PRESENTATION AND OUTCOMES OF PRIMARY SPONTANEOUS INTRACEREBRAL HAEMORRHAGE AT CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

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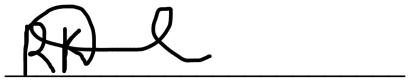
A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, in partial fulfilment of the requirement for the degree of Master of Medicine in the Department of Neurosurgery

Johannesburg, 2020

DECLARATION

I, Rambelani Khohomela, declare that this research report is my own work, in design and execution. It is being submitted for the degree of Master of Medicine (Neurosurgery) of the University of the Witwatersrand, Johannesburg. It has not been submitted for any degree or examination at this or any other University.



Signature

25 May 2020

Date

DEDICATION

This work is dedicated to my wife, Cathrine, and my two daughters Andani and Arehone, for their unwavering support and love.

ABSTRACT

AIM

To determine the presentation and outcomes of patients with primary spontaneous intracerebral haemorrhage referred for neurosurgical management in Charlotte Maxeke Johannesburg Academic Hospital.

METHOD

This was a 6-month prospective study of 45 patients referred to the CMJAH Neurosurgical Unit with a CT scan confirmed diagnosis of spontaneous intracerebral haemorrhage. Patients who met the inclusion criteria were then assessed for relevant data such as demographic, clinical and radiological data. Outcome was then assessed and prognostic factors for poor outcomes were analysed.

RESULTS

There were 13 (28.89%) female patients and 32 (71.11%) male patients. The mean age was 52 ± 11.44 yrs. 32 (71.11%) patients were black, 8 (17.78%) were White, 4 (8.89%) were Coloured and 1 (2.22%) was Indian. Collapse and weakness were the most common modes of presentation and occurred in 19 (42.22%) and 18 (40%) patients respectively. Supratentorial bleeds accounted for 35 (77.78%) patients while 10 (22.22%) patients suffered infratentorial bleeds. The anatomical location of the haemorrhages was: putamen 23 (51.11%), cortical 6 (13.33%), Pontine 5 (11.11%), thalamus 6 (13.33%), cerebellum 5 (11.11%). Craniotomy was performed in 3 (6.67%) patients and 4 (8.89%) patients had EVD inserted. There was poor outcome in 35(77.78%) patients with 22 (48.89%) dead, 1 (2.22%) vegetative and 12 (26.67%) severely disabled. Results from logistic regression showed that; age, GCS, mass effect, IVH, ICH volume and hydrocephalus were significantly associated with poor outcome.

CONCLUSION

Our study has shown that spontaneous ICH presents a common clinical problem in our environment with associated significant morbidity and mortality.

AKNOWLEDGEMENTS

I want to thank God for making this work possible. I am also profoundly grateful to my supervisors, Prof John Ouma and Dr. Kaunda Ibebuike, for their help and relentless guidance with this study. I want to express my heartfelt gratitude to both of you for your patience, kindness and wisdom towards the completion of this research as well as my training. I also want to thank the entire consultants and registrars in the University of Witwatersrand Department of Neurosurgery for their encouragement, understanding and inputs.

I thank God for blessing me with a beautiful and supportive family. My wife Cathrine, you have been a pillar of the family during my years of study and beyond. I would not have done it without you. To my daughters Andani and Arehone, you have been very understanding and loving during my frequent absence from your life.

ABBREVIATIONS

AIDS – Acquired Immune Deficiency Syndrome

CAA – Cerebral Amyloid Angiopathy

CMJAH – Charlotte Maxeke Johannesburg Academic Hospital

CSF – Cerebrospinal Fluid

CT Scan – Computed Tomography Scan

EVD – External Ventricular Drain

GCS – Glasgow Coma Scale

GOS – Glasgow Outcome Scale

HIV – Human Immune Deficiency Virus

ICH – Intracerebral haemorrhage

ICP – Intracranial Pressure

ICU – Intensive Care Unit

IVH – Intraventricular Haemorrhage

NIHSS – National Institutes of Health Stroke Scale

PHE – Perihaemorrhagic Edema

RCT – Randomised Control Trial

SA – South Africa

SD – Standard deviation

SSA – Sub-Saharan Africa

USA – United Sates of America

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1. INTRODUCTION

1.1. Definition and Classifications

Spontaneous intracerebral haemorrhage refers to bleeding into brain parenchyma without trauma or surgery[1,2]. This manifests clinically as haemorrhagic stroke.

Spontaneous intracerebral haemorrhages (ICH) can further be subdivided into primary or secondary. Primary spontaneous intracerebral haemorrhage refers to haemorrhage inside cerebral parenchyma or ventricles, without an underlying causative pathology, such as tumour, vascular malformation, or aneurysm[1–3]. 80% of spontaneous intracerebral haemorrhages are primary. Hypertensive related bleeds account for the overwhelming majority of these cases with a very few being related to amyloid angiopathy. Secondary spontaneous intracerebral haemorrhage refers to haemorrhages which are caused in the presence of a structural abnormality such as a tumour, aneurysm or vascular malformation[1–3]. This study will be limited to primary spontaneous intracerebral haemorrhages.

1.2. Epidemiology

Spontaneous intracerebral haemorrhage affects more than a million people annually worldwide. It is more disabling than ischaemic stroke[2,3]. It accounts for 10% – 15% of all strokes in USA[2,3], 18 – 24% in Japan[4] and Korea[5]. Sub-Saharan African studies show an even greater proportion of spontaneous intracerebral haemorrhage as a percentage of all strokes[6–12]. This is postulated to be due to the higher levels of uncontrolled hypertension in Africa and other developing countries.

ICH incidence differs depending on geographic region. Developed countries have incidence rates of 10 per 100 000 person years. Developing countries have incidences which are double this[13]. Furthermore, these incidences are increasing in poor countries compared to wealthy countries where the trend is to show a decline. The highest number of ICH cases and mortality is in Sub-Saharan Africa and Asia[14].

Factoring in the results from the studies mentioned above, it is not surprising that ICH has different incidence amongst racial groups. A large population based study showed that incidence rates were highest amongst Asians followed by whites then blacks and Hispanics [15]. An American study showed that black Americans had higher rates of ICH than whites[16]. This difference was attributed to higher prevalence of uncontrolled hypertension in black people[16].

The incidence of ICH increases with age. A Dutch study by Jolink et al, showed increasing ICH rates with age[17]. Hemphill showed that ageing increases risk for ICH[18]. ICH affects more men than women. Jolink et al, reported higher incidence of ICH in men than women across all different age groups[17].

Spontaneous intracerebral haemorrhage causes a higher level of morbidity and mortality as compared to ischaemic stroke[1–3]. ICH mortality varies between countries and time periods. High income countries report lower mortality rates, 20 – 30%, compared to low income countries, 40 -50%[13]. In high income countries the trend has been for this mortality rate to decrease. Some studies report mortality rate of up to 70%[7,9,19]. Of the patients who survive 75% will be left functionally dependent and less than 20% will achieve functional independence[1,3].

1.3. Prognostic factors

Several studies have looked at the issue of prognosis in ICH[18,20,21]. Increasing age, low level of consciousness, low GCS score, abnormalities in arterial blood pressures, temperature, respiration at presentation, severity of weakness, speech disturbances, gaze palsies, brainstem involvement, higher volume of ICH, infra-tentorial origin of ICH, intra-ventricular or sub-arachnoid extension of ICH, midline shift, higher ICH Score have all been studied by various workers as important markers of bad prognosis after ICH[18]. To date over 19 prognostic scores have been developed[21]. The ICH Score is the most popular. The ICH Score (See Table 1) takes six factors into account as investigated by Hemphill et al[18]. These six factors were found to be independent predictors of poor outcome in the study[18]. This score is the most widely used and validated score[20].

Table 1: Intracerebral Haematoma Score

Characteristic	**Finding**	**Points**
GCS	3 – 4	2
	5 – 12	1
	13 – 15	0
Age	>80	1
	<80	0
Location	Infratentorial	1
	Supratentorial	0
ICH Volume	>30cc	1
	<30cc	0
Intraventricular blood	Yes	1
	No	0
Total Score		0 – 6 points

1.4. Problem

There is a shortage of data on primary spontaneous intracerebral haemorrhage in Africa[22]. Most of the African studies do not make a distinction between haemorrhagic and ischaemic stroke and thus group stroke as an overall entity. Several studies have looked at the epidemiology of stroke in Africa[22,23]. Historically strokes, both ischaemic and haemorrhagic, were more common in high income countries compared to low income ones. However, in recent times there has been a change in this pattern with stroke rates declining in developed countries while rates increase in developing countries. South Africa is regarded as a developing country and this means stroke rates are bound to be an increasing problem on the already overburdened healthcare system. This makes any study looking at this topic prudent.

The annual burden of stroke in SA is 25,000 deaths with 95,000 years lived with disability[24]. Stroke is the second leading cause of death in SA following HIV/AIDS[25,26]. These figures represent both ischaemic and haemorrhagic stroke as a whole. Uncontrolled high blood pressure and obesity, are the biggest risk factors for stroke burden in rural SA[26]. There is also a paucity of data specifically for primary spontaneous intracerebral haemorrhage in SA. This study aims to bridge this knowledge gap and hopefully shed some light into this topic. The relevance of this study may be justified from the highlighted clinical problems primary spontaneous ICH presents in our setting including the expected rise in this trend. It has devastating consequences on the patient many of whom do not have the social infrastructure to deal with these effects.

1.5. Justification

The study will assist us in the following aspects:

- Presentation: We will better understand who presents with this condition, risk stratification and primary prevention programs.
- Management and short-term outcomes: We will be able to critique our management style in light of outcomes and benchmark ourselves against others; are we doing too much/too little/helping/not helping patients at all? Are we using resources properly, ICU for poor grade ICH?
- Prognostic factors: We will better understand the prognostic factors for good/bad/disabled/death outcome in our settings, and understand if this is due to our management decisions or the innate nature of the disease. We will be better able to triage patients in future and allocate theatre and ICU resources to those with the best chances of survival, and we will be able to counsel families based on accurate local data

1.6. Risk factors and pathophysiology

Modifiable risk factors are risk factors that can be changed with lifestyle modification. These include smoking, hypertension, and alcoholism. Non-modifiable risk factors are fixed and cannot be addressed by lifestyle changes. These include increasing age and male sex[27–29]. Genetic risk factors have also been postulated with Apolipoprotein E being implicated in ICH[30]. African series also show similar risk factors with an addition of HIV infection which is very prevalent in Sub-Saharan Africa[7].

Increasing old age and uncontrolled hypertension are the most significant risk factors for developing ICH[1–3,27]. Degenerative cerebral vascular changes are caused by ageing.

Hypertension exacerbates this process and leads to degradation and necrosis of small perforating vessels in the brain. This leads to small aneurysms which are friable and can end up bleeding and causes ICH[2,3,31].

1.7. Clinical presentation and haematoma location

The presentation of primary spontaneous intracerebral haemorrhage is a function of haematoma size and anatomical location. The most frequent locations are the basal ganglia, thalamus, lobar, pons and cerebellum[1–3,31].

Putaminal Haemorrhage

- Most common location for primary spontaneous ICH
- 50% – 60% of cases
- Nearly always associated with hypertension
- Abrupt onset of severe headache with or without nausea and vomiting
- Neurological deficit develop overtime as haematoma expands
- Contralateral progressive hemiparesis, hemisensory loss, homonymous hemianopsia
- Alteration of consciousness ranging from lethargy to coma
- Intraventricular extension leading to acute hydrocephalus

Thalamic Haemorrhage

- 10% - 15% of all primary spontaneous ICH
- Almost uniformly as a result of chronic hypertension
- Headache is the initial symptom with the neurological deficits varying depending on haematoma size and direction of haematoma dissection through parenchyma
- Can also extend into ventricles leading to acute hydrocephalus

Caudate Haemorrhage

- 5% - 7% of all primary spontaneous ICH
- Always hypertension related
- Headache, nausea and vomiting are initial symptoms followed by disorientation
- Can extend into ventricles leading to acute hydrocephalus

Lobar Haemorrhage

- Presentation varies depending on exact location and size of haematoma
- Haemorrhages found mostly in subcortical white matter of the parietal, temporal, and occipital lobes which accounts for the lower incidence of coma and fixed neurological deficits
- Headache, vomiting and seizures due to superficial location of haematoma
- Low incidence of coma on presentation, hemiparesis is usually mild
- Associated with hypertension, CAA and coagulopathy

Cerebellar Haemorrhage

- Posterior fossa is a small space
- High incidence of coma
- Almost always the result of hypertension
- Initially headache and nausea, then progressive dizziness, neck stiffness and dysarthria
- One third present in a coma

Brainstem Haemorrhage

- Most commonly results from hypertension

- Pontine location more frequent than medullary and midbrain
- Pontine haemorrhage most devastating of all haemorrhages
- Most patients present in a coma and outcome is extremely poor

1.8. Current management of primary spontaneous intracerebral haemorrhage

Patients with ICH should ideally be managed in a specialised stroke unit with all the support facilities such as neuro ICU, radiology services etc. The care should be by a multi-disciplinary team including; stroke neurologists, neuroradiologists, interventional radiologists, neurosurgeons, neurocritical care physicians, physiotherapists, occupational therapists, speech and language therapists etc.

Medical management strives to avoid the complications of ICH. Complications of primary spontaneous intracerebral haemorrhage can be divided into neurological and non-neurological. The American Heart Association developed guidelines for the management of spontaneous ICH.

Most of the patients with primary spontaneous intracerebral haemorrhage have elevated blood pressures[1–3,31]. These elevated blood pressures are associated with haematoma expansion. A significant number of patients experience haematoma expansion and this occurs within 4 hours of initial haemorrhage. Uncontrolled hypertension tends to exacerbate this haematoma expansion which is why it is important for patients to have prompt blood pressure control as soon as is safely possibly. The question of how aggressively blood pressure should be dropped and how quickly is still being debated. Several major studies have tried to resolve this with no clear answer[32,33].

1.9. Neurosurgical management

Primary spontaneous intracerebral haemorrhage is a medical problem unless there is a sequalae that would benefit from surgical intervention such as massive haemorrhage, haemorrhage with intraventricular extension, and hydrocephalus. Haemorrhage in the brain parenchyma can benefit from drainage, either via craniotomy or minimally invasive techniques such endoscopic aspiration or stereotactic aspiration, while intraventricular extension of blood can be drained by an external ventricular drain (EVD). This would help to reduce the clot burden and mass effect and thus decrease ICP.

Two major studies have looked at craniotomy for ICH, the STICH I (Surgical Trial in Intracerebral Haemorrhage) (2005) and STICH II (Surgical Trial in Lobar Intracerebral Haemorrhage)[34,35]. In the STICH I, there was no difference between medical and surgical treatment but subset analysis showed there might be a benefit in operating patients with superficial lobar haematoma[34]. STICH II looked at this subset of patients who had superficial lobar haematomas. There was no difference in the two treatment arms[35]. Two meta analyses of randomized controlled trials comparing craniotomy to medical treatment showed a modest benefit with surgery[36,37].

Minimally invasive techniques are in current development and carry the advantage of less trauma to the brain. The largest trial, The Minimally Invasive Surgery and rtPA for Intracerebral Haemorrhage Evacuation (MISTIE III) trial, showed that this technique was not beneficial[38].

Hence the neurosurgery unit at CMJAH may be consulted by the referring doctors on account of a massive bleed, intraventricular extension, hydrocephalus, and other causes of raised intracranial pressure such as cerebral oedema.

2. AIMS

To determine the presentation and outcomes of patients with primary spontaneous intracerebral haemorrhage referred for neurosurgical management in Charlotte Maxeke Johannesburg Academic Hospital.

3. OBJECTIVES

1. To determine the age, gender, race and ethnic distribution at presentation in patients with primary spontaneous intracerebral haemorrhage referred for neurosurgical management in CMJAH
2. To determine the clinical findings, and radiological brain CT Scan findings at presentation in patients with primary spontaneous intracerebral haemorrhage referred for neurosurgical management in CMJAH
3. To determine the neurosurgical management decisions amongst patients entered in the study
4. To determine the outcome at discharge
5. To determine factors associated with the poor outcome at discharge

4. METHODS

4.1. Study design

A 6-month descriptive prospective study design was used.

4.2. Study location

The research was conducted in CMJAH. It is one of the two principal teaching hospitals of the University of the Witwatersrand, Johannesburg. It is regarded as a central hospital and offers both tertiary and quaternary services to the population of both Gauteng province and by virtue of referral patterns from other adjacent provinces namely; North West, Free State, Limpopo and Mpumalanga

4.3. Study population

The population studied comprised of patients with radiologically confirmed spontaneous ICH who were referred by the managing physicians for neurosurgical management in CMJAH. These patients were referred from CMJAH medical wards, casualty or surrounding referral hospitals. Secondary causes of ICH were excluded by higher imaging; CT angiograms (CTA), digital subtraction angiography (DSA) and magnetic resonance imaging (MRI).

4.4. Sample size

A sample of 45 individuals was required to assess prevalence and the outcome at a 5% level of significance assuming a 50% prevalence of the outcome as determine by previous studies in the general population. It is an observational study and we are assuming a 10% error rate.

Inclusion Criteria

- All consecutive patients referred by the managing physicians to the Neurosurgical Unit at CMJAH with a CT Scan confirmed spontaneous ICH, within the study period.

Exclusion Criteria

- Patients with bleeding dyscrasias

Limitations

The study had several limitations:

- The number of study participants was small
- The duration of the study was short (6 month)
- Outcome was measured at discharge
- Study was hospital based

4.5. Haematoma volume calculation

Hematoma volume was calculated using the A*B*C/2 method[39].

4.6. Measuring tool or instrument

A structured questionnaire was used to capture clinical and radiological details of the participants in the study.

4.7. Data collection

- This occurred over a period of six months at CMJAH
- Patients were screened to see if they met study inclusion criteria
- The patients and or the relatives were then approached for consent to be included into the study
- The patients were then assessed by the author
- The data collected/variables include
    - Demographic data – age, gender, race/ethnicity
    - Clinical data – presentation, GCS, ICH Score, risk factors, management decisions, outcomes
    - Radiological data – Location, size, IVH, Mass effect, hydrocephalus
    - Outcome – Glasgow outcome score
        - Poor outcome = GOS 1 – 3
        - Good outcome = GOS 4 – 5

4.8. Ethics

The research protocol was submitted to Human Research Ethics Committee (Medical) of the University of the Witwatersrand for ethics clearance. The clearance certificate number is: M190207

5. DATA ANALYSIS

The data was analysed, with a statistician, by the use of computer aided statistical analysis of the variables. The data was entered into an Excel spreadsheet and then exported to the Stata (Version 15) Statistical Software. Categorical variables such as gender were described as frequency, percentages or charts. While nominally distributed continuous variables such as age were reported as mean ± standard deviation but non-nominally distributed variable were presented as median (interquartile range). Association between categorical variables such as gender and the outcome were determined using a Pearson's Chi-square test and logistic regression at 5% level of significance. Independent association between variables and the outcome were determined using logistic regression at 5% level of significance. Fischer's exact test was used in certain instances for cross tabulations when the numbers where less than 5.

6. RESULTS

6.1. Demographic profiles

Table 2: Demographic profile of study participants

Variable	Characteristics	Frequency	Percent (%)
Gender			
	Female	13	28.89
	Male	32	71.11
Age in years			
	19 – 30	1	2.22
	31 – 50	19	42.22
	51 – 80	24	53.33
	>80	1	2.22
Ethnicity			
	Black	32	71.11
	White	8	17.78
	Indian	1	2.22
	Coloured	4	8.89

6.1.1. Gender

Forty-five (45) patients (see Table 2) were enrolled into the study during the 6-month study period. All these patients met our study inclusion criteria. Thirty-two (71.11%) patients were males while 13 (28.89%) patients were female.

6.1.2. Age

The age of participants ranged from 21 – 81 years with a mean age of 52 ± 11.44 years, and a median of 52 years. The age of males ranged from 39 – 77 years with a mean age of 53.72 ±

9.26 years, and a median age of 52 years. The age of females ranged from 21-81 years with a mean age of 48.15 ± 15.32 years, and a median age of 45 years.

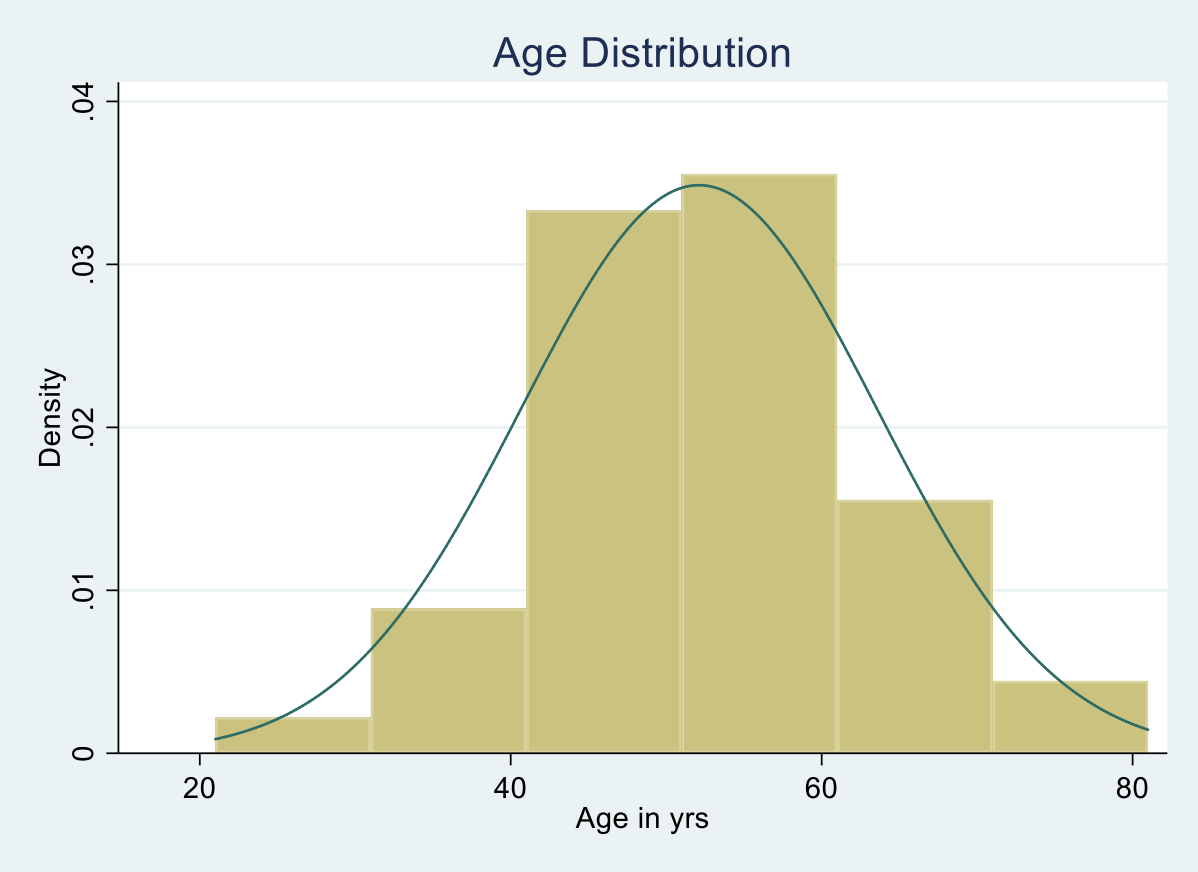

Figure 1: Graph indicating distribution of age

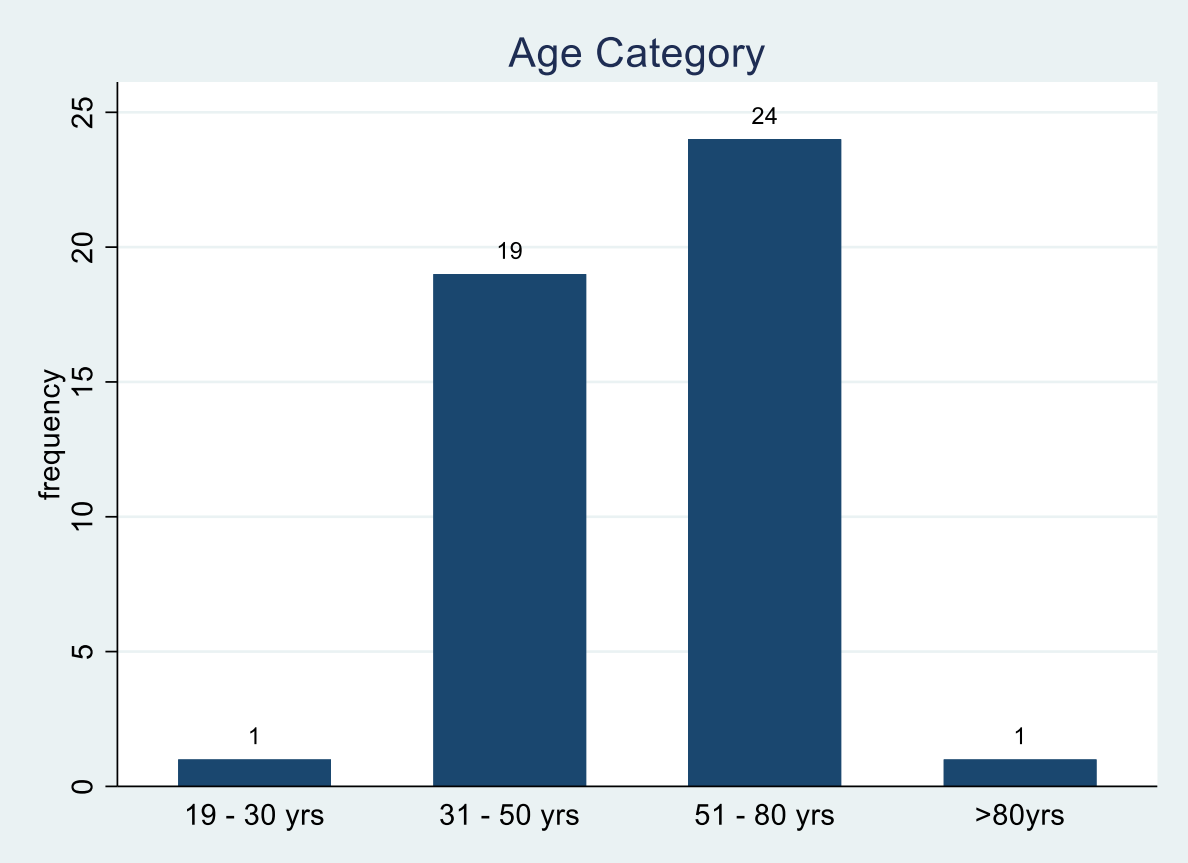

Figure 2: Graph indicating distribution of age categories

6.1.3. Race/Ethnic distribution

Thirty-two (71.11%) patients (see Table 2) were blacks, 8 (17.78%) patients were whites, 1 (2.22%) patient was Indian while the remaining 4 (8.89%) patients were Coloured.

6.2. Clinical Presentation

Table 3: Clinical presentation of patients

Variable	Characteristics	Frequency	Percent (%)
Presenting symptom			
	Collapse	19	42.22
	Weakness	18	40.00
	Headache	3	6.67
	Seizure	3	6.67
	Speech difficulty	2	4.44
GCS			
	13-15	19	42.22
	9-12	10	22.22
	3-8	16	35.56
ICH Score			
	0	11	24.44
	1	12	26.67
	2	8	17.78
	3	6	13.33
	4	8	17.78

Collapse (see Table 3) was the presenting symptom in 19 (42.22%) patients, followed by weakness 18 (40%), headache 3 (6.67%), seizures 3 (6.67%) and speech difficulty 2 (4.44%). The ICH Score was 0 in 11 patients (24.44%), 1 in 12 patients (26.67%), 2 in 8 patients (17.78%), 3 in 6 patients (13.33%) and 4 in 8 patients (17.78%). No ICH Score of 5 or 6 were documented.

Nineteen patients (42.22%) presented with mild GCS (GCS 13 – 15). 10 patients (22.22%) presented with moderate GCS (GCS 9 – 12). 16 patients (35.56%) presented with severe GCS (GCS 3 – 8).

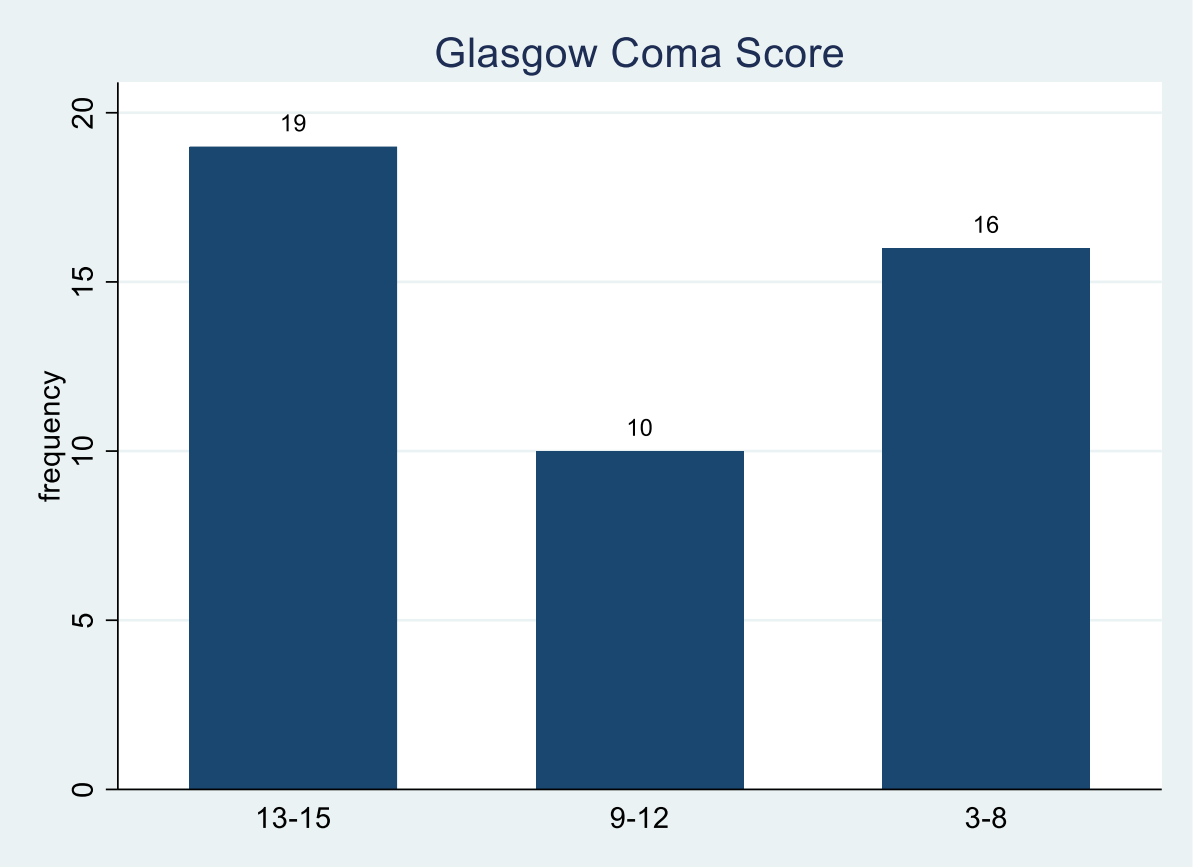

Figure 3 Graph indicating GCS severity at presentation

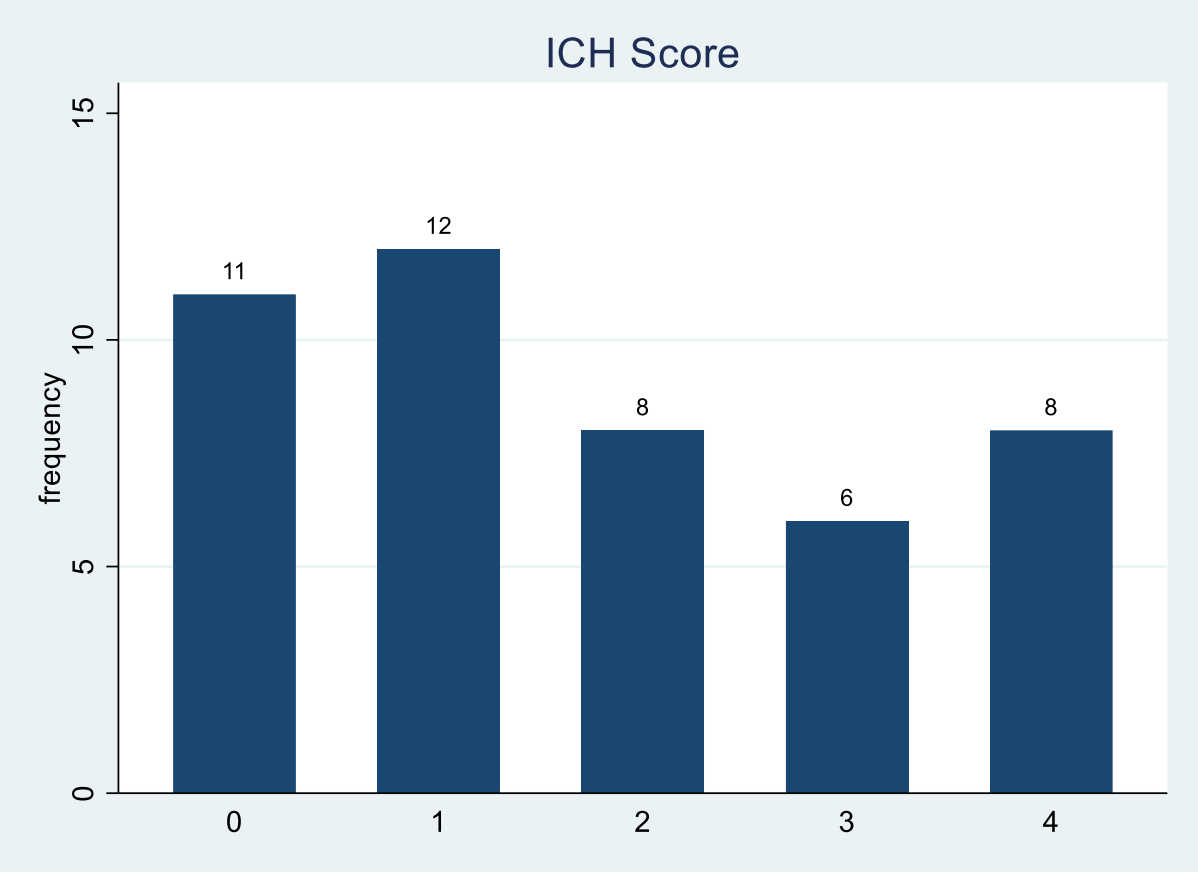

Figure 4 Graph indicating ICH Score at presentation

6.3. Radiographic profiles

Table 4: Anatomical location of haemorrhage

Variable	Location	Frequency	Percent (%)
Compartment			
	Supratentorial	35	77.78
	Infratentorial	10	22.22
Specific location			
	Putamen	23	51.11
	Thalamus	6	13.33
	Cortical	6	13.33
	Cerebellum	5	11.11
	Pontine	5	11.11

6.3.1. Location

Thirty-five (77.78%) patients suffered supratentorial bleeds while 10 (22.22%) patients suffered infratentorial bleeds (see Table 4). The anatomical location of the bleeds was: putamen 23 (51.11%), cortical 6 (13.33%), Pontine 5 (11.11%), thalamus 6 (13.33%), cerebellum 5 (11.11%).

6.3.2. Other CT Scan characteristics

Table 5: CT Scan findings

Variable	**Characteristics**	**Frequency**	**Percent** (%)
Size of ICH			
	<30ml	37	82.22
	>30ml	8	17.78
Intraventricular Haemorrhage			
	Yes	25	55.56
	No	20	44.44
Mass Effect			
	Yes	28	62.22
	No	17	37.78
Hydrocephalus			
	No	28	62.22
	Yes	17	37.78

Thirty-seven (82.22%) patients (see Table 5) had bleeds less than 30ml while 8 (17.78%) had bleeds more than 30ml. The mean size was 26.51ml ± 24.35ml. The range was 2ml – 100ml. The median was 20ml. Mass effect was present in 28 cases (62.22%). Intraventricular haemorrhage was present in 25 cases (55.56%). Hydrocephalus was present in 17 cases (37.78%).

6.4. Management decisions

Table 6: Management decisions

Variable	Characteristics	Frequency	Percent (%)
Craniotomy			
	No	42	93.33
	Yes	3	6.67
EVD			
	No	41	91.11
	Yes	4	8.89
Best Medical Therapy			
	Yes	39	86.67
	No	6	13.33

The neurosurgical management decisions for the 45 patients is as shown in Table 6. Thirty-nine (86.67%) patients were managed conservatively, while 3 (6.67%) patients underwent craniotomy and 4 (8.89%) patients had EVD inserted. One patient had an EVD inserted and then underwent a formal craniotomy.

6.5. Outcomes

Table 7: Outcomes based on Glasgow Outcome Score

Variable	Characteristics	Frequency	Percent (%)
GOS			
	Dead	22	48.89
	Vegetative	1	2.22
	Severe disability	12	26.67
	Moderate disability	6	13.33
	Good recovery	4	8.89
Outcome			
	Poor outcome	35	77.78
	Good outcome	10	22.22

Twenty-two (48.89%) patients (see Table 7) died, while other outcomes were 1 (2.22%) patient for persistent vegetative state, 12 (26.67%) patients for severe disability, 6 (13.33%) patients for moderate disability and 4 (8.89%) had good recovery. In terms of good or poor outcomes 35 (77.78%) patients had poor outcomes while 10 (22.22%) had good outcomes.

Table 8: Cross tabulation of GOS and ICH Score

	ICH Score					
GOS	**0**	**1**	**2**	**3**	**4**	**Total**
Dead	1	4	5	4	8	22
Vegetative	0	0	0	1	0	1
Severe disability	3	5	3	1	0	12
Moderate disability	4	2	0	0	0	6
Good recovery	3	1	0	0	0	4
Total	11	12	8	6	8	45

A cross tabulation of GOS and ICH Score is as shown in table 8. Out of the 11 patients with an ICH Score of 0, a total of 4 patients had poor outcome including 1 death, while a total of 7 patients had good outcome (4 moderate disability, 3 good recovery). From the cohort of 12 patients with ICH Score of 1, 9 patients had poor outcome including 4 deaths, while 3 patients had good outcome. All 8 patients with ICH Score of 3 had poor outcome (5 dead, 3 severe disability), and all 6 patients with ICH Score of 3 also had poor outcome (4 dead, 1 vegetative, 1 severe disability). The 8 patients with ICH Score of 4 all demised. No patients had ICH Score of 5 or 6.

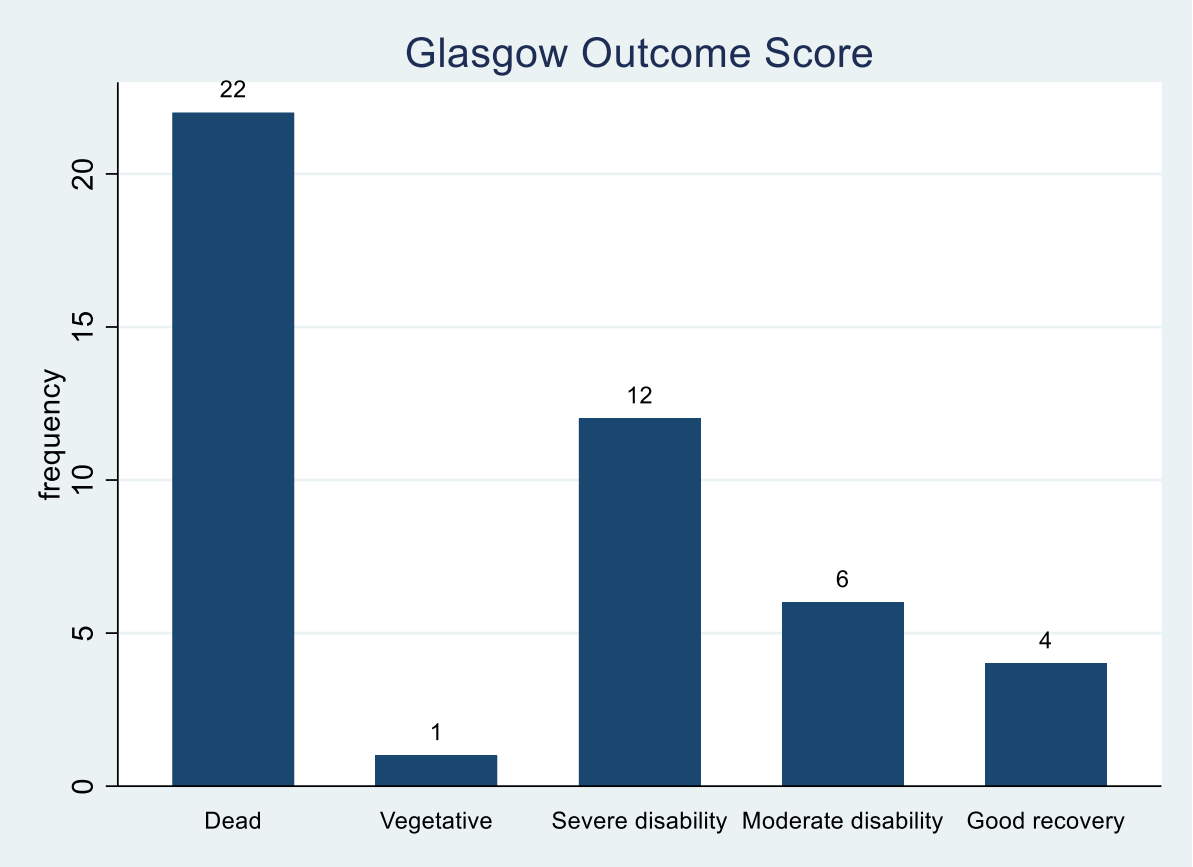

Figure 5 Graph indicating Glasgow Outcome Score in the study participants

6.6. Factors associated with outcomes

Table 9: Factors associated with outcomes

Variable	Characteristics	Nonadjustable Odds Ratio (95% Confidence Interval)	Likelihood Ratio P value
Gender			
	Female	1 (reference)	0.93
	Male	1.07 (0.23; 5.00)	
Ethnicity			
	Black	1 (reference)	0.52
	White	1.96 (0.21; 18.72)	
	Indian/Coloured	0.42 (0.06; 3.03)	
Age			
		1.07 (1.00; 1.16)	0.04
GCS			
		0.60 (0.39;0.92)	0.0003
Systolic BP			
		1.02 (0.99; 1.05)	0.19
Diastolic BP			
		1.01 (0.97; 1.04)	0.71
Compartment			
	Supratentorial	1 (reference)	0.26
	Infratentorial	3.11 (0.34; 28.13)	
Location			
	Putamen	1 (reference)	0.91
	Thalamus	1.76 (0.17; 18.32)	
	Cortical	0.70 (0.10; 4.90)	
	Cerebellum	1 (empty)	
	Pontine	1.41 (0.13; 15.26)	
IVH			
	No	1 (reference)	
	Yes	19.64 (2.21; 174.71)	0.0006
Mass Effect			
	No	1 (reference)	
	Yes	30.37 (3.32; 277.30)	0.0001
ICH Volume			
		1.16(1.03;1.30)	0.0002

Results from the logistic regression (see Table 9) showed that none of the gender (P=0.93), ethnicity (P=0.52), systolic blood pressure (P=0.19), diastolic blood pressure (P=0.71), cerebral compartment (P=0.26) nor anatomical location (P=0.91) were significantly associated

with poor outcome. Age (OR1.07, 95% CI: 1.00 - 1.16, P=0.04), GCS (OR: 0.60, 95% CI: 0.39 - 0.92, P=0.0003), IVH (OR: 19.64, 95% CI: 2.21 - 174.71, P=0.0006), Mass Effect (OR: 30.37, 95% CI: 3.32 - 277.30, P=0.0001) and ICH volume (OR: 1.16, 95% CI: 1.03 - 1.30, P = 0.0002) were significantly associated with poor outcome. Hydrocephalus was also shown by Fisher's exact test (0.007) to be significantly associated with poor outcome (P=0.005).

7. DISCUSSION

7.1. Demographic profile

7.1.1. Gender

ICH has a higher incidence in males than females. In a Dutch study, the annual incidence was higher in males than females for all ages[17]. A study conducted in Sweden showed that incidence rates of ICH were higher in males than in females[40]. In our study 71.11% of the patients were males and 28.89% were females. These findings are in keeping with other studies reported in the literature. In a meta-analysis representing 36 studies, men were found to have higher incidence of ICH compared to females. The difference was more pronounced in Japanese studies[15]. A Chilean study reported 56.5% of participants were males[41].

Sub-Saharan Africa studies have shown different trends. Erkabu et al, carried out a study in Ethiopia which had 57.7% male participants[42]. Albertino et al, in a study conducted in Maputo, Mozambique reported more females (55.2%) than males (44.2%), one of two studies to show this reversal[9]. A Zambian study carried out in Lusaka reported that 40.9% of the participants were males[7]. A study from Ibadan in Nigeria reported that 60.3% of their participants were males[22]. Nkusi et al, in a study carried out in Kigali, Rwanda had 54.1% of the patients who were males[43]. A study from Dakar Senegal reported that 56.25% were male[10].

A Malaysian study had a 50 – 50 gender split[44]. In a Texas community study 50% of the participants were male[45]. It is clear that the overwhelming majority of cases of ICH are in males. What is not clear is the reason for this propensity.

7.1.2. Age

The incidence of ICH increases with increasing age. Jolink et al, reported increasing incidence rates with ageing[17]. Our findings showed that the mean age for the study was 52 years. Patients in the Maputo study had a mean age of 54.7 years[9]. In the Zambian study the mean age was 56 years[7]. Soto et al, in the Chilean study reported a mean age of 66 years[41]. Adeleye et al reported a mean age of 55.7 years[22]. Nkusi et al, in Rwanda reported a mean age of 59.7 years[43]. Sagui et al, in Senegal reported a mean age of 51 years[10]. A community based study in Texas, USA indicated that the mean age was 73 years[45]. The study by Sia et al, had a mean age of 61.6 years[44]. It seems that studies in developed world have a higher mean age as compared to the studies from developing nations. Our findings are consistent with studies from developing nations.

7.1.3. Race/Ethnic distribution

Differences in the incidence of spontaneous ICH, among ethnicities, has been reported. Flaherty et al, in a study in USA found that African Americans had a higher reported incidence rates compared to white people[16]. Asians however have higher reported rates of ICH than either race in the US[16]. The high frequency of ICH among the black race (71.11%) in our study may reflect the predominantly black population in our environment. Whites had the next highest frequency (17.78%) followed by coloureds (8.89%). Indians had the lowest rate (2.22%). It is difficult to draw any conclusions on our findings due to the confounding. Race is a proxy for economic differences especially in our setting. Our study population is not a true reflection of the demographics of the country. Furthermore, hospital-based population does not reflect the general population outside the hospital. Taking this into account it is difficult to make any conclusions.

7.2. Clinical presentation

Clinical presentation is a function of the size and anatomical location of the ICH. The next major determinant is the swiftness of emergency response teams. In our study, collapse was the most common presenting symptom (42.22%) followed by weakness (40%), seizure (6.67%), headache (6.67%) and speech difficulty (4.44%). Most literature report weakness as the most common presenting symptom which correlates with the anatomical location of the haemorrhage being basal ganglia. Adeleye et al, reported limb paresis, headache and vomiting as the most common presenting symptoms[22]. Nkusi et al, reported that collapse was the most common presentation followed by hemiparesis, disturbed speech and headache[43]. Erkabu et al, reported hemiparesis as the most common presentation (52.8%) followed by loss of consciousness (26%), aphasia (17%), headache (4%) and seizure(0.8%)[42]. Sia et al, reported weakness as the most common presentation followed by loss of consciousness, headache and speech disturbance. Taking these findings into account shows that our findings are similar to other studies.

The mean GCS at presentation of our study participants was 10. This correlated with 35.56% of our patients presenting with a severe GCS (3 – 8), 22.22% with a moderate GCS (9 – 12) and 42.22% with a mild GCS (13 – 15). These findings were comparable to other studies especially those from Sub-Saharan Africa. Zahuranec et al, reported a mean GCS of 12.5[45]. Adeleye reported that 57% of patient presented in a coma with GCS less or equal to 8[22]. Our findings correlate with collapse as the most frequent form of presentation. Collapse suggests a larger size haemorrhage or situation were a small haemorrhage was allowed to increase in size due to inadequate response of emergency services or failure to control hypertension.

7.3. Radiographic profile

7.3.1. Location

Haematoma location was supratentorial in 77.78% of the cases and infratentorial in the remainder 22.22%. This compares with the study by Soto et al who reported supratentorial location of haemorrhages in 81.5% of the time with infratentorial accounting for 18.5%[41]. Also Adeleye reported supratentorial location in 90.5% of the cases[22]. The commonest location in our study was putamen (51.11%) followed by thalamus and cortical each with 13.33% and lastly cerebellum and pontine both with 11.11% each. These findings are comparable to other studies. Adeleye et al reported basal ganglia location as commonest site followed by lobar location[22]. In Soto et al's study, basal ganglia was the most frequent site followed by lobar, thalamus, cerebellum and pons[41]. An Ethiopian study by Deresse and Shaweno reported basal ganglia location as the most common site accounting for 38% of the bleeds, followed by thalamic (29.6%), lobar (18.3%), pons (5.6%), midbrain (4.2%), cerebellum (2.8%), IVH (1.4%)[19]. The Texas community study by Zahuranec et al indicated that deep cerebral location was the most common location (55%) followed by lobar, brainstem, cerebellum and multifocal[45]. Erkabu reported that basal ganglia was the most common location (50.4%) followed by multiple location (25%), lobar (20.3%) and brainstem(1.6%)[42]. Sia et al reported basal ganglia/thalamus as most common location. This was followed by lobar, brainstem and cerebellum[44]. However, in contrast to our findings, Nkusi et al reported lobar location as the most common location (38.2%), followed by basal ganglia (29.1%), thalamic (27.2%) and pontine (5.4%)[43]

7.3.2. Other CT scan characteristics

The other characteristics from the CT scan findings were also consistent with other studies reported. Our findings showed that 82.22% of patients had haematoma volume less than 30ml. 55.56% had IVH. Mass effect was documented in 62.22%. Hydrocephalus was present in 37.78%. Adeleye reported mass effect in 78.3% of the cases and IVH in 65.1% of the cases, the median volume of the bleed was 28ml[22]. Our median volume was 20ml. These results from Nigerian study are very similar to ours. Soto reported IVH in 52.6% of the cases[41]. Nkusi et al, in Rwanda reported IVH rate of 46%[43]. These rates of IVH are also consistent with our findings.

7.4. Management decisions

Management options for ICH include craniotomy, minimal invasive techniques, external ventricular drains and conservative management. There are no standardised guidelines for the surgical management of ICH and most units have their own independent decision-making process. We passively analysed our decision-making process. We found that 6.67% of patients underwent craniotomy and 8.89% had EVD inserted while 86.67% were managed by utilizing best medical therapy. It is very difficult to critique any of the decisions as all units make decisions based on their own local patient profile. Due to this there is wide variability in terms of management decision-making across most of the studies. Adeleye in Ibadan, Nigeria reported that 36.5% of the patients had operative management. This was mostly craniotomies and few EVD placements[22]. A Chilean study reported 3.1% craniotomy rate and 2.1% EVD rate[41]. A Swedish study looking at all neurosurgical centres in Sweden showed that 5% of patients with ICH underwent surgical intervention. There was a similar incidence of surgical intervention across all the neurosurgical centres in Sweden[40]. This makes our findings consistent with this nationwide Swedish study.

7.5. Outcomes

ICH carries a high level of morbidity and mortality especially when compared to ischaemic stroke. Mortality ranges from 20-30% in high income countries to 70% in low income countries[1]. Most of the studies report on mortality as an outcome. In our study we have included GOS category 1-3 and reported it as poor outcome. Based on this we have established that 77.78% had poor outcomes. The overall mortality rate was 48.89% while 2.2% were in a vegetative state and 26.67% were severely disabled. Our mortality rate compares with Hemphill et al, in the USA and also Sia et al, done in Malaysia. Hemphill and Sia reported mortality rates of 45% and 43.9% respectively[18,44]. A study done in Hong Kong reported a mortality rate of 22%[46]. This is significantly lower than our findings. This is probably related to the high-income status of Hong Kong. A study conducted in India reported a 35.5% bad outcome[47]. The Zambian study reported a 71.6% poor outcome with 53.4% dead while 2.3% were in vegetative state and 15.9% had severe disability[7]. The Mozambican study reported a 28-day mortality rate of 72%[9]. The Ethiopian study reported 67.9% poor outcome with 23.5% dead and 44.4% severely disabled[19]. A Senegalese study reported a 56% mortality[10]. A Rwandan study showed a mortality rate of 55.6% at 1 year follow up with in-hospital mortality reported as 19.4%[43]. The Swedish multicentre study reported a mortality rate of 10 – 28%[40]. Cross tabulation of GOS and ICH Score in our study showed that our patients were demising with even lower scores for ICH Score. In Hemphill study there was no mortality for ICH Score of 0[18]. Our study had a 9.09% mortality for ICH Score of 0. We had a mortality rate of 33%, 62.5%, 66%, and 100% for ICH Score of 1 – 4 respectively. We did not have participants with higher scores. Hemphill had a mortality rate of 13%, 26% , 72%, 97% and 100% for ICH Score of 1 – 6 with both 5 and 6 having 100% mortality[18]. These findings can be attributed perhaps to the difference in our demographic as our patients are younger. Another possibility is poor emergency response to the initial ICH which converts potentially salvageable patients into

patients that cannot be saved. This shows that the ICH Score in our setting would not be an adequate predictor of outcome especially at its lower end.

7.6. Factors associated with outcomes

Many prognostic factors have been reported in multiple studies. To date 19 prognostic scores have been suggested, each based on factors that are predictive of bad outcomes[21]. The ICH Score by Hemphill is the most popular such score. This score has been validated in many different environments and has stood the test of time. In the study by Hemphill et al, they found that; ICH volume, Age, GCS, Infratentorial location of bleed and IVH were all associated with poor outcome[18]. Our findings showed similar factors to be associated with poor outcome. These included; Age. GCS, Mass effect, IVH, ICH volume and hydrocephalus.

Age is associated with poor outcomes in some studies whereas it has been found not to be a predictor of poor outcome in others. Most studies document increasing severity of injury with increasing age. Hemphill reported that age was an independent predictor beyond 80 years whereas for us it is an independent predictor with a younger patient cohort. This feature has been one of the criticisms of ICH Score by Girish Menon in India who also found the same issue of a younger population[48].

GCS is a standard neurological assessment tool and carries the most weight in the ICH Score. GCS is part of many prognostic neurological scores for different conditions. It carries significant weight in all these scores with ICH Score being no exception. We found a very strong correlation between GCS and mortality.

Mass effect and ICH volume were independent predictors of poor outcome in our patients. Hemphill didn't find a correlation between mass effect and poor outcome, however an association was made between ICH volume and poor outcome in his cohort[18]. Mass effect and perihaematomal oedema have been associated with poor outcomes in several studies. Staykov et al, found that mass effect could potentially double in certain instances and was closely related to ICH volume and ultimately to poor outcome[49]. A study by Gebel et al supported these findings indicating the dangers of perihaematomal oedema[50]. IVH is an independent predictor of poor outcome. IVH can lead to hydrocephalus and oedema. Both hydrocephalus and perihaematomal oedema are associated with bad outcomes. IVH is also associated with larger ICH volumes. All the above make IVH a poor prognosis predictor as noted by our study and that of Hemphill[18].

8. CONCLUSION

Our study has shown that spontaneous ICH presents a common clinical problem in our environment which carries a very significant morbidity and mortality. Our patient demographic is the same as those of other published data. There were more men in our study which is in keeping with international trends in both Western and Sub-Saharan Africa. The average age of our patients seems younger as compared to studies coming out of the developed world. However, comparing this to Sub-Saharan African studies, we have similarities with our peers. This may be due to higher rates of hypertension amongst black people. This may be an economic factor and not necessarily genetic based.

Collapse and weakness were the most common presenting symptoms. Most patients presented with a declining level of consciousness and hence collapse featuring very highly in their clinical presentation. This ties in with the anatomical location of most of our bleeds being in basal ganglia and thalamus area. These locations accounts for the observed presentation. The decreased LOC during presentation could be attributed to delay in presentation due to poor emergency services.

The overwhelming majority of our study participants were managed medically. A small number underwent surgical intervention with either craniotomy or EVD. These interventions had no impact on eventual outcome. The outcome of the study participants was dominated by poor outcome. Almost half of the patients died with a further 20% being severely disabled. This confirms the high rate of mortality of ICH especially in a developing world setting such as ours. Although most developed world studies quote lower poor outcome figures, studies from developing world and especially Sub-Saharan Africa report similar results as ours.

Factors associated with outcomes included age, GCS, mass effect, IVH, ICH volume and hydrocephalus. These features are not surprising as they have all been previously associated with poor outcomes in previous studies. In this regard our study compared very well with other international studies.

9. RECOMMENDATIONS

One of the limitations of the study is the limited duration, small number of patients and also limited resources in carrying out the study. We recommend a more expansive follow up study of the topic over a prolonged period of time with a greater number of participants that are followed up for a lengthy period of time.

There are no dedicated stroke units in most public hospitals. We recommend establishment of centres of excellence were such patients are managed in a multidisciplinary stroke centre.

We recommend written guidelines at institutional level of how to manage ICH both medically and surgically. There seemed to be no clear direction in terms of tackling some of the key management issues in ICH such as blood pressure control, anticoagulation and when to intervene surgically.

We recommend a dedicated ambulance service to deal with ICH which would be staffed with emergency personnel who are familiar with the emergency treatment of the condition. These providers need to be well versed in critical care basics such as intubation and ventilation and managing hypertensive crises. They need to have the skills to immediately diagnose strokes and using stroke scores such as NIHSS and ICH Score. Likewise, emergency unit personnel need to be well versed in these skills and scores so that they can stabilise and order the initial investigations without delay.

We recommend an awareness campaign about stroke and its dangers with an emphasis on risk factors. This campaign should encourage people to live healthy lifestyle and have regular health check. Hypertension and diabetes education with reference to its link to ICH should be stressed.

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APPENDICES

APPENDIX A

DATA COLLECTION SHEET

1. Demographics

Study Number:

Age:

0 – 18yrs	19 – 30yrs	31 – 50yrs	51 – 80yrs	>80yrs

Sex:

Ethnicity:

Occupation:

Marital Status:

2. Clinical Findings

Primary Complaint: H/A, LOC, Collapse, weakness, speech difficulty, others (specify)

Time since onset:

Glasgow Coma Scale:

Vitals: BP P RR Temperature

Risk factors: HPT: Yes/No Diabetes: Yes/No Smoking: Yes/No

Others (specify):

Laboratory investigations: Hb WCC Plt

Na K Cl Ur Cr

Clotting Profile/INR

Neurological deficit:

3. Radiological Findings

Location: Putamen/Thalamus/Cortical/Cerebellum/Pontine/Medulla

Size: >30cc or <30cc

IVH: Yes/No

Mass effect: Yes/No

Hydrocephalus: Yes/No

Others (specify)

4. Management

Craniotomy: Yes/No

External ventricular drain: Yes/No

Medical management/close ICU observation: Yes/No

Others (specify)

5. Outcome

Glasgow Outcome Scale

Score	Description
1	Dead
2	Persistent vegetative state
3	Severe disability (conscious but disabled), needing assistance with activities of daily living
4	Moderate disability (disabled but independent), no assistance with activities of daily living Disabilities include varying degrees of dysphasia, hemiparesis, or ataxia as well as intellectual and memory deficits and personality changes
5	Good recovery, resumption of normal activities even though there may be minor neurologic or psychological deficits

APPENDIX B

Glasgow Coma Scale

Eye opening	Spontaneously To speech To pain No response	4 3 2 1
Verbal response	Orientated time person and place Confused Inappropriate words Incomprehensible sounds No response	5 4 3 2 1
Motor response	Obeys commands Moves to localized pain Flexion withdrawal from pain Abnormal flexion (decorticate) Abnormal extension (decerebrate) No response	6 5 4 3 2 1
Total Score		___ 15

Intracerebral Haemorrhage Score

Feature	Finding	Points
GCS	3 – 4 5 – 12 13 – 15	2 1 0
Age	>80 <80	1 0
Location	Infratentorial Supratentorial	1 0
ICH Volume	>30cc <30cc	1 0
Intraventricular blood	Yes No	1 0
Total Score		0 – 6 points

Glasgow Outcome Scale

Score	Description
1	Dead
2	Persistent vegetative state
3	Severe disability (conscious but disabled), needing assistance with activities of daily living
4	Moderate disability (disabled but independent), no assistance with activities of daily living Disabilities include varying degrees of dysphasia, hemiparesis, or ataxia as well as intellectual and memory deficits and personality changes
5	Good recovery, resumption of normal activities even though there may be minor neurologic or psychological deficits

APPENDIX C

LETTER TO HOSPITAL SUPERINTENDENT

30 November 2018

The Superintendent

Charlotte Maxeke Johannesburg Academic Hospital

17 Jubilee Road

Parktown

Johannesburg

Dear Sir/ Madam

I am Dr Rambelani Khohomela, a third-year registrar in the department of Neurosurgery at The University of the Witwatersrand. With your kind permission, I wish to conduct a research project in the hospital titled: **"Presentation and outcomes of primary spontaneous intracerebral haemorrhage at Charlotte Maxeke Johannesburg Academic Hospital".**

The research is a requirement for the award of the MMed degree of the university.

I hereby request your permission to use patients' hospital records for this study. This is a prospective study, so patients or family members of patients will be asked to give informed

consent to participate in this research study. Information sheets for participants as well as consent forms will be provided.

Attached to this letter are copies of the protocol, patient information sheet and consent forms.

Information gathered from this study might prove beneficial for future management of patients suffering from this condition.

I hope for a favourable response in this regard.

Kind Regards

Dr Rambelani Khohomela

Registrar

APPENDIX D
INFORMATION SHEETS

PATIENT INFORMATION SHEET

Title of study: Presentation and outcomes of primary spontaneous intracerebral haemorrhage at Charlotte Maxeke Johannesburg Academic Hospital

Principal Investigator: Dr. Rambelani Khohomela

Address: Department of Neurosurgery, University of the Witwatersrand, Johannesburg

Introduction:
I am Dr Rambelani Khohomela from Department of Neurosurgery, University of the Witwatersrand, Johannesburg and doing ~~a~~ research on the presentation and outcomes of spontaneous intracerebral haemorrhages in patients referred to the Neurosurgery Department at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). Since your brain scan shows that you are a patient suffering from this disease, I would like to invite you to join this research study.

Background information
Primary spontaneous intracerebral haemorrhage refers to haemorrhage within the brain parenchyma or ventricles in the absence of underlying causative pathology, such as tumours, vascular malformations, or aneurysms. It is a type of stroke. It causes headache, loss of consciousness, neurological deficit symptoms depending on where it is located in the brain. Hypertension is the most common risk factor. There are many forms of management of this condition including observation, medical and surgical treatment.

Purpose of this research study
The purpose of study is to find out about primary spontaneous intracerebral haemorrhage in patients referred for neurosurgical intervention in CMJAH: presentation, management and outcomes We hope that the study outcomes will enable us to better understand the condition and provide better care to our patients in the future.

Procedures
In this study, all consenting patients with a diagnosis of primary spontaneous intracerebral haemorrhage will be included. A record of their demographic data, their symptoms including findings on brain scan will be kept for the study. As part of treatment some of the patients may undergo an operation where the blood clot will be drained or an external ventricular drain is inserted into the ventricle. We will then assess the outcomes after these management techniques.

Possible risks or benefits
Collection of information is by our standard protocol in the routine assessment and care of our patients. No extra demands will be made on you. There is no direct financial or other benefit for the participant of the study. However, any investigation which is specific for the study will be done free of cost to the patients.

Right of refusal to participate and withdrawal

You are free to choose whether to participate in the study. You may refuse to participate without any loss of benefit which you are otherwise entitled to. You will receive the same standard care and treatment which is considered best for you irrespective of your decision to participate in the study. You may also withdraw any time from the study without any adverse effect on your management.

If you do decide to participate, you will be asked to sign a Consent Sheet.

Confidentiality
The information about you will remain confidential. Nobody except the Investigator and the Supervisor will have access to it. Your name and identity will also not be disclosed at any time. However, the data may be seen by Ethical review committee and may be published in journal and elsewhere without giving your name or disclosing your identity.

Available Sources of Information
If you would be interested to learn about the results of the study, I would be pleased to provide a summary on request.
If you have any further questions you may contact the Investigator (Dr. R Khohomela), Department of Neurosurgery, University of the Witwatersrand, Johannesburg on tel no. 082 694 8622, or by e-mail on Rambsta@gmail.com. Alternatively, you may contact the Supervisor, Dr J Ouma, on tel no. 082 493 5394, or by e-mail on glioma42@gmail.com

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg ("Committee"). A principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.

If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Dr Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Thank you for reading this Study Information Sheet.

May 2019

APPENDIX E

ASSENT TO PARTICIPATE IN RESEARCH STUDY

Title of study: Presentation and outcomes of primary spontaneous intracerebral haemorrhage at Charlotte Maxeke Johannesburg Academic Hospital

Assent to participation

I, **……** hereby agree to be part of the study, as described in the Information Sheet given to me. I have been given a chance to ask questions and was happy with the answers given to me.

I understand that I may leave the study at any time I want to.

Minor's signature or thumb print: _____
Date: _____
Principal Investigator's Signature: _____
Date: _____

Refusal to participate

I, **……** hereby do not agree to be part of this study.

Minor's signature or thumb print: _____
Date: _____
Principal Investigator's Signature: _____
Date: _____

APPENDIX F

INFORMED CONSENT FORM

Research Project: Presentation and outcomes of primary spontaneous intracerebral haemorrhage at Charlotte Maxeke Johannesburg Academic Hospital

Principal Investigator: Dr Rambelani Khohomela

Consent Given

I, ... hereby give consent for the use of my medical records for the purposes of this research project, as described in the Study Information Sheet given to me. The research has been explained to me and I understand what my participation involves.

Participant's signature or thumb print: _____

Date: _____

Principal Investigator's Signature: _____

Date: _____

Consent Not Given

I, ... hereby do not give consent for the use of my medical records for the purposes of this research project.

Participant's signature or thumb print: _____

Date: _____

Principal Investigator's Signature: _____

Date: _____

PARENT/GUARDIAN/NEXT OF KIN CONSENT FORM

Research Project: Presentation and outcomes of primary spontaneous intracerebral haemorrhage at Charlotte Maxeke Johannesburg Academic Hospital

Principal Investigator: Dr Rambelani Khohomela

Consent Given

I, ... hereby give consent for the use of patient ..... 's medical records for the purposes of this research project, as described in the Study Information Sheet given to me. The research has been explained to me and I understand what the patient's participation involves.

Parent/Guardian/Next of Kin's signature or thumb print:

_____

Date: _____

Principal Investigator's Signature: _____

Date: _____

Consent Not Given

I, ... hereby do not give consent for the use of patient ..... 's medical records for the purposes of this research.

Parent/Guardian/Next of Kin's signature or thumb print:

_____

Date: _____

Principal Investigator's Signature: _____

Date: _____

DEFERRED CONSENT FORM

Research Project: Presentation and outcomes of primary spontaneous intracerebral haemorrhage at Charlotte Maxeke Johannesburg Academic Hospital

Principal Investigator: Dr Rambelani Khohomela

Consent Given

I, ... hereby give consent for the use of my medical records for the purposes of this research project, as described in the Study Information Sheet given to me. The research has been explained to me and I understand what my participation involves.

Participant's signature or thumb print: _____

Date: _____

Principal Investigator's Signature: _____

Date: _____

Consent Not Given

I, ... hereby do not give consent for the use of my medical records for the purposes of this research project.

Participant's signature or thumb print: _____

Date: _____

Principal Investigator's Signature: _____

Date: _____

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Rambelani Khohomela (Student number: 1530913) am a student registered for the degree of MMed (Neurosurgery) in the academic year 2020.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: _____ Date: 25/05/2020

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Dr R Khohomela

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M190207

NAME: (Principal Investigator)	Dr R Khohomela
DEPARTMENT:	School of Clinical Medicine Department of Neurosciences Division of Neurosurgery Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	Presentation and outcomes of primary spontanous intracerebral haemorrhages at Charlotte Maxeke Johannesburg Academic Hospital
DATE CONSIDERED:	2019/02/22
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Drs J Ouma and K Ibebuike
APPROVED BY:	CB Penny Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2019/04/30

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. I agree to submit a yearly progress report. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **February** and will therefore reports and re-certification will be due early in the month of **February** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

30/04/2019
Date

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES

1530913:MMed_Dissertation_Final.docx

ORIGINALITY REPORT

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5	Deresse, Birrie, and Debebe Shaweno. "Epidemiology and in-hospital outcome of stroke in South Ethiopia", Journal of the Neurological Sciences, 2015. Publication	<1%
6	www.kjim.or.kr Internet Source	<1%
7	Lovisa Tobieson. "Surgically Treated Intracerebral Haemorrhage : Pathophysiology	<1%