=72) and 37.28% (n=86) patients in the age groups, 25-34, 35-44 and 45-54, respectively. This is similar to previous studies (Hart and Miller, 1983 & Connor et al, 2004). The prevalence of young stroke patients in our study is 32.25%. This is higher compared to 8.5% (113/1331) found by Bevan et al (1990) in a retrospective study of stroke patients over a six year period, 1982 and 1987. In the latter study, the patients’ age ranged from 15 to 45 year, whereas in this study, the age range was 15 to 54 years of age. The prevalence of young stroke patients in Hoffmann’s (2000) study was comparable to our study at 25% (320:1 260). The age range was 15 to 49, whereas in our study it was 15 to 54 years of age.

In this study, there is a predominance of females with a female to male ratio of 1.33:1, but the gender difference is statistically insignificant. The SASPI field study found a crude male to female ratio of 1:1.8, but it should be noted that the SASPI field study was a community-based study at Agincourt and included age groups from 15 and above (Connor et al, 2004). Male gender has been shown to be a risk factor in a number of studies (Ayala et al, 2002). In this study, stroke in women occurred at a younger age compared to men and the mean age difference was 4.98 years.

The majority of our patient population came from Soshanguve. This is the youngest of the townships in the hospital’s drainage area formed in 1974. The name is an acronym of its constituent ethnic groups, viz, Sotho, Shangaan, Nguni and Venda. This township alone has a population of approximately 600 000 people (Censors, 2001).

This study found hypertension to be the most important risk factor with the highest frequency, 33.33% (n=76). The figures are similar to Hoffman’s findings of a prevalence of 31% among patients in a similar setting in South Africa (Hoffman, 1998). Previous studies have shown that hypertension is the most prevalent risk factor in both the young and old (Rosman, 1986; Qureshi et al, 1995, Zanebe et al, 2005 & Connor et al, 2009). The prevalence of hypertension as a risk factor in this study is lower than findings from a similar study conducted by Qureshi et al (1995) among young black patients in Atlanta, who found a frequency of 55%. This study was conducted in a well-developed country. Ten years earlier,
a similar study was conducted in the same hospital where the current study was conducted. The frequency for hypertension as a risk factor was 42.4%. In this study, hypertension was a risk factor in 75% (n=12/16) of patients with cerebral haemorrhage and 29.72% (n=63/212) with cerebral infarction. This is consistent with the study in Atlanta (Qureshi, 1995). Twenty four (31.58%) patients with hypertension were investigated with transthoracic echocardiography, 30.26% (n=23) and 11.84% (n=9) with carotid doppler ultrasound. Such low frequency of radiological investigation can be attributable to limited resources, human as well as budgetary constraints.

Hyperlipidemia is the second most common risk factor in this study at 26.75% (n=61). This is a worrying occurrence since previous studies both in the developed and developing countries showed hyperlipidemia to be less frequent among blacks. Panthak et al (2009) found a frequency of 17% among black patients in their study, 17.1 % and 21% among Hispanics and whites, respectively. However this finding should be interpreted in context as only 39.91% (n=91) young stroke patients were tested for lipid profile (lipogram). Taj et al (2010) in a study on risk factors for stroke in Pakistan, found that dyslipidemia was the third frequent risk factor at 31.5%. Palleiro et al (2007) also found hyperlipidemia to be among the most common risk factors in their study on young ischaemic stroke. A study among young stroke patients (18 to 45 years) in Taiwan found hyperlipidemia to be the most common risk factor at 53.1% (Lee et al, 2002). Previous studies showed that the prevalence of hyperlipidemia was low among African American. Pathak et al (2009) in Florida among young stroke patients (25 to 49 years) found a frequency of 17%. Contrary to previous studies, Prisant et al (2000) had shown that there was similar prevalence of hypercholesterolemia in blacks and whites, but blacks have been neglected in most pharmacological studies on hyperlipidemia. White et al (2005) in northern Manhattan found hypercholesterolemia to be significantly more prevalent in Hispanics and blacks than whites. Further studies are needed in order to investigate this matter further.

In this study 23.24% (n=53) of patients had a cardiac risk factor, and women were more affected than males. However, the gender difference was statistically insignificant. Previous studies have found cardio-embolism to be the cause of cerebral infarction in a third of young strokes (Martin et al, 1997). Further, previous studies have shown that cardioembolic stroke is proportionally more common in women (Appelros et al, 2009). Echocardiography was performed in 90.57% (n=48) patients with cardiac disease (n=53) and was abnormal in 66.67% (n=32) of the cases. Electrocardiography was performed in 67.92% (n=36) and was
abnormal in 58.33% (n=21) of the patients. The finding in this regard is in line with findings in other accepted studies (Rosman, 1986 & Qureshi et al, 1995).

Thirty one (13.6%) of the patients smoked cigarette and there was a predominance of male to female ratio of 4.16:1 and the gender difference was statistically significant. Connor et al (2009) found smoking frequencies of 23% among young black patients in Johannesburg. Joubert (1991) found frequencies of 27.8% at GaRankuwa hospital. The lower smoking frequency in this study is in agreement with findings by Peer et al (2009) that smoking was on the decline in South Africa.

Neurosyphilis was a risk factor in 12.28% (n=28) of the patients. Rapid plasmin regain (RPR) and Treponema pallidum haemagglutination (TPHA) were performed in 65.79% (n=150) and 33.77% (n=77) patients, respectively. Cerebrospinal fluid (CSF) VDRL was analysed in 7.89% (n=18) patients and was positive in two patients. Eighteen (64.29%) of the patients with neurosyphilis were co-infected with HIV. Meningitis was risk factor in 6.14% (n=14). Twelve (85.71%) of the patients with meningitis were also HIV positive. All the young black patients with meningitis had cerebral infarction. Grau et al (1998) showed that recent infection is an independent risk factor for a stroke. Bova et al (1996) found prevalence of acute infection of 24.2% in their study and that it was a risk factor for ischaemic stroke.

Diabetes mellitus was a risk factor in 9.21% (n=21) of patients. Glycaemic control (HBA1c) was evaluated in 63.16% (n=12) of patients with diabetes mellitus. It was abnormal in 7 patients. Of the 288 young black stroke patients, only 12.72% were tested for glycaemic control.

Eighteen (7.89%) patients were reported to consume alcohol. There was a predominance of males with a male to female ratio of 5:1. The gender difference was statistically significant. Alcohol consumption was a risk factor in 8.02% (n=17) young black patients and 15 of the patients had other risk factors with the exception of 3 patients who had alcohol consumption as the sole risk factor. Consumption of alcohol was the sole risk factor in one (6.25%) patient with cerebral haemorrhage.

Family history of stroke was reported in 6.14% (n=14) of patients in the study. Puerperium and autoimmune conditions were a risk factor in 12 (4.26%) of the patients. Autoimmune conditions were predominant in female than males, but statistically insignificant. The
majority of patients with autoimmune conditions were in the age group 25-34 years. In one (8.33%) patient, puerperium was associated with a hypertensive (putaminal) haemorrhage and the rest of the patients (91.67%) had ischaemic strokes. Six (50%) of the 12 patients had hypertension as an additional factor. Kittner et al (1996) found that the risks of both cerebral infarction and haemorrhage are increased in the puerperal period.

Obesity was observed in only 2.63% (n=6) of the patients. Black stroke patients were more likely than Whites and Hispanics to have been diagnosed with high blood pressure and morbid obesity (Cossrow and Falkner, 2004). A study conducted in northern Manhattan found that abdominal (trunkal) obesity was an independent, potent risk factor for ischaemic stroke in all race-ethnic groups (Suk et al, 2003). The prevalence of obesity and the obesity-related cardiovascular diseases are greater in African Americans and Hispanic/Mexican Americans than in Caucasians (Cossrow and Falkner, 2004). The low frequency of obesity in this study is attributed to the fact that body mass index was not assessed and therefore should be interpreted in context.

Trauma was reported in 1.75% (n=4) of patients and there was equal gender distribution. Three of the patients were in the age group 33-44 years and the fourth patient was in the age group 25-34 years. Two of the patients did not have other risk factors and it was reported that one of the patients presented 2 days post motor vehicle accident. All the patients had cerebral infarction on CT scanning. Carotid Doppler was not performed in these patients. Marino et al (2006) found that of the 89 patients in their study who sustained moderate to severe head trauma a total of 28 cerebral infarctions were found in 17 (19%) cases.

Two patients (0.88%) had a family history of stroke. A number of studies have shown an association (Vergheese et al, 1986 & Kang et al, 2009). Another 0.88% (n=2) had herpes ophthalmicus and they were HIV positive and their CD4 counts were 162 cells/ul and 581 cells/ul, respectively. In a number of studies herpes ophthalmicus was associated with cerebral infarction secondary to vasculitis (Lin et al, 2010).

The two patients with atrial fibrillation were female and in the age group 25-34 and 45-54. Previous studies found atrial fibrillation to be more common in whites than among Hispanics and blacks (White et al, 2005)

Only one (0.44%) patient had an ischaemic stroke associated with oral contraceptive use. Hyperlipidemia was an associated risk factor in this patient. Oral contraceptives, especially
those containing high doses of oestrogen in concert with other risk factors like cigarette smoking and arterial hypertension are associated with a relative risk of stroke (Bousser et al, 2000). Migraine was reported in one (0.44%) patient with ischaemic stroke in the age group 19-24. The patient with migraine had no other risk factors. Chang et al (1999), reported that between 20% to 40% of strokes in women with migraine seemed to develop directly from a migraine attack and was associated with ischaemic and not haemorrhagic stroke.

Hundred and nine (47.81%) young stroke patients were investigated for HIV infection and 74.07% (n=80) tested positive. Of the 43 patients with no known risk factors, 53.49% (n=23) were HIV positive and that constituted 10.09% (n=228) of the total population of young strokes. The mean CD4 count of the HIV positive patients was 178.95 cells/ul. Fifty seven (71.25%) patients had a CD4 count below 200 and in 28.75% (n=23) patients, the CD4 count was above 200 cells/ul. The general body of evidence presented in previous studies in South Africa and abroad does not regard HIV infection as an independent risk factor for stroke, rather as a cofactor (Mochan et al, 2003; Tipping et al, 2005; Patel et al, 2005). In this study, however, 10.09% of the patients did not exhibit any known risk factor for stroke.

In this study prothrombotic profile was performed in 12.72% (n=29). Protein S and C were assessed in 6.58% (n=15) and 7.02% (n=16) patients, respectively. They were positive in only 2 patients respectively. These investigations are performed when indicated, not on a routine basis.

Antinuclear antibodies were measured in 26.75% (n=61) and were positive in 19.67% (n=12) patients. In a study conducted by Montalban et al (1994), of the 481 patients tested, 7.2% (n=35) patients were positive for antinuclear antibodies. The study however included all age groups. Autoimmune screening is also performed when indicated (Montalban et al, 1994).

This study demonstrates a high proportion of cerebral infarctions. This finding is similar to other studies of young strokes (Qureshi et al, 1996). Cerebral haemorrhage accounted for 7.02% of the stroke. In previous studies higher figures for cerebral haemorrhage were obtained. In the Kalafong study (Rosman, 1986) and Johannesburg hospital study (Connor et al, 2009), cerebral haemorrhage accounted for 32% and 27%, respectively. In this study the low prevalence of cerebral haemorrhages is probably due to the exclusion of subarachnoid haemorrhages. Seventy five per cent (n=12) of the cerebral haemorrhages (n=16) were due to hypertension. This is similar to the findings in the Johannesburg hospital study (Connor et al, 2009).
Echocardiography was performed in 21.05% (n=48) of patients (n=228). It was abnormal in 75% (n=36) patients of the 48 patients tested. Electrocardiography was performed in 20.61% (n=47) and it was abnormal in 63.82% (n=30) patients. Carotid Doppler was performed in 7.08% (n=16) and was abnormal in 31.25% (n=5) patients. Angiography was not done in all the patients. In the Kalafong study 79.31% (n=92/116) were scanned, 2 patients underwent carotid sonography, angiography was performed in 11 patients and lumber punctures in 20 patients in a retrospective study in Atlanta on young black stroke patients, CT scan was performed in all patients, 27% (n=16) of patients with cerebral infarction were evaluated with transthoracic echocardiography, carotid Doppler ultrasonography was performed in about 14% (n=35) of patients and angiography in 4 patients (Qureshi et al, 1995). Radiological investigations are performed when indicated.

There is seasonal variation in the occurrence of strokes in young black patients at Dr. George Mukhari hospital. Most of the strokes occurred in the summer and autumn seasons and the month of January had the highest frequency of strokes. Strokes in Western and European countries show a predominance of strokes to be during the cold months, i.e., winter and spring (Oberg et al, 1999). Controversies regarding seasonal occurrence occurs and thus further studies are required in that regard (Connor, 2002).

**Conclusion**

The study suggests that there has been a significant increase in the number of stroke patients over the years. There was no gender difference among the young black stroke patients.

Hypertension remains a dominant risk factor for stroke. The diagnosis and treatment of this common condition (hypertension) can be associated with certain challenges peculiar to poor communities. Connor et al (2006) found that a lot of rural South African communities had malfunctioning blood pressure measuring devices and ill-fitting cuffs, thus making the monitoring of blood pressure challenging and inaccurate. This is over and above the shortage of medical supplies. We add our voice in recognition of the fact that this prevailing situation needs to be addressed.

Cardiac disease is the third most frequent risk factor. This is in line with other studies that show that a third of young stroke patients had a cardiac cause. Cardiac assessment therefore remains paramount in the management of young stroke patients.
Even though there was a statistically significant gender difference with regards cigarette smoking and alcohol usage, this did not translate to a marked difference in the occurrence of strokes between the sexes. This could be partly explained by the fact that only 13.6% of patients smoked and 6.14% consumed alcohol.

HIV infection seems to be an independent risk factor for stroke in young stroke patients (35.09%, n = 80/228) at Dr. George Mukhari hospital. Further studies are needed to understand the mechanisms involved.

Despite the retrospective nature of the study, valuable information regarding the distribution of risk factors has been obtained. These findings can be further verified by prospective studies on the subject.

Based on the findings of the study, the following recommendations are made:

- High blood pressure awareness programmes are important as a preventative measure against strokes.
- Even after a stroke has occurred there still exists a window of opportunity that could be better exploited by awareness campaigns and allocation of resources.
- A national interlinking computerised system that will contain the clinical and radiological particulars of patients with strokes could facilitate collaborative studies on the condition.
REFERENCES


19. Cossrow N, Falkner B. Race/Ethnic issues in obesity and obesity-related comorbidities. The Journal of Clinical Endocrinology & Metabolism 2004;89:2590-2594

20. Dobson R. Stroke and heart attack admissions are linked to cold weather. BMJ 2004;329:760.


49. Lewis S, Arnott D, Godfrey C, Britton J. Public health measures to reduce smoking prevalence in the UK: how many lives could be saved? Tob Control 2005;14:251-254

76. Rosman KD. The epidemiology of stroke in an urban black population. Stroke 1986;17:667-669


