“ANATOMICAL RELATIONSHIP AND CLINICAL OUTCOME OF PATIENTS WITH INTRACEREBRAL HEMORRHAGE WITH INTRAVENTRICULAR EXTENSION. - A CROSS SECTIONAL STUDY AT KLES DR.PRABHAKAR KORE HOSPITAL AND MRC”

By

REG NO. BG0108004

Dissertation

Submitted to the
KLE University, Belagavi, Karnataka

In Partial Fulfillment
of the requirements for the degree of

M. D.
in
GENERAL MEDICINE

DEPARTMENT OF MEDICINE,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELAGAVI, KARNATAKA

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ENDORSEMENT

This is to certify that the dissertation entitled **"ANATOMICAL RELATIONSHIP AND CLINICAL OUTCOME OF PATIENTS WITH INTRACEREBRAL HEMORRHAGE WITH INTRAVENTRICULAR EXTENSION. - A CROSS SECTIONAL STUDY AT KLES DR. PRABHAKAR KORE HOSPITAL AND MRC"** is a bonafide research work done by **CANDIDATE REG NO. BG0108004**.

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LIST OF ABBREVIATIONS USED

AAICH	-	Anticoagulant associated intracerebral hemorrhage
ADL	-	Activities of daily life
AVM	-	Arteriovenous malformation
Bl.Urea	-	Blood urea
CAA	-	Cerebral amyloid angiopathy
CAT	-	Computerized axial tomography
cm^3	-	Cubic centimeter
CPP	-	Cerbral persufusion pressure
CSF	-	Cerebrospinal fluid
CT	-	Computed tomography
CTA	-	Computed tomography angiography
CVA	-	Cerebrovascular accident
CVD	-	Cerebrovascular disease
DC	-	Direct count
DM	-	Diabetes mellitus
DVT	-	Deep venous thrombosis
ECG	-	Electrocardiogram
EEG	-	Electroencephalogram
ESR	-	Erythrocyte sedimentation rate
FBS	-	Fasting blood sugar
FEIBA	-	Factor VII inhibitor bypass activity
FFP	-	Fresh frozen plasma
GCS	-	Glasgow Coma Scale
GERFHS	-	Genetic and Environmental Risk Factors for Hemorrhagic Stroke

GOS	-	Glasgow Outcome Scale
HbA1c	-	Glycosylated haemoglobin
HDL	-	High density lipoprotein
HTN	-	Hypertension
i.e.,	-	That is,
ICASS	-	Indian Collaborative Acute Stroke Study
ICH	-	Intracerebral hemorrhage
ICP	-	Intracranial pressure
INR	-	International normalized ratio
IR	-	Inversion recovery
IVC	-	Inferior vena cava
IVE	-	Interventricular extension
IVH	-	Intraventricular hemorrhage
LAD	-	Left anterior descending artery
LDL	-	Low density lipoprotein
LVH	-	Left ventricular hypertrophy
MCV	-	Mean corpuscular volume
mg%	-	Milligram percentage
mg/dL	-	Milligrams per deciliter
mL	-	Milliliter
mmHg	-	Millimeters of mercury
mmol/L	-	Millimole per litre
MRI	-	Magnetic resonance imaging
mRS	-	Modified rankin scale
n	-	Total number
p	-	Probability value
PCCs	-	Prothrombin complex concentrates

PE	-	Pulmonary embolism
PPBS	-	Post prandial blood sugar
RBS	-	Random blood sugar
tPA	-	Tissue plasminogen activator
SAH	-	Subarachnoid hemorrhage
SBP	-	Systolic blood pressure
SD	-	Standard deviation
SE	-	Spin echo
SPAF	-	Stroke Prevention in Atrial Fibrillation
SPIRIT	-	Stroke Prevention in Reversible Ischemia Trial
Sr. Creat	-	Serum creatinine
Sr. Potass	-	Serum potassium
Sr. Sodium	-	Serum sodium
TGs	-	Triglycerides
TIAs	-	Transient ischemic attacks
VKA	-	Vitamin K antagonists
VLDL	-	Very low density lipoprotein
vs.	-	Versus
WARSS	-	Warfarin-Aspirin Recurrent Stroke Study
WHO	-	World Health Organization

ABSTRACT

Background and objectives

Spontaneous ICH remains a formidable disease that continues to disable and kill the majority of its victims. Stroke places a tremendous burden on health resources throughout the world. Most cases are attributed to hypertension or amyloid angiopathy. ICH occurs most frequently in the putamen (35 to 50%), followed by lobar (30%), thalamus (10 to 15%), pons (5 to 12%), caudate (7%), and the cerebellum (5%).Various studies showed that outcome in patients with ICH is related to age, clinical presentation, alcoholism, hematoma volume, IV extension etc. The objectives of present study were to study the relationship between anatomical site, clinical presentations, hematoma volume and intraventricular extension with outcome of the patients based on modified rankin scale.

Methods

The present cross sectional study was conducted on patients with intracerebral hemorrhage admitted to medicine and neurology wards in KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi from Jan 2015 to Dec 2015. Relevant data was collected by a detailed interview with either patient or the attender, clinical examination and with the help of a predesigned and pretested proforma. Anatomical site of intracerebral hemorrhage and volume of ventricular bleed will be made out from CT/MRI scans. Clinical outcome was assessed based on Modified rankin scale score. Statistical test –Mann whitney-U test and Chi-square tests also may be used for analysis.

Results

We found ICH was common in the age group 51-70 years. The ICH was more common in males compared to females with M:F ratio 3.66:1. The most common clinical presentations were with neuro deficits, speech disorder and cranial nerve dysfunction. Hypertension was the most important risk factor found among patients. Most of patients with hypertension were newly detected cases. The duration and severity of hypertension didn't have any bearing on the study group. The age and gender of the patient didn't show any influence on the outcome of the patients in our study. The outcome of the patients were significantly affected by presentation of patients with neurodeficits/altered sensorium.The volume of bleed significantly influenced the outcome of the patients. ICH with intraventricular extension had poorer outcome as compared to ICH without intraventricular extension.

Conclusion

In the present involving 56 patients with intracerebral bleed, the outcome was significantly influenced by clinical presentation, volume of ICH, intraventricular extension and midline shift in the CT/MRI. The age, gender and habits didnt show any correlation with the outcome of the patient. We feel it is worthy to study by adjusting comorbid conditions like hypertension, age, sex, habits and site of bleed to know whether these patients have true association. Owing to our small sample size, studies with large sample size is required to overcome these limitations.

Keywords

Haemorrhagic stroke; Intracerebral bleed; Interventricular extension;

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INTRODUCTION

Spontaneous ICH remains a formidable disease that continues to disable and kill the majority of its victims.[1] Stroke is the third leading cause of mortality and morbidity in developed countries after coronary heart disease and cancer. Stroke places a tremendous burden on health resources throughout the world. It will also be a major public health problem in developing countries like India with the changing epidemiological transition along with an increasing life expectancy due to decline in communicable and nutritional diseases.[2] Community surveys from different regions of India showed crude prevalence rate for 'stroke' presumed to be of vascular origin in the range of 200 per 100,000 population. Likewise analysis of data from university hospitals in India suggests that 1.5% of all hospital cases, 4.5% of medical and about 20% of neurological admissions are of acute stroke. Spontaneous ICH accounts for approximately 15 to 20% of all strokes. The morbidity pattern revealed that stroke increases with increasing age and predominantly constituted ischemic strokes (73.1%). Stroke in the young constituted 27.8%.[2]

Most cases are attributed to hypertension or amyloid angiopathy. ICH occurs most frequently in the putamen (35 to 50%), followed by lobar (30%), thalamus (10 to 15%), pons (5 to 12%), caudate (7%), and the cerebellum (5%).[3]

Treatment of this disease continues to be controversial and without any proved success such as improvement in the disease mortality or the resulting disability in survivors.[4]

Modifiable risk factors for stroke include hypertension, cardiovascular disease, diabetes, hyperlipidemia, cigarette smoking and alcohol abuse. Important non modifiable risk factors for stroke include age, gender, ethnicity and heredity. Improved detection and modification of risk factors could reduce the impact of this disease.

Primary prevention is the most effective medical intervention. Nevertheless, as the population continues to age and patients remain undertreated for hypertension, the incidence of ICH is likely to increase resulting in significant socioeconomic impact on society in the coming years. A growing body of evidence suggests that genetic factors play an important role in the occurrence of certain forms of ICH, such as lobar hemorrhage.[5] Epidemiological studies, prospective as well as case control studies reported an inverse association between serum cholesterol level and risk of hemorrhagic stroke. Unlike ischemic strokes or other causes of hemorrhagic stroke such as subarachnoid hemorrhage (SAH), where major advancement of treatment has led to improved outcomes, the increased incidence of ICH has not been matched with any considerable improvement in treatment.[6]

Technology did not exist to diagnose less severe hemorrhages during life, especially if the lesions did not communicate with the cerebrospinal fluid (CSF) [prior to the introduction of computed tomography (CT) scan]. Computed tomography now allows accurate localization of small and medium sized hemorrhages. Computed tomography not only shows clinicians whether a lesion is hemorrhage, but also accurately shows the location, size, spread within the brain, drainage into the ventricles, spaces around the brain, presence of edema and mass effect. While old infarcts and hemorrhages can look similar on CT. Therefore, it is an important task for the physician to predict the functional outcome from a single CT scan of the brain done at the time of the hospital admission.[7] Magnetic resonance imaging (MRI), with its capability of showing the presence of hemosiderin can help define whether lesions are old hemorrhages. When the subject of ICH is reviewed in light of results with newer imaging techniques, the old rules are found to apply mainly to larger hemorrhages, which is only a small fraction of ICH.[8]

Howeever, in India, so far very few studies have been done on intracerebral hemorrhage with intraventricular extension. Furthermore, the studies that have been already done varies regarding the outcome depending on the site and volume of hemorrhage.

The above facts prompts, extensive research to explore insights of ICH in the context of determining primary preventive measures, predictors of early outcome and treatment of ICH. Hence the present study was planned to know the relationship between anatomical site of intracerebral bleed and clinical outcome, clinical outcome in patients with intracerebral hemorrhage with and with out intra ventricular extension, relationship between volume of intraventricular bleed and clinical outcome, various clinical presentations of patients with intracerebral hemorrhage so as to reduce the burden of this disease.

OBJECTIVES

The objectives of present study were;

1. To study relationship between anatomical site of intracerebral bleed and clinical outcome based on modified rankin scale and thereby assess prognosis in them.

2. To study the clinical outcome in patients with intracerebral hemorrhage with and with out intra ventricular extension based on modified rankin scale and thereby assess prognosis in those patients.

3. To study relationship between volume of intraventricular bleed and clinical outcome based on modified rankin scale and thereby assess prognosis.

4. To study various clinical presentations of patients with intracerebral hemorrhage.

REVIEW OF LITERATURE

Historical perspectives

The term “Stroke” or “Cerebrovascular accidents” has come to signify the abrupt impairment of brain function caused by a variety of pathological changes involving one (focal) or several (multifocal) intracranial or extracranial blood vessels.[9]

The first known description of stroke was given by Hippocrates who took the word “Apoplexy” from common non medical use where it meant **“**Astonished**,** Suddenly benefit of one’s senses**”** and applied it descriptively to stroke.

- Jacob Werter, a Swiss physician was the first person to suggest that apoplexy was caused by disease of blood vessel in the brain.
- Thomas Willis described the circle of wills in 1664.
- Seddicot described spontaneous intracerebral haemorrhage in 1813.
- In 1828 Abberonbie, described the obliterative arterial disease of cerebral arteries.
- In 1825, Bonillord described localisation of lesion and aphasia.
- In 1860, Von Graafe used Helmoltz ophthalmoscope.
- 1877 Osler reported a case of Subarachnoid and intracerebral haemorrhage due to ruptured aneurysm.
- In 1914, Ramasy hunt was the first to describe comprehensive description of spontaneous carotid occlusion without crest disease of the intracranial vessel producing cerebral infarction.

- Dandy performed the first air ventriculogram.
- Denny brown introduced the concept of vascular insufficiency.
- Dr. GodFrey Honnsfield, a British physicist in 1972 introduced computerized axial tomography (CAT) technique into neuro radiology which resulted in award of noble prize in 1979. This lead to more precise categorization of ischaemic and hemorrhagic cerebrovascular accident (CVA).

Within the last decade, the magnitude of research has grown exponentially. The term apoplexy has faded, and the term stroke has become common place in the medical setting.[10]

Definition

WHO defines stroke as rapid development of clinical signs of focal (or global) brain function disorders, with symptoms which last 24 hours or longer or lead to death, without other clear cause, except signs of blood vessel damage.[11]

Stroke is the third leading cause of mortality in the United States. Of the approximately 700,000 strokes occurring each year, about 550,000 are first strokes. About 400,000 strokes are ischemic.[12] Stroke is the leading cause of adult disability with more than 4 million stroke survivors in the United States alone. Approximately 90% of stroke survivors are left with some residual deficit.[13]

Cerebrovascular disease (CVD) ranks first in frequency and importance among the neurological disorders that cause disability. About 50% of the patients with neurological disorders admitted in general hospitals are of this type.[13]

- Primary ICH – Spontaneous non-traumatic bleeding into brain parenchyma.
- Primary ICH is mostly the result of chronic hypertension and amyloid angiopathy which accounts for almost 78 to 88% of cases.[14]

Intracerebral hemorrhage (ICH) is defined as the spontaneous extravasation of blood into the brain parenchyma. Non-traumatic forms of ICH account for 10% to 30% of all stroke hospital admissions,[15] leading to catastrophic disability, morbidity, and a mortality of 30% to 50% at 30 days.[15] Death at 1 year varies by different location: 51% for deep, 57% for lobar, 42% for cerebellar and 65% for brain stem hemorrhages.[16] In a recent population-based study, the overall incidence of ICH was estimated to be 12 to 15 cases per 100,000 population.[17] The cost of ICH alone is estimated to be USD $6 billion per year in the United States alone[18] related to both acute and chronic medical care costs, as well as the loss of productivity.[18]

Epidemiology

Worldwide

The prevalence of major varieties of CVD is uncertain and varies depending upon the source of data. Data from hospitals and neurology clinics are subjected to selection bias and are likely to overemphasize strokes that are more severe and require hospitalization. In addition the numbers of patients likely to be underestimated as patients with mild strokes may not avail these services. Therefore general population survey data are more representative but often suffer from small number of less common types of stroke making precise estimates of frequency of various stroke subtypes difficult.[19]

Intracerebral hemorrhage accounts for 10–15% of all strokes in Western populations and is defined as the non-traumatic, abrupt onset of severe headache, altered level of consciousness, or focal neurological deficit associated with a focal collection of blood within the brain parenchyma on neuroimaging or at autopsy which is not due to trauma or hemorrhagic conversion of a cerebral infarction.[20] The incidence of ICH is defined as the percentage of a population experiencing a first ICH in a given time period (usually a year). When reviewing studies of ICH incidence it is important to consider the criteria utilized, as investigators may include or exclude hemorrhages associated with vascular malformations, anticoagulants, thrombolytic agents, or illicit drugs. Comparisons of incidence rates are further complicated by methodological differences in case ascertainment, imaging rates, variations in population structure, and the range of ages reported. Given these limitations, incidence rates of ICH in the Western hemisphere during the CT era have generally ranged from 10 to 30 cases per 100000 persons.[21]

Intracerebral hemorrhage incidence rates are higher in eastern Asia, where ICH has historically accounted for a larger percentage of all strokes than in Western populations. This balance may be changing due to declining rates of ICH in the East. The incidence of ICH declined between the 1950s and the 1980s. Studies of incidence trends in subsequent years have produced mixed results. There was a trend toward a reduction in ICH incidence in Oxfordshire, England between 1981 and 2006. Intracerebral hemorrhage incidence also declined during the 1990s in several Chinese cities. However, similar declines have not been seen in other studies. The stabilization of ICH incidence in the last two decades is at least partially attributable to the detection and proper classification of small hemorrhages with modern neuroimaging. Risk for ICH appears to be marginally greater in men than in women, driven by an excess of deep hemorrhages. In the United States blacks and Hispanics have significantly higher rates of ICH than whites. Among blacks and Hispanics, the excess risk of ICH is most notable in young and middle-aged persons. The predominant location of ICH within the brain varies in different populations. In the United States, Europe, and Australia, deep cerebral ICH (hemorrhage originating in the periventricular white matter, caudate nucleus, internal capsule, putamen, globus pallidus, or thalamus) is most common, followed closely by lobar hemorrhages originating in the gray matter or subcortical white matter. In a large population-based study in Japan, however, lobar hemorrhage accounted for only 15% of ICHs.[21]

In most populations, cerebellar hemorrhage accounts for approximately 10% of ICH and brainstem hemorrhage for 5–10% of ICH. In the United States, the greatest excess risk of ICH in blacks and Hispanics as compared to whites occurs in deep cerebral and brainstem locations.[21]

India

The Indian subcontinent is a vast land with rapidly increasing population. Ascertainment of the true incidence of any disease in such a large population is associated with innumerable problems and CVD is no exception. There is inadequate data to reflect the true incidence of CVD in the Indian population. This is because, most of them are studies carried out in large urban teaching hospitals. Well-designed population based study was done in Vellore, South India that was conducted in two phases. In the first phase, a total urban and rural population of 258,576 was evaluated. After examination by neurologist, 147 cases of hemiplegia were detected. The prevalence rate of hemiplegia was calculated as 56.9 per 100,000 populations (68.5 in male and 44.8 in female). The prevalence rate was more in urban area than in rural area and increased with age. Subsequently during the second phase, the population was kept under surveillance for two years, prevalence and annual incidence rate of 84 and 13 respectively per 100,000 populations was reported.[22]

Cerebrovascular disease constituted 0.9 to 4.5% of total medical admissions. Ischemic stroke from thrombosis and embolism constituted between 57.3% and 82.7% of all strokes. The incidence of hemorrhagic stroke was between 13.6% and 37.9% of total stroke cases. Most of these studies were retrospective.[23]

Based on neuroimaging findings, recent studies have determined the stroke subtypes and the ratio of cerebral infarct to hemorrhage range as 1.86:1-2.21:1.[24-26] Hence, cerebral hemorrhage is proportionately much higher in the Eastern Indian community than in Western countries, where the ratio of infarct to hemorrhage is 5:1. Suitable neuroimaging data were available only in 50-60% of cases in these surveys. Incidentally, the high incidence of cerebral hemorrhage also has been noted among Chinese.[27]

The Kolkata study[26] demonstrated that the basal ganglia-thalamic region was, by far, the commonest site (75%) of hemorrhage. In contrast, the subcortical region was the commonest site of infarction (75.6%). This predilection for subcortical infarct also is common in other Asian races. A study based on noninvasive tests to determine subtypes of ischemic stroke from a hospital-based registry of Southern India has attributed 41% of strokes to large artery atherosclerosis, 18% to lacunar causes, 10% to cardioembolic causes, and 4% to causes such as Takayasu syndrome, MoyaMoya disease, carotid dissection, hyperhomocysteinemia, anticardiolipin antibody, and protein S deficiency. The rest 27% of the cases of ischemic stroke were of undetermined origin.[28]

Among cardioembolic stroke, rheumatic heart disease (29%) and ischemic heart disease (27%) are predominant causes.[28]

The studies conducted in the last decade in large academic centers from northern and southern India both have documented a high frequency of intracranial vessels affected on the basis of noninvasive vascular studies.[28,29] This is consistent with findings in other Oriental countries. The Indian Collaborative Acute Stroke Study (ICASS); a multicentric study conducted among 2,162 admitted stroke patients across southern, northern, and western India; observed ischemic stroke in 77%, hemorrhagic stroke in 22%, and unspecified stroke in 1% cases based on cerebral computed tomography (CT).[30]

Hence, in India, the pooled data incorporating all the studies reveal that ischemic stroke occurs in 68-80% and hemorrhagic stroke in 20-32%. Ischemic stroke comprise large vessel (41%), lacunar (18%), cardioembolic (10%), other determined (10%), and undetermined (20%) subtypes. The extracranial carotid disease is the etiological factor in 25-26% and intracranial carotid disease in 30% of ischemic stroke cases.[31]

Hospital statistics of CVD in India when compared to the West are more apparent than real as 80 to 85% of Indian population are living in rural areas and may not reach city hospitals which are equipped with facilities for complete workup of the patients with stroke. Ischemic infarctions are still predominant in overall picture of CVD.[12] The incidence of stroke in young in India is higher when compared to the Western figure. It has been found that strokes are fairly common in young Indians below 40 years since they constitute 18.8 to 32% of all stroke cases.[32]

Classification of cerebrovascular disease

Cerebrovascular disease from the clinical point of view can be classified as thrombosis, embolism and hemorrhage.

International classification of disease by World Health Organization[33]

1. ***Intracerebral Hemorrhage***

- Primary includes those associated with hypertension and/or alcoholism
- Excludes any specified causes
- Due to arterial malformation or arteriovenous malformation (AVM)
- Due to moya moya disease or other arterial obstruction
- Due to amyloid angiopathy
- Due to trauma
- Others
- Unknown

2. ***Subarachnoid Hemorrhage***

- Due to berry aneurysm
- Due to AVM
- Due to trauma

Cerebral Hemorrhage

Intracranial bleed could be subarachnoid hemorrhage, intraparenchymal hemorrhage or intraventricular hemorrhage. Seventy to ninety percent of spontaneous ICHs are associated with hypertension.[34] Analysis of eleven separate series of hypertensive ICH revealed that 64% occur in basal ganglia, 13% in thalamus, 16% in hemispheric white matter, 10 to 12% in pons and 8 to 10% in cerebellum.[34]

Risk factors in cerebrovascular diseases

<u>Age and race</u>

Age is the greatest risk factor for ICH. Incidence rates increase dramatically among persons older than 60. As discussed previously, there are geographic and racial variations in ICH incidence. Studies to date have not determined whether these variations can be explained entirely by known risk factors or whether there are additional factors, possibly genetic, which remain undiscovered.

<u>Hypertension</u>

Hypertension is the most important and prevalent modifiable risk factor for ICH. In the biracial population of Greater Cincinnati during 1988, the presence of hypertension among patients with ICH was remarkably similar for whites (73%), African-Americans (71%), men (72%), and women (73%). Untreated hypertension is a greater risk factor than treated hypertension, and hypertensive patients who discontinue their medications have greater risk than those who continue them. Among modifiable risk factors for ICH, hypertension accounts for the greatest attributable risk for hemorrhage in deep hemispheric and brainstem locations. The role of hypertension in lobar ICH is less clear, but accumulating evidence suggests hypertension is also a risk factor for hemorrhage in this location (albeit less potent). The relative effect of hypertension as a risk factor for ICH is greater in younger patients than the elderly.[21]

Treatment trials for hypertension have shown reduced ICH risk with improved blood pressure control. The use of illicit sympathomimetic drugs, particularly cocaine and amphetamines, has been associated with hemorrhagic stroke in some (but not all) studies. This relationship may be due to drug-induced hypertension or drug-induced cerebral vasculitis.[21]

Cerebral amyloid angiopathy

Once thought to be a rare cause of ICH, cerebral amyloid angiopathy (CAA) is now considered an important cause of lobar hemorrhage in the elderly. Its principal pathological feature is the deposition of amyloid protein in the media and adventitia of leptomeningeal arteries, arterioles, capillaries, and, less often, veins. The hypothesized pathogenesis of ICH due to CAA involves destruction of the normal vascular structure by deposition of amyloid in the media and adventitia and subsequent miliary aneurysm formation or double barreling and fibrinoid necrosis. The brittle blood vessels and microaneurysms may then be prone to rupture in response to minor trauma or sudden changes in blood pressure. Cerebral amyloid angiopathy may also be responsible for transient neurological symptoms and dementia with leukoencephalopathy.[21]

Amyloid protein becomes increasingly frequent in cortical blood vessels with advancing age, affecting only 5–8% of persons with age 60–69 years but 57–58% of those age 90 years or older. The deposition of amyloid is most prominent in the parieto-occipital regions and is rarely found in the basal ganglia or brainstem. Cerebral amyloid angiopathy equally affects men and women.[21]

Apolipoprotein E and CAA

Several studies have examined the relationship of Apolipoprotein E E2 and E4 with lobar ICH and CAA. In a population-based, case-control study of hemorrhagic stroke in Greater Cincinnati/Northern Kentucky (the Genetic and Environmental Risk Factors for Hemorrhagic Stroke, or GERFHS, study), cases of lobar ICH were age-, race-, and gender-matched to controls from the same population, allowing investigators to control for putative ICH risk factors and determine the prevalence of Apolipoprotein E genotype in the population from which cases were identified. After controlling for the presence of hypertension, hypercholesterolemia, frequent alcohol use, smoking history, and other risk factors, Apolipoprotein E4 was found to be an independent risk factor for lobar ICH but not non-lobar ICH. In addition, haplotypes inferred using 12 markers over the 50 untranslated region, promoter region, and exons of the Apolipoprotein E gene identified significant association with lobar ICH, which suggests that regulation of the gene may affect the risk of disease.[35]

Aneurysms and vascular malformations

Although ruptured berry aneurysms typically cause SAH, on occasion bleeding is directed into the brain parenchyma without significant subarachnoid extension. Vascular malformations associated with ICH include arteriovenous malformations (AVMs), cavernous malformations, dural arteriovenous fistulae, venous malformations, and capillary telangiectasias.Reports of ICH mechanism suggest that aneurysms and vascular malformations are particularly important as a cause of ICH among young people. In a prospective autopsy series, 4% of all brains were found to have vascular malformations, of which 63% were venous malformations. This contrasts starkly with lesions that cause hemorrhage as reported by autopsy. While venous malformations are the most common lesions in the general population, they are associated with only a small percentage of ICH cases. Similarly, cerebral telangiectasias are more common at autopsy than AVMs or cavernous malformations but rarely hemorrhage. The natural history, clinical evaluation, and management options for intracranial vascular malformations have been recently reviewed.[21]

Anticoagulant-andthrombolytic associated ICH

The use of warfarin for prevention of ischemic stroke among patients with atrial fibrillation increased significantly during the late 1980s and 1990s following publication of the Stroke Prevention in Atrial Fibrillation (SPAF) trials, European Atrial Fibrillation Trial, and other important studies on this topic. Warfarin distribution in the United States quadrupled on a per-capita basis during the 1990s [61]. During the same period, the incidence of anticoagulant associated intracerebral hemorrhage (AAICH) quintupled in the Greater Cincinnati region. In most trials of warfarin for treatment of atrial fibrillation or myocardial infarction the risk of AAICH has ranged from 0.3% to 1.0% per patient year, with risk on the lower end of this spectrum in more recent studies. Several trials have tested warfarin for secondary stroke prevention in patients with cerebral ischemia of non-cardiac origin. The Warfarin-Aspirin Recurrent Stroke Study (WARSS) compared aspirin to warfarin (goal INR 1.4–2.8), and found no difference between groups in effectiveness or risk of major hemorrhage (including ICH). The Stroke Prevention in Reversible Ischemia Trial (SPIRIT) compared aspirin to high intensity warfarin (goal INR 3.0–4.5). It was stopped before completion because of a 7.0% annual risk of major hemorrhage in the warfarin group, including a 3.7% annual risk of intracranial bleeding. Studies of anticoagulation outside of clinical trials show that well-managed warfarin at conventional INRs can produce acceptable rates of ICH (similar to or slightly higher than in trials); however, the hemorrhage risk must be balanced against the benefit of anticoagulation for each patient. The relative risk of ICH in anticoagulated patients as compared to the general population is approximately 7–10. Data from clinical trials and community surveillance suggest that clinical factors that increase the risk of AAICH are advanced age, prior ischemic stroke, hypertension, leukoaraiosis, and higher intensity of anticoagulation. The addition of antiplatelet agents to warfarin probably increases the risk compared to warfarin alone. Strict management of blood pressure and INR in anticoagulated patients reduces the risk of hemorrhage. Thrombolysis for myocardial infarction carries a small but definite risk of intracranial hemorrhage. Rates of intracranial hemorrhage in this setting have generally ranged from 0.4% to 1.5% of patients treated with various regimens of thrombolytic agents and anticoagulants. Risk factors for hemorrhage after thrombolysis for myocardial infarction include older age, female sex, black race, hypertension, prior stroke, excessive anticoagulation, and lower body weight. In the large GUSTO-1 trial, the majority of such hemorrhages were intraparenchymal (81%) or intraparenchymal plus subdural

(15%), with relatively few pure subdural (3%) or pure intraventricular (1%) bleeds. Among intraparenchymal hemorrhages, the majority (77%) occurred in lobar regions of the brain. Intraventricular (49%) and subarachnoid (11%) extension of bleeding was relatively common. Thrombolytic treatment of ischemic stroke carries a greater risk of intracranial hemorrhage than thrombolysis for myocardial infarction.[21]

Antiplatelet drugs

Antiplatelet drugs probably increase the risk of ICH by a small amount. The absolute risk of intracranial hemorrhage among elderly persons taking aspirin has been estimated at 0.2–0.3% annually (vs. 0.15% in similar persons not taking antiplatelets or anticoagulants).[21]

Cerebral microbleeds

The use of gradient echo MRI to detect small, asymptomatic hemorrhages in the brain parenchyma ("microbleeds") has received considerable recent attention. Gradient echo MRI accentuates signal dropout from chronic blood products and is more sensitive at detecting small hemorrhages than standard T2 sequences. The prevalence of microbleeds in the general population is best estimated from two studies of middle-aged and elderly adults without known cerebrovascular disease or dementia, in which microbleeds were found in 6.4% and 4.7% of the respective populations. Microbleeds are associated with both ischemic (especially lacunar) and hemorrhagic cerebrovascular disease as well as hypertension, leukoaraiosis, advancing age, and male gender. Microbleeds are common in hemorrhagic stroke, occurring in 54–71% of ICH patients. They appear to be equally prevalent in cases of deep cerebral and lobar hemorrhage, and are therefore not specific for amyloid angiopathy or hypertensive ICH; however, in some studies the location of microbleeds has correlated with the site of symptomatic hemorrhage (i.e., deep cerebral micro bleeds are associated with deep cerebral ICH while lobar microbleeds are associated with lobar ICH). Many clinicians consider microbleeds to be markers of small-vessel disease and a hemorrhage-prone state.[21]

Although microbleeds have been associated with a variety of demographic variables and disease states, their practical value in predicting hemorrhage risk is less clear. A small, prospective Chinese study scanned 121 acute stroke patients with gradient echo MRI and found that 35.5% had microbleeds. Over a mean follow-up of 27.2 months, 4 patients (9.3%) with microbleeds had a subsequent ICH, compared to 1 patient (1.3%) without microbleeds (p¼0.053). The power of microbleeds to predict subsequent hemorrhagic and ischemic cerebrovascular disease and the value they might add to risk–benefit analyses for antiplatelet or anticoagulant use are important questions which remain unanswered.[21]

<u>Prior cerebral infarction</u>

Prior cerebral infarction is associated with a 5- to 22-fold increased risk of ICH [32,95,96]. The strong relationship between ICH and cerebral infarction is not surprising since hemorrhage and infarction share similar risk factors, such as hypertension. In the GERFHS case-control study in Greater Cincinnati 15% of ICH patients had a history of previous ischemic stroke; the multivariate odds ratio for ICH in patients with prior stroke compared to controls was 7.0. While hypercholesterolemia is a risk factor for cardiac disease and ischemic stroke, hypocholesterolemia appears to increase risk of ICH. Potential explanations for the association of low cholesterol and ICH include reduced platelet aggregation, increased fragility of the cerebral vasculature, and confounding by medical illness or nutritional deficiencies. Given these findings, there is theoretical concern that widespread use of cholesterol lowering medications may increase rates of ICH. Analysis of the GERFHS study showed that hypercholesterolemia was protective for ICH, but that statin use was not associated with increased ICH risk.[21]

Heavy alcohol use

Numerous studies have identified a relationship between alcohol use and the risk of hemorrhagic stroke. There is probably a dose– response relationship with increased risk among heavy but not light drinkers. Heavy alcohol use has also been implicated in early hematoma expansion, possibly due to adverse effects upon platelet and liver function.[21]

Tobacco use

There may be a weak association between tobacco use and ICH but data have been conflicting. It is suggested that current smoking (as opposed to past smoking or never smoking) increases the risk of ICH in a dose-dependent manner.[21]

Diabetes mellitus

Diabetes is associated with greater risk of ICH in some case-control studies. A review of available data produced an overall risk ratio of 1.3 with borderline statistical significance. The association of diabetes and ICH may vary by age group and location of hemorrhage.[21]

Heritability

There is a genetic component to ICH risk but its absolute value is small. Among probands in the GERFHS case-control study,[35] 6% of patients had an affected first-degree relative and 6% an affected second-degree relative. Among cases the odds ratio for an affected first-degree relative was high (6.3) but the population attributable risk was low (0.05). The association of apolipoprotein genotypes with lobar ICH was previously discussed.[21]

Serum cholesterol

In prospective studies, hemorrhagic stroke has been found to occur at higher rates in persons with low levels of blood total cholesterol than in persons with higher levels.[36,37] This finding was first noted following World War II among rural Japanese, who had very low serum cholesterol levels by Western standards (less than 160 mg/dL) and also had a marked increase in incidence of ICH.[38]

The Kaiser medical care program, a cohort study included 61,751 enrollees, aged 40 to 89 years and free of cardiovascular disease at baseline. Sixteen year incidence of combined non-fatal and fatal ICH was investigated in relation to serum cholesterol measured in multi-phasic health checkups made in 1977 through 1985. From 1978 through 1993 (average of 10.7 years), there were 386 events (201 in men, 29% fatal; 185 in women 42% fatal). By multivariate proportional hazard life table regression analysis, serum cholesterol level below the sex specific 10^{th} percentile (less than 178 mg/dL) in men compared with higher cholesterol level, was associated with a significantly increased risk of ICH in men aged 65 years or older (relative risk 2.7; 95% confidence interval 1.4 to 5%). An excess risk was also observed among elderly women at the lowest cholesterol range but a chance finding could not be ruled out. No relationship was found among men or women aged 40 to 64 years and statistical interaction of low serum cholesterol with hypertension was found in either sex.[39] The mechanism of harmful effect of low serum cholesterol upon cerebral arteries is not clearly understood; very low serum cholesterol appears to be an underlying condition that can facilitate weakening of the arterial wall leading to the rupture of the small intraparenchymal cerebral arteries. There is, however, some evidence that very low serum cholesterol plays a role in the pathogenesis of ICH through its adverse effects on erythrocyte fragility and the development of arterionecrosis. It was suggested that low serum cholesterol (which might reflect poor nutrition, especially inadequate intake of animal food) could enhance the vulnerability of small intraparenchymal cerebral arteries and lead to the development of stroke in the presence of hypertension.[40]

Site of Intracranial Hemorrhage

The most common form of ICH is the putaminal hemorrhage. Predilection sites for ICH include the basal ganglia (40 to 50%), lobar regions (20 to 50%), thalamus (10 to 15%), pons (5 to 12%), cerebellum (5 to 10%) and other brainstem sites (one to five percent).[1] A study on ICH showed that the most common site of bleeding was putamen (35 to 50%) followed by subcortical white matter (30%), thalamus (10%), pons (5 to 12%), cerebellum (10%) and brain stem (six percent).[41]

Drugs

Intracranial hemorrhage secondary to cocaine[42] and amphetamine[43,44] addiction is reported in literature. Drug abuse is an important consideration in non-traumatic parenchymal ICH, representing approximately 0.5% of overall ICH, but a higher percentage of ICH is seen in adolescents and young adults.[64,65] Although drug associated cerebral vasculitis is well recognized for heroin, methamphetamine and ephedrine, vast majority of cocaine related ICH is not associated with any vasculitis or vasculopathy.[45,46] Rather, it seems that a sudden increase in blood pressure above recent baseline, even if not to markedly hypertensive levels or direct pharmacologic effects is the trigger for ICH in this setting. Other prescription and non-prescription drugs such as phenyl-propranolamine and other blood pressure raising or adrenergic agonist drugs have been associated with ICH, especially with persistent use or overdose.[47-49] Alcohol, the most common drug of abuse in the society has been associated with an increased risk of parenchymal (and subarachnoid) ICH.[50,51]

Clinical presentation and natural history of intracerebral hemorrhage

The Harvard Cooperative Stroke Registry reported on the clinical findings associated with stroke.[52] The clinical features used to define ICH were presentation with a gradual progression (over minutes or days) or sudden onset of focal neurological deficit, usually accompanied by signs of increased intracranial pressure such as vomiting or diminished consciousness. As many as 91% of patients were hypertensive (blood pressure 160/100mmHg or higher) at the onset of their stroke.[21]

Vomiting was far more common in ICH and SAH (51% and 47% respectively) than for ischemic stroke (4–10% of cases). While SAH presented with headache at onset in 78% of cases, 33% of cases of ICH also had a headache at onset compared to 3–12% of ischemic stroke subtypes. Finally, SAH and ICH both presented with coma in 24% of cases compared to 0–4% of ischemic stroke subtypes.

A particular characteristic of ICH was the smooth or gradual progression of stroke in 63% of cases, with sudden onset in 34% of cases. A smooth or gradual onset of stroke was seen in only 5–20% of ischemic stroke subtypes and 14%of SAH. Thus, ICH is the stroke sub type most likely to worsen significantly in the first 24 hours.[21]

There are two separate aspects of differential diagnosis of stroke.

1. Vascular disease must be distinguished from other neurologic illnesses.
2. The different types of vascular disease must be separated from one another.

Differentiation of vascular disease from other neurologic illness:

The three criteria by which the stroke is identified are

1. Temporal profile of stroke syndrome
2. Evidence of focal brain disease
3. The clinical setting.

A clear history of premonitory phenomena, mode of onset and the evaluation of neurologic disturbance in relation to patient’s medical status are required.

There are few categories of neurologic diseases whose temporal profile mimic that of CVD. Tumors, infection, inflammation, degeneration and nutritional disease are not likely to manifest themselves precipitously. A stroke developing over a period of several days usually progresses in a stepwise fashion, increments of deficits added from time to time. A slow gradual downhill course over a period of one week or more indicates that the lesion is probably not vascular.

Differentiation of thrombosis, embolism and hemorrhage

It is difficult to frame definite rules to differentiate cerebral hemorrhage, ischemic and embolic infarction. However with history and detailed clinical examination majority of the cases can be diagnosed at the bed side.

Clinical presentation of symptoms by subtype[21]

	thrombosis	Lanune	Embolus	ICH	SAH
Maximal at obset	**40%**	**38%**	**79%**	**34%**	**80%**
Stepwise	**34%**	**32%**	**11%**	**3%**	**3%**
Gradual	**13%**	**20%**	**5%**	**63%**	**14%**
Fluctuating	**13%**	**10%**	**5%**	**0%**	**3%**

a. CLINICAL

Cerebral thrombosis

The important diagnostic criteria of atherothrombotic infarction are:

- History of prodromal Transient ischemic attacks (TIAs).
- Intermittent stepwise evolution of neurologic deficit with recovery and improvement between worsening rather than steady progression.
- Relative preservation of consciousness unless upper part of basilar territory is involved.
- Onset during sleep.
- On arising or during a period of hypotension, evidence of atherosclerosis.
- Normal Cerebrospinal fluid (CSF).

However, TIAs are seen in only 30% of cases, consciousness may be impaired in massive cerebral infarction, CSF will be blood stained in hemorrhagic infarction.

Cerebral embolism

The clinical syndrome is characterized by abrupt development of completed stroke within few seconds. Transient ischemic attacks are uncommon. Presence of atrial fibrillation, myocardial infarction, and endocarditis favour the diagnosis of embolism. Evidence of recent embolism in other organs, rapid improvement from stroke, relative preservation of consciousness favours the diagnosis.

Cerebral hemorrhage

Presence of hypertension (70 to 80% of patients), frequent occurrence of headache, absence of prodromal phenomena, rapid development of neurologic deficit over a period of minutes to hours, onset during waking hours, deepening stupor or coma, nuchal rigidity except when in deep coma, suggest the diagnosis of ICH.

In a series of 244 cases of proven ICH it was possible to identify four major presenting groups.[53]

1. Sudden onset without loss of consciousness (89 cases)
2. Sudden onset with loss of consciousness (117 cases)
3. Gradual onset without loss of consciousness (23 cases)
4. Gradual onset with later loss of consciousness (4 cases)

The exact onset of remaining 12 cases was unknown. Thus, in about 50% cases patients did not lose consciousness at or within 24 hours of ictus. Severe headache was a feature of only 50% cases and vomiting was always universal.[54]

Subarachnoid hemorrhage

Typical presentation of subarachnoid hemorrhage is sudden severe headache, widespread or predominant on one side or the posterior part of the head and stiff neck. There are no cerebral symptoms or signs in pure SAH. However, localizing findings occur in ICH or cerebral infarction secondary to SAH.

b. INVESTIGATIONS

Computerized tomography (CT)

The advent of computed tomography in the early 1970's greatly facilitated the diagnosis and management of stroke and added significantly to the understanding of the pathophysiologic brain alteration. Computed tomography scan is the most important non-invasive technique that distinguishes stroke resulting from cerebral infarction and hemorrhage. It also helps to differentiate other lesions that may clinically present as stroke.

Computed tomography scan readily demonstrates acute hemorrhage as hyperdense signal intensity. Multifocal hemorrhages at the frontal, temporal or occipital poles suggest a traumatic etiology. Hematoma volume in cubic centimeters can be approximated by a modified ellipsoid equation: (A x B x C)/2, where A, B and C represent the longest linear dimensions in centimeters of the hematoma in each orthogonal plane. Perihematomal edema and displacement of tissue with herniation also can be appreciated. Iodinated contrast may be injected to increase screening yield for underlying tumor or vascular malformation.[55]

Contrast enhanced CT greatly aids reorganization of other type of brain lesions. It may present hemorrhages as a round or irregularly shaped, homogenous, hyperdense and non-calcified lesions. The hyperdense region is related to protein content of hemoglobin. The typical sequence of evolution and resolution of ICH is as follows:

1) First week: Hyperdense hematoma with surrounding oedema and mass effect, but no enhancement.
2) Second to fourth week: Decrease in density of hematoma, resolution of oedema, mass effect and evidence of post-contrast peripheral rim enhancement.
3) One month and later: The hematoma appears as an isodense or hypodense lesion with no mass effect and decreased intensity of enhancement.

Magnetic resonance imaging (MRI)

Most remarkable feature of MRI brain images are the striking grey-white matter differentiation seen with the inversion recovery sequence (IR). Acute hemorrhages exhibit a ring of increased proton density, as well as a rim of decreased T_1 value surrounding a central core of longer T_1 on spin echo (SE), T_2 has been very prolonged but is usually shorter than the prolongations associated with oedema. The hemorrhages and hemorrhagic infarcts appear as areas of increased image-intensity on IR scans. The time of transitions from relatively short T_1 and T_2 times in chronic hemorrhages is undetermined. The transition point depends on various factors like age of hemorrhage, hematocrit and hemoglobin content of blood, initial blood volume in the tissue, extent and degree of tissue injury and presence of oedema.[79] These characteristics diminish the possibility of determining hemorrhagic lesion. Identification of small hemorrhages restricted to or embedded in normal white matter may be difficult.

The MRI appearance of hemorrhage on conventional T1 and T2 sequences evolves over time because of chemical and physical changes within and around the hematoma. Conventional T1 and T2 sequences are not highly sensitive to hemorrhage in the first few hours, but newer gradient refocused echo sequences appear to be able to detect ICH reliably within the first one to two hours of onset. Arteriovenous malformations and cavernous angiomas may be identified by the presence of multiple flow voids adjacent to the hematoma. Paramagnetic contrast may be injected to increase screening yield for underlying tumor or vascular malformation. Gradient echo sequences may reveal multiple foci of hypointensity attributable to hemosiderin deposition from prior silent cerebral microbleeds. A multilobar distribution of hypointense foci on gradient echo imaging may provide supportive evidence of cerebral amyloid angiopathy, while multiple deep foci may suggest an underlying hypertensive arteriopathy.[55]

A study compared MRI and CT in a series of 175 patients of strokes in which MRI was more sensitive than CT in the early detection of cerebral hemorrhage.[56] Computed tomography is the method of choice to rule out ICH but MRI is more specific in later stages of hemorrhages.

MRI Appearance of ICH

Phase	Time	Hemoglobin	T1	T2
Hyperacute	<24 hours	Oxyhemoglobin (intracellular)	Isointense or hypointense	Hyperintense
Acute	1-3 days	Deoxyhemoglobin (intracellular)	Isointense or hypointense	Hypointense
Early subacute	>3 days	Methemoglobin (intracellular)	Hyperintense	Hypointense
Late subacute	>7 days	Methemoglobin (extracellular)	Hyperintense	Hyperintense
Chronic	>14 days	Hemosiderin (extracellular)	Isointense or hypointense	Hypointense

Hematoma growth in Intracerebral hemorrhage was traditionally viewed as a monophasic event with a brief episode of bleeding followed by increasing edema and clinical deterioration. This view is no longer accepted. Clinical predictors of early hematoma growth have been difficult to consistently identify. In one retrospective study hypertension (systolic blood pressure 160) was associated with enlargement. This finding has not been prospectively confirmed. Significant delayed edema may occur days to a week after initial bleeding and has been associated with neurological deterioration.[21]

Morbidity and mortality

Intracerebral hemorrhage is often clinically devastating. Thirty-day case fatality rates range from 40% to 50%, with approximately half of deaths occurring within two days of onset. Patients with ICH fare worse than those with ischemic stroke, and few are left without disability. Mortality after ICH was reportedly as high as 90% in the pre-CT area. The lower mortality in more recent studies likely reflect a combination of identification bias in the pre-CT era (with mild hemorrhages misclassified as ischemic infarcts) and improved supportive care.[21]

Prognostic indicators

A variety of reports have examined clinical and radiographic factors associated with prognosis after ICH. Predictors of poor outcome include advanced age, poor neurological status at presentation (as measured by Glasgow Coma Scale [GCS] score), larger hematoma size, early hematoma growth, intraventricular extension of hemorrhage, anticoagulant use, and brainstem location of hemorrhage. In a population-based study in Greater Cincinnati, the volume of ICH in combination with the GCS predicted overall 30-day mortality with 96% sensitivity and 98% specificity. Patients with a volume of 60 cm^3 and a GCS score 8 had a predicted mortality of 91% while those with a volume of $\leq 30 cm^3$ and a GCS score 9 had a predicted mortality rate of 19%. For ICH with a volume of $\geq$ 60 cm^3, the 30-day mortality for deep hemorrhages was 93% and for lobar hemorrhages was 71%. Several prediction models for outcome after ICH have been developed but have not gained widespread clinical use. Nonetheless, in a recent study more deaths caused by ICH were associated with withdrawal of care or a “comfort care” approach (68%)

than progression to brain death (29%) or medical complications (3%). The "self-fulfilling prophecy" in neurological catastrophes like ICH has been described as the preconceived notion that medical care is futile, followed by withdrawal of care and death of the patient. The complicated determinants of morbidity and mortality following ICH, together with expectations of the patient, family, and physicians require careful consideration in each case.[57,21]

Mortality of ICH based on volume and location of hematoma[57]

Location	Overall 30 day mortality (n=188)	≤ 30 cm^3 ICH	30-60 cm^3 ICH	≥60 cm^3 ICH
Lobar (n=66)	39%	23%	60%	71%
Deep (n=76)	48%	7%	64%	93%
Pontine (n=9)	44%	43%	100%	N/A
Cerebellum (n=11)	64%	57%	75%	N/A

Risk of ICH recurrence

Because ICH is less common and more deadly than ischemic stroke, studies estimating ICH recurrence risk have been more difficult to perform. A review of studies tracking ICH recurrence found an aggregate risk of 2.4% per patient-year. The studies selected excluded patients with "secondary" causes of ICH such as vascular malformations or anticoagulation. Most studies have found ICH recurrence is more common following lobar ICH than non-lobar ICH. In the cited review, risk of recurrence among patients presenting with lobar ICH was 4.4% per year, compared to 2.1% annually for those with non-lobar hemorrhage. Risk of new cerebral ischemia (1.1% per year) was lower than the risk of recurrent ICH. One study found that Apolipoprotein E2 orE4 genotypes increase the risk of recurrence following lobar ICH, presumably because of their association with amyloid angiopathy. The 21% two-year recurrence risk after lobar ICH in this study was greater than other reports and likely reflects the highly selected patient cohort.[21]

Primary intraventricular hemorrhage

Primary intraventricular hemorrhage (IVH) is rare among adults, comprising 2–3% of ICH admissions. Signs and symptoms of IVH frequently include headache, vomiting, and altered level of consciousness. Many patients are hypertensive or coagulopathic and some have vascular malformations defined by angiography. Hydrocephalus and elevated intracranial pressure are frequent and potentially fatal complications.[21]

Management of intracerebral hemorrhage[58]

Emergency Diagnosis and Assessment

Recommendations

1. A baseline severity score should be performed as part of the initial evaluation of patients with ICH.

2. Rapid neuroimaging with CT or MRI is recommended to distinguish ischemic stroke from ICH.

3. Contrast-enhanced *CT* angiography (CTA) and contrast-enhanced CT may be considere to help identify patients at risk for hematoma expansion, and

CTA, CT venography, contrast-enhanced CT, contrastenhancent MRI, magnetic resonance angiograph and magnetic resonance venography, and catheter angiography can be useful to evaluate for underlying structural lesions including vascular malformations and tumors when there is clinical or radiological suspicion.

Hemostasis and Coagulopathy, Antiplatelet Agents, and DVT Prophylaxis:

Recommendations

1. Patients with a severe coagulation factor deficiency or severe thrombocytopenia should receive appropriate factor replacement therapy or platelets, respectively.

2. Patients with ICH whose INR is elevated because of vitamin K antagonists (VKA) should have their VKA withheld, receive therapy to replace vitamin K–dependent factors and correct the INR, and receive intravenous vitamin K. PCCs may have fewer complications and correct the INR more rapidly than FFP and might be considered over FFP rFVIIa does not replace all clotting factors, and although the INR may be lowered, clotting may not be restored in vivo; therefore, rFVIIa is not recommended for VKA reversal in ICH

3. For patients with ICH who are taking dabigatran, rivaroxaban, or apixaban, treatment with FEIBA, other PCCs, or rFVIIa might be considered on an individual basis. Activated charcoal might be used if the most recent dose of dabigatran, apixaban, or rivaroxaban was taken <2 hours earlier. Hemodialysis might be considered for dabigatran

4. Protamine sulfate may be considered to reverse heparin in patients with acute ICH**.**

5. The usefulness of platelet transfusions in ICH patients with a history of antiplatelet use is uncertain.

6. Although rFVIIa can limit the extent of hematoma expansion in noncoagulopathic ICH patients, there is an increase in thromboembolic risk with rFVIIa and no clear clinical benefit in unselected patients.Thus, rFVIIa is not recommended

7. Patients with ICH should have intermittent pneumatic compression for prevention of venous thromboembolism beginning the day of hospital admission. Graduated compression stockings are not beneficial to reduce DVT or improve outcome

8. After documentation of cessation of bleeding, lowdose subcutaneous low-molecular-weight heparin or unfractionated heparin may be considered for prevention of venous thromboembolism in patients with lack of mobility after 1 to 4 days from onset

9. Systemic anticoagulation or IVC filter placement is probably indicated in ICH patients with symptomatic DVT or PE. The decision between these 2 options should take into account several factors, including time from hemorrhage onset, hematoma stability, cause of hemorrhage, and overall patient condition**.**

Blood pressure

Recommendations

1. For ICH patients presenting with SBP between 150 and 220 mm Hg and without contraindication to acute BP treatment, acute lowering of SBP to 140 mm Hg is safe and can be effective for improving functional outcome.
2. For ICH patients presenting with SBP >220 mm Hg, it may be reasonable to consider aggressive reduction of BP with a continuous intravenous infusion and frequent BP monitoring

General Monitoring and Nursing Care

Recommendation

1. Initial monitoring and management of ICH patients should take place in an intensive care unit or dedicated stroke unit with physician and nursing neuroscience acute care expertise

Glucose Management: Recommendation

2. Glucose should be monitored. Both hyperglycemia and hypoglycemia should be avoided

Seizures and Antiseizure Drugs

Recommendations

1. Clinical seizures should be treated with antiseizure drugs.
2. Patients with a change in mental status who are found to have electrographic seizures on EEG should be treated with antiseizure drugs
3. Continuous EEG monitoring is probably indicated in ICH patients with depressed mental status that is out of proportion to the degree of brain injury
4. Prophylactic antiseizure medication is not recommended

Management of Medical Complications

<u>Recommendations</u>

1. A formal screening procedure for dysphagia should be performed in all patients before the initiation of oral intake to reduce the risk of pneumonia.
2. Systematic screening for myocardial ischemia or infarction with electrocardiogram and cardiac enzyme testing after ICH is reasonable.

ICP Monitoring and Treatment

<u>Recommendations</u>

1. Ventricular drainage as treatment for hydrocephalus is reasonable, especially in patients with decreased level of consciousness
2. Patients with a GCS score of ≤8, those with clinical evidence of transtentorial herniation, or those with significant IVH or hydrocephalus might be considered for ICP monitoring and treatment. A Cerbral persufusion pressure (CPP) of 50 to 70 mm Hg may be reasonable to maintain depending on the status of cerebral autoregulation
3. Corticosteroids should not be administered for treatment of elevated ICP in ICH.

IVH

<u>Recommendations</u>

1. Although intraventricular administration of rtPA in IVH appears to have a fairly low complication rate, the efficacy and safety of this treatment are uncertain
2. The efficacy of endoscopic treatment of IVH is uncertain.

Surgical Treatment of ICH

Recommendations

1. Patients with cerebellar hemorrhage who are deteriorating neurologically or who have brainstem compression and/or hydrocephalus from ventricular obstruction should undergo surgical removal of the hemorrhage as soon as possible.
2. For most patients with supratentorial ICH, the usefulness of surgery is not well established Specific exceptions and potential subgroup considerations are outlined below in recommendations 3 through 6.
3. A policy of early hematoma evacuation is not clearly beneficial compared with hematoma evacuation when patients deteriorate
4. Supratentorial hematoma evacuation in deteriorating patients might be considered as a life-saving measure.
5. DC with or without hematoma evacuation might reduce mortality for patients with supratentorial ICH who are in a coma, have large hematomas with significant midline shift, or have elevated ICP refractory to medical management
6. The effectiveness of minimally invasive clot evacuation with stereotactic or endoscopic aspiration with or without thrombolytic usage is uncertain

Prevention of Recurrent ICH

Recommendations

1. When stratifying a patient's risk for recurrent ICH may affect management decisions, it is reasonable to consider the following risk factors for ICH recurrence: (1) lobar location of the initial ICH; (2) older age; (3) presence

and number of microbleeds on gradient echo MRI; (4) ongoing anticoagulation; and (5) presence of apolipoprotein E ε2 or ε4 alleles

2. BP should be controlled in all ICH patients Measures to control BP should begin immediately after ICH onset A long-term goal of BP <130 mm Hg systolic and 80 mm Hg diastolic is reasonable
3. Lifestyle modifications, including avoidance of alcohol use greater than 2 drinks per day, tobacco use, and illicit drug use, as well as treatment of obstructive sleep apnea, are probably beneficial
4. Avoidance of long-term anticoagulation with warfarin as a treatment for nonvalvular atrial fibrillation is probably recommended after warfarin-associated spontaneous lobar ICH because of the relatively high risk of recurrence
5. Anticoagulation after nonlobar ICH and antiplatelet monotherapy after any ICH might be considered, particularly when there are strong indications for these agents
6. The optimal timing to resume oral anticoagulation after anticoagulant-related ICH is uncertain. Avoidance of oral anticoagulation for at least 4 weeks, in patients without mechanical heart valves, might decrease the risk of ICH recurrence
7. If indicated, aspirin monotherapy can probably be restarted in the days after ICH, although the optimal timing is uncertain
8. The usefulness of dabigatran, rivaroxaban, or apixaban in patients with atrial fibrillation and past ICH to decrease the risk of recurrence is uncertain
9. There are insufficient data to recommend restrictions on the use of statins in ICH patients

Rehabilitation and Recovery

Recommendations

1. Given the potentially serious nature and complex pattern of evolving disability and the increasing evidence for efficacy, it is recommended that all patients with ICH have access to multidisciplinary rehabilitation
2. Where possible, rehabilitation can be beneficial when begun as early as possible and continued in the community as part of a well-coordinated ("seamless") program of accelerated hospital discharge and home-based resettlement to promote ongoing recovery

Outcome in intracerebral hemorrhage

Overall outcome in ICH is poor with mortality rates for spontaneous ICH generally remaining up to 50%.[59] Volume of ICH, age, GCS score on admission, pulse pressure and blood pressure on admission have all been demonstrated to be important independent predictors of survival in ICH in studies incorporating multivariate analysis. More recent studies have been investigated and confirmed prior reports that the presence and degree of intraventricular extension[57] and degree of hydrocephalus[60] are independent predictors of outcome in spontaneous ICH in addition to parenchymal hemorrhage volume. Etiologically, ICH from thrombolysis or coagulopathy has especially a poor outcome, owing largely to the greater mean volume of these hemorrhages.[61] Medical co-morbidities, especially cardiopulmonary diseases adversely affect the outcome and are often exacerbated in the setting of acute ICH.

The mass effect resulting from hematoma volume, oedematous tissue surrounding the hematoma and obstructive hydrocephalus with subsequent herniation is the chief secondary cause of death in the first few days after ICH.[62]

Deep venous thrombosis (DVT) is rather a common complication of immobility after stroke. DVT predisposes patients to the risk of pulmonary embolism (PE), which may be fatal. In a Swedish study, with the causes of death verified by autopsy, three percent of stroke patients succumbed to PE within 3 months.[63] Another potentially fatal complication after stroke is pneumonia, which was, after the primary bleed, the second most common cause of death within one month after ICH in the Oxfordshire Community Stroke Project.[64] After 30 days had elapsed, pneumonia was the commonest cause of death of ICH patients.

Mortality during the first month after ICH varied from 14 to 52%.[65-67] Majority of the deaths occured in the early phase after ICH, with up to 27% during the first 24 hours.[65] A study reported that 11% of patients died during the first 24 hours after hemorrhage, 19% within 3 days and 33% within two weeks.[68] In the Oxfordshire Community Stroke Project, 24% of the patients with ICH died within the first 24 hours and 39% within the first week.[69] In a Swedish population-based study, 18% of the patients with ICH died within the first two days[70] and another study[71] reported two day mortality of 24%.

Independent predictors of 30 days mortality includes the size and location of the hemorrhage, midline shift in cranial CT scan, intraventricular spread of the hemorrhage, low GCS score on admission and high blood glucose on admission.[72-75]

The predictors for long-term survival (more than six months) after primary ICH includes the initial level of consciousness, the severity of handicap caused by the stroke in the early phase, the patient's age, the volume and location of hematoma.[68,72]

A prospective study of 166 cases using multivariate analysis to assess death and functional outcome after spontaneous ICH showed that seventy-one patients (43%) died, sixty nine patients (42%) had a satisfactory outcome and twenty six patients (16%) had a poor functional outcome. Early survival (30 day) was correlated with morphologic parameters on the initial CT (hemorrhage size, midline shift and intraventricular spread of the hemorrhage), while six month survival was correlated with age. Using logistic regression, five independent predictors of satisfactory outcome at six months were, age, hemorrhage size, intraventricular spread of the hemorrhage, limb paresis and communication disorders. Of these, age was the most important predictor by far.[76]

A study was conducted to identify current models for prediction of short term outcome after ICH and to evaluate their clinical applicability and relevance in treatment decisions. The study concluded that most models are easy to apply and can generate a high probability of death or poor outcome. However, only a small proportion of patients have such a high probability and 30 day case fatality is not always correctly predicted. Therefore, current models have limited relevance in triage, but can be used to estimate the chances of survival of individual patients.[77]

Glasgow Coma Scale (GCS)

The GCS is the most widely used scoring system in quantifying level of consciousness following traumatic brain injury. It is used primarily because it is simple, has a relatively high degree of interobserver reliability and because it correlates well with outcome following severe brain injury.

It is easy to use. Other factors which alter the patient's level of consciousness interfere with the scale's ability to accurately reflect the severity of a traumatic brain injury. Shock, hypoxemia, drug use, alcohol intoxication, metabolic disturbances may alter the GCS score independently of the brain injury.

In a prospective study, the prognostic value of clinical characteristics and CT scan findings in 50 patients of ICH had been examined with follow up over six months period. Each patient had been individually followed up for eight weeks. Age of more than 60 years, GCS Score of six or less (in a modified Scale of 10) at the time of admission, ICH volume greater than 30 ml, midline shift in CT scan of more than three mm, presence of intraventricular hemorrhage (IVH) and hydrocephalus had an adverse impact on outcome. Young age, GCS score of more than eight, ICH volume of less than 20 ml, presence of lobar hemorrhage and absence of IVH/hydrocephalus were associated with relatively favourable outcome.[78]

Functional outcome

The Modified Rankin Scale (MRS) and Glasgow Outcome Scale (GOS) provide the most practical instruments for outcome evaluation after stroke.[79] The MRS uses a zero to five point scale (zero = no symptoms, five = severe disability, requires constant attention).[80] The Glasgow Outcome Scale consists of five well-defined outcomes: death, persistent vegetative state, severe disability, moderate disability and good recovery.[81]

Studies reported that 73 to 78% of the patients who survived for at least 6 months after ICH were functionally independent (good recovery and moderate disability according to GOS: moderately disabled, able to take care of themselves at home, move outdoors, do shopping and use public transportation), while 22 to 27% were dependent [severe disability and vegetative state: severely disabled persons need assistance for some activities of daily life (ADL) every day].[68] A study observed 78% of the survivors to be in the categories I to III [82] and 22% to be in the categories IV to V on MRS. They reported that most of the severely handicapped patients had died by the end of the follow-up, which explained the small final percentage of patients with poor functional outcome.

METHODOLOGY

The present study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

Study design and duration

The study design was a hospital based cross-sectional study.

Study period

This study was done for the period of one year from January 2015 to December 2015.

Place

The present study was carried out in the Department of Medicine and Neuromedicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi a tertiary care teaching hospital attached to Jawaharlal Nehru Medical College, Belagavi.

Source of Data

Patients presenting with spontaneous intracerebral hemorrhage with or without intraventricular extension above 18 years of age in the Department of General Medicine and Department of Neruomedicine, KLES Dr Prabhakar Kore Hospital and MRC, Belagavi

Sample size

A total of 56 patients with spontaneous intracerebral hemorrhage were studied.

Sampling procedure

The sample size was determined considering total number of cases of intracerbral hemorrhage admitted during last 3 years. That is, 169 patients weer admitted with intracerbral hemorrhage during last 3 years. Which translates about 56 average number of cases per year. Hence the sample size of 56 was considered for this study.

Selection criteria

Inclusion Criteria

- Patients with spontaneous intracerebral hemorrhage with or without intraventricular extension.
- Patients aged 18 and above.

Exclusion Criteria

- Primary intraventricular hemorrhage.
- Intraventricular hemorrhage secondary to subarachnoid hemorrhage
- Cerebral infarct with secondary hemorrhage leading to intraventricular extension
- Traumatic intraventricular hemorrhage.

Ethical clearance

Prior to the commencement, the study was approved by the Institutional Ethics Committee, Jawaharlal Nehru Medical College, Belagavi.

Informed consent

The patients who fulfilled the selection criteria were informed about the nature of study and a written informed consent was obtained (Annexure–I).

Data collection

The selected patients were interviewed for the demographic data, history of presenting illness and other comorbid conditions. Further these patients underwent clinical examination followed by systemic examination. These findings were noted on a predesigned and pretested proforma (Annexure-II).

Investigations

Venous blood samples (10 mL) were collected immediately on admission to intensive care unit from the selected patients and were subjected following investigations.

- Fundoscopy
- Complete Blood Count
- Routine Urine Examination
- Blood Sugar
- Blood urea
- Serum creatinine

- Lipid profile
- Serum electrolytes
- 12 lead ECG
- CT/MRI

Outcome variables

Antomical site of intracerebral hemorrhage

Anatomical site of intracerebral hemorrhage was made out from CT/MRI scans.

Volume of ventricular bleed

Volume score of ventricular bleed was made out from CT/MRI scans. The score involves grading[83] the amount of blood in each ventricle as;

- 0, no blood;
- 1, sedimentation of blood in the posterior part;
- 2, partly filled with blood; or
- 3, completely filled with blood.

The total amount of intraventricular blood (the IVH score) was the total of the four scores and ranged from 0 (no IVH) to 12 (all four ventricles completely filled with blood)

The volumetric analysis was also done to find out hematoma volume. ICH volume was determined using the ABC/2 method.[84]

ICH location

ICH location was determined by the anatomic structure that contained majority of hematoma.

Clinical outcome

Clinical outcome was assessed based on modified rankin scale.

Modified Rankin Scale[85-86]

- 0 No symptoms at all
- 1 No significant disability despite symptoms; able to carry out all usual duties and activities
- 2 Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
- 3 Moderate disability; requiring some help, but able to walk without assistance
- 4 Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
- 5 Severe disability; bedridden, incontinent and requiring constant nursing care and attention
- 6 Dead.

Statistical methods

The data obtained was coded and entered into Microsoft excel spreadsheet and data was analysed using SPSS version 21. The categorical data was expressed in terms of rates, ratios and percentages and the continuous data was expressed in terms of mean ± standard deviation. The comparison of categorical data was done using Chi-square test or Fisher's exact test. Continuous data was compared using independent sample 't' test. At 95% confidence interval, a probability (p) value of $\leq$ 0.050 was considered as statistically significant.

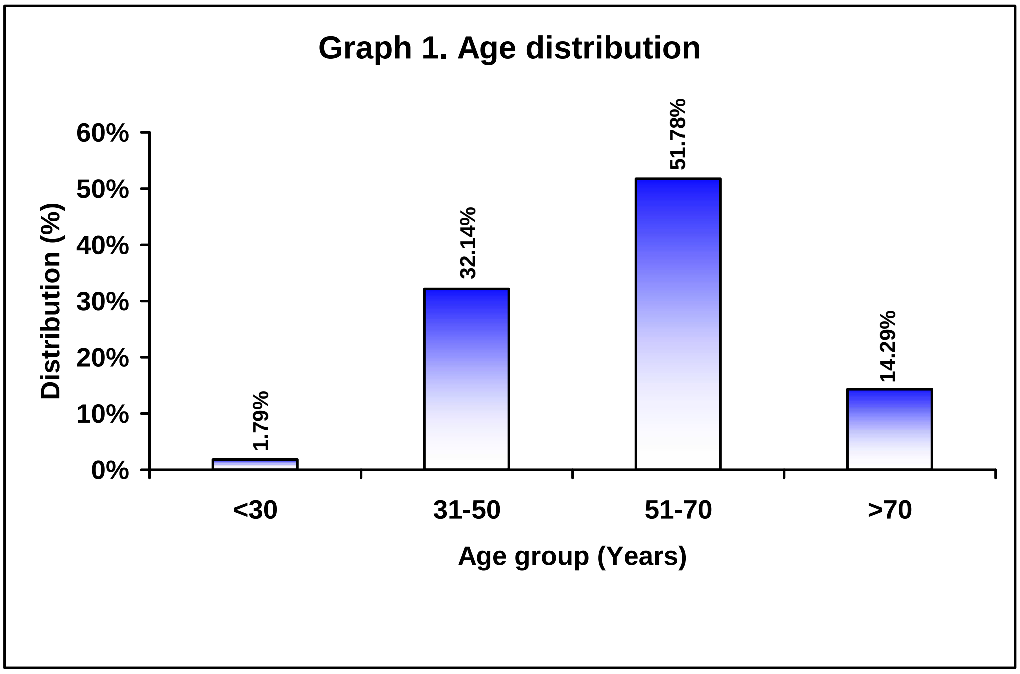
RESULTS

The present study was conducted on 56 patients presenting with intracerebral hemorrhage with or without intraventricular extension, in KLES Dr Prabhakar Kore hospital and MRC Belagavi during the period Jan 2015 to Dec 2015.

The data obtained was tabulated as below.

Table 1. Age distribution

Age group (Years)	Distribution (n=56)	
	Number	**Percentage**
<30	1	1.79
31 to 50	18	32.14
51 to 70	29	51.78
>70	8	14.29
Total	**56**	**100.00**

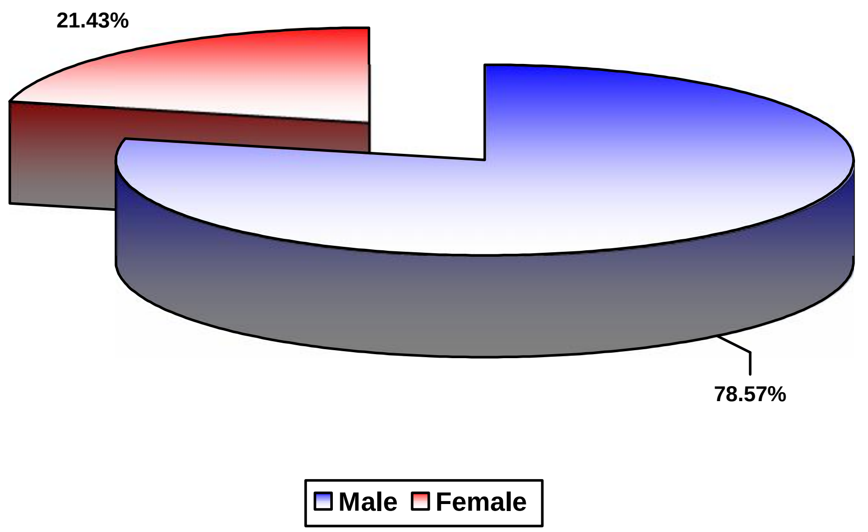


In the present study maximum number of patients were in the age group 51 to 70 years that is 29 (51.78%). The youngest patient was 28 years old and the oldest was 85 years.

Table 2. Sex distribution

Sex	Distribution (n=56)	
	Number	Percentage
Male	44	78.57
Female	12	21.43
Total	**56**	**100.00**

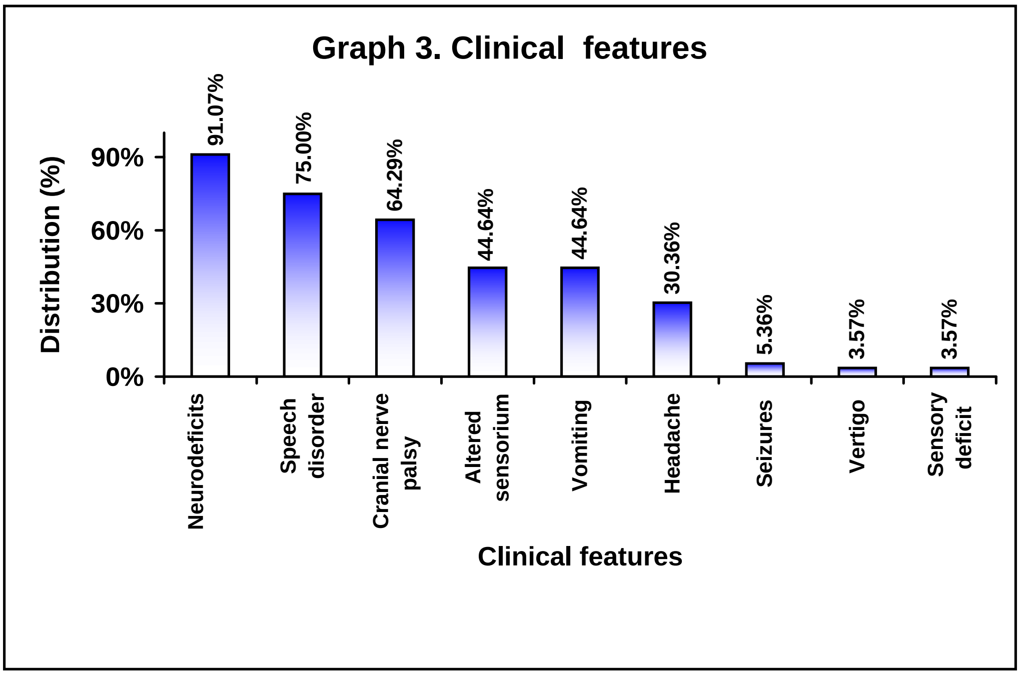
Graph 2. Sex distribution



In the present study out of 56 cases 44 (78.57%) were males and 12 (21.43%) were females. Male preponderance was seen with Male to Female ratio of 3.66:1.

Table 3. Clinical features

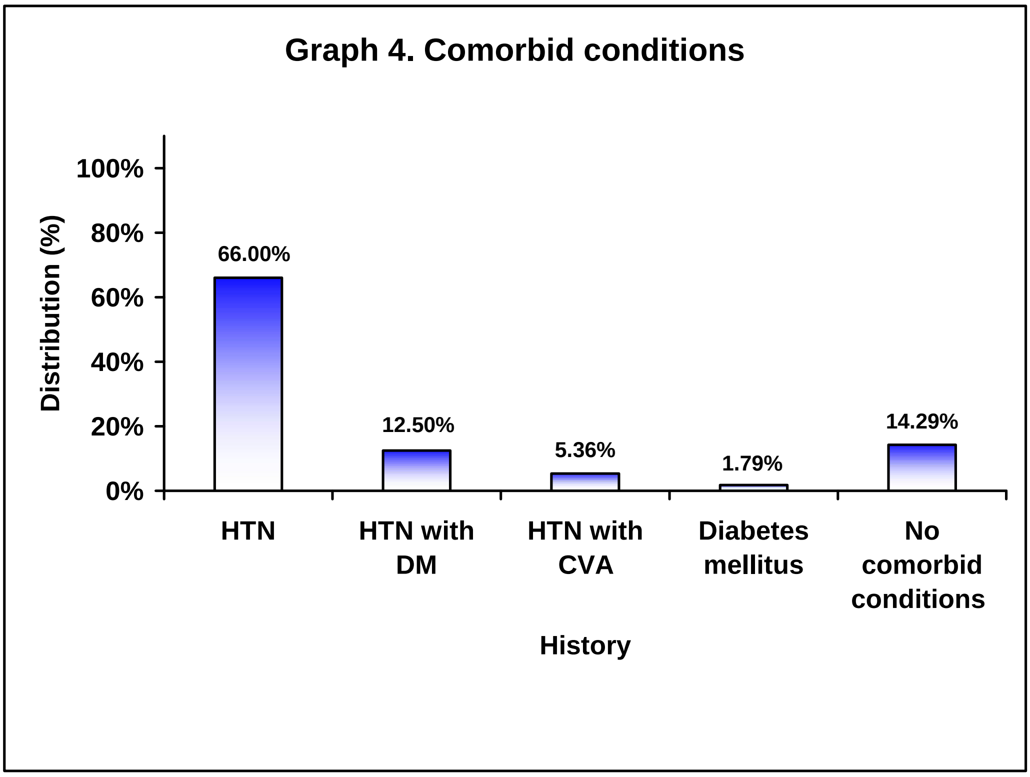
Clinical features	Distribution (n=56)	
	Number	Percentage
Neurodeficits	51	91.07
Speech disorder	42	75
Craninal nerve palsy	36	64.29
Altered sensorium	25	44.64
Vomiting	25	44.64
Headache	17	30.36
Seizures	3	5.36
Vertigo	2	3.57
Sensory deficit	2	3.57



In our study the most of the patients presented with neurodeficits 51 (91.07%), followed by speech disorder 42 (75%), cranial nerve palsy 36 (64.29%), vomiting 25 (44.64%), headache 17 (30.36%) and only 3 (5.36%) with seizures.

Table 4. Comorbid conditions

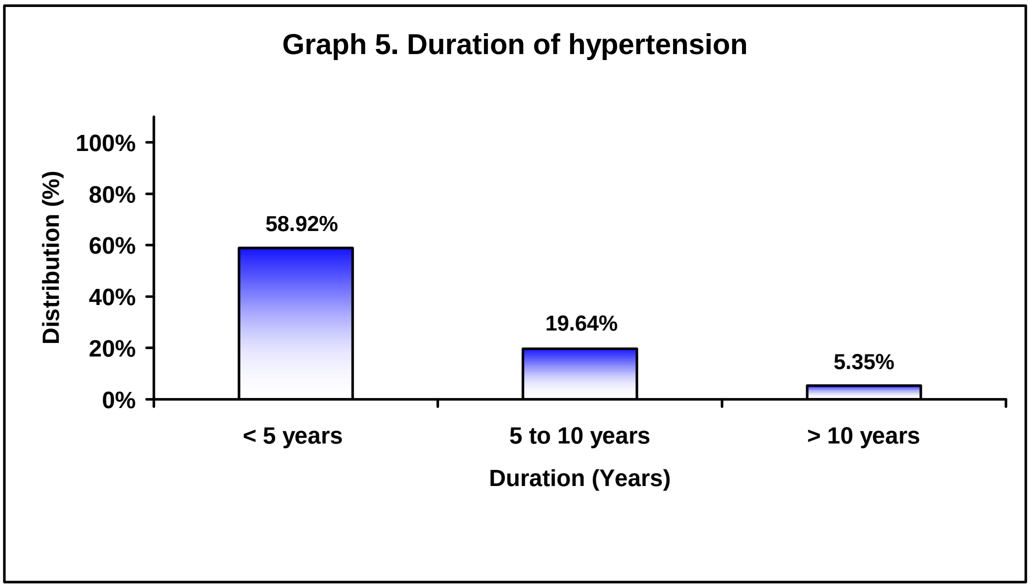
History	Distribution (n=56)	
	Number	**Percentage**
Hypertension	37	66.0
Hypertension with DM	7	12.5
HTN with old CVA	3	5.36
Diabetes mellitus	1	1.79
No co-morbid condition	8	14.29
Total	**56**	**100**



In the present study most of the patients with ICH had hypertension 37 (66%). The other comorbid conditions are shown as above.

Table 5. Duration of hypertension

Duration (years)	Distribution (n=56)	
	Number	Percentage
< 5 years	33	58.92
5 – 10 years	11	19.64
> 10 years	3	5.35

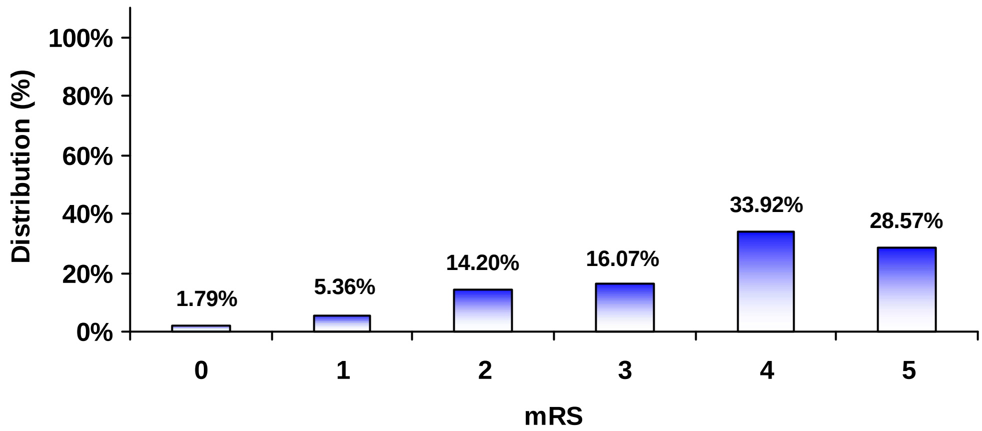


In the present study most of the patients had duration of hypertension less than 5 years 33 (58.92%). The duration of hypertension in other patients is depicted above.

Table 6. Distribution of patients according to modified rankin scale (mRS)

mRS	Distribution (n=56)	
	Number	Percentage
0	1	1.79
1	3	5.36
2	8	14.2
3	9	16.07
4	19	33.92
5	16	28.57
Total	**56**	**100.00**

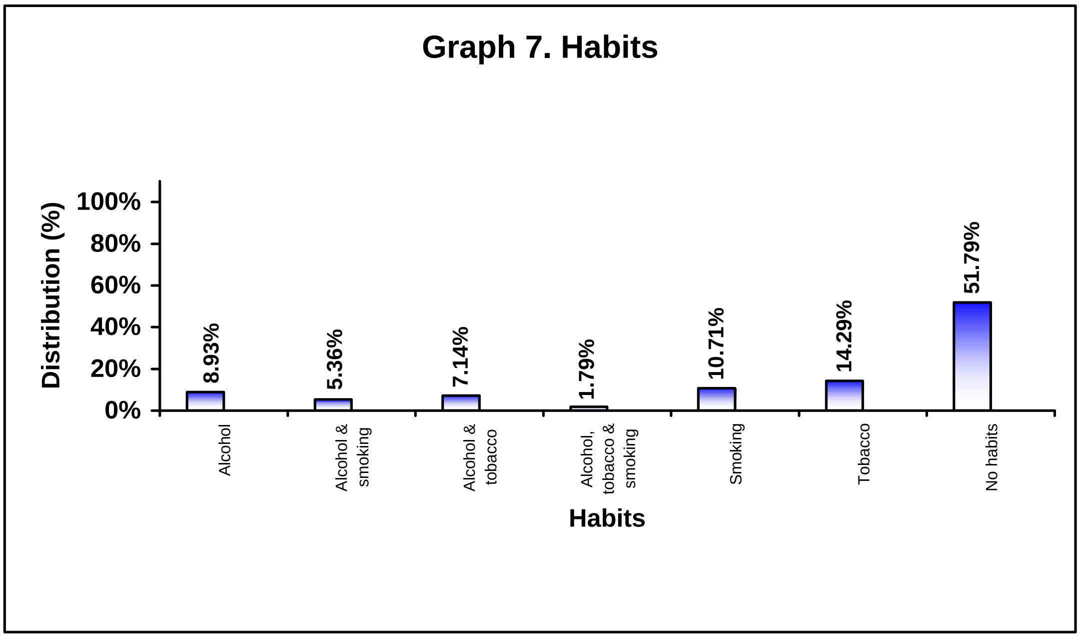
Graph 6. Distribution of patients according to modified rankin scale (mRS)



In the present study most of the patients had mRS score of 4 that is 19 (33.92%). The mRS score of rest of the patients is depicted above.

Table 7. Habits

Habits	Distribution (n=56)	
	Number	Percentage
Alcohol	5	8.93
Alcohol and smoking	3	5.36
Alcohol and tobacco	4	7.14
Alcohol , tobacco and smoking	1	1.79
Smoking	6	10.71
Tobacco	8	14.29
No Habits	29	51.79
Total	**56**	**100**

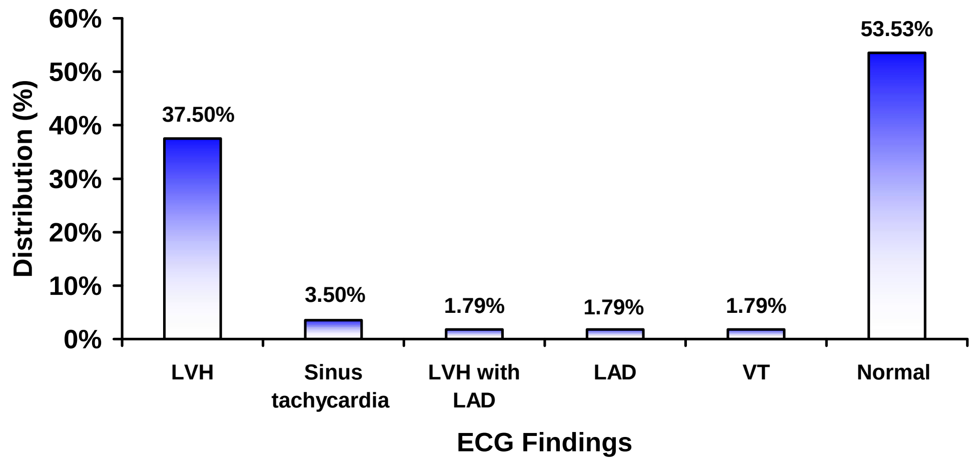


In the present study tobacco chewing 8(14.29%) was the single most common habit found among the patients with ICH. However 29 patients (51.79%) didn't have any habits.

Table 8. ECG Findings

ECG Findings	Distribution (n=56)	
	Number	Percentage
LVH	21	37.5
Sinus tachycardia	2	3.5
LVH with LAD	1	1.79
LAD	1	1.79
VT	1	1.79
Normal	30	53.53
Total	**56**	**100**

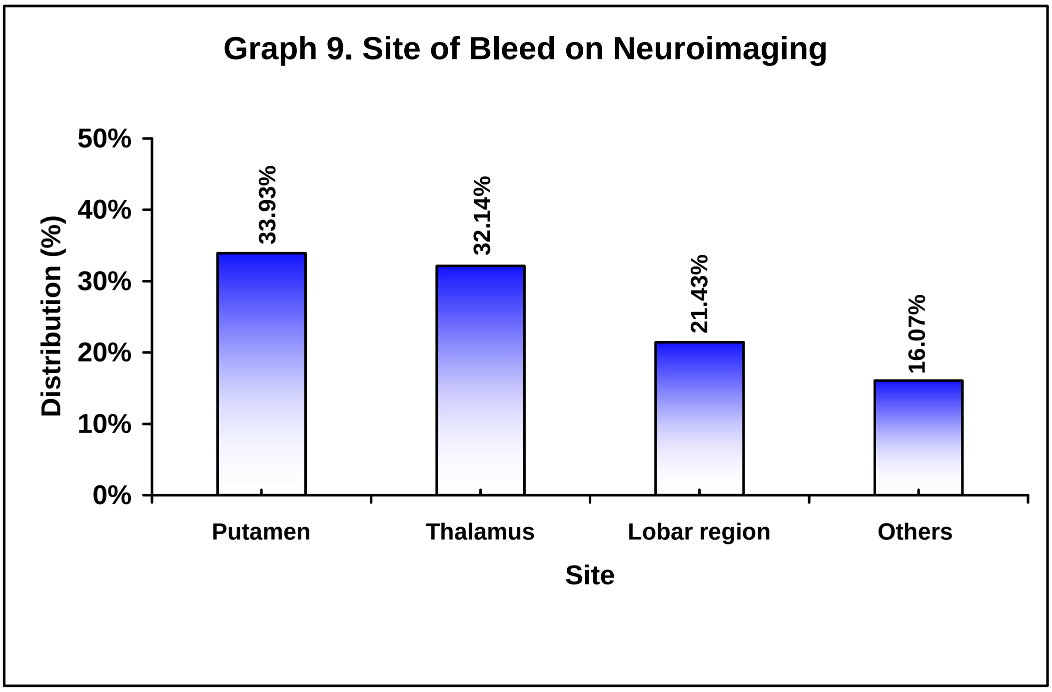
Graph 8. ECG findings



In our study most of the patients had a normal ECG 30 (53.53%). The most common ECG abnormality was LVH (37.5%). Other ECG abnormalities are shown in the above table.

Table 9. Site of Bleed on Neuroimaging

Site	Distribution (n=56)	
	Number	Percentage
Putamen	19	33.93
Thalamus	18	32.14
Lobar Region	12	21.43
Others	9	16.07

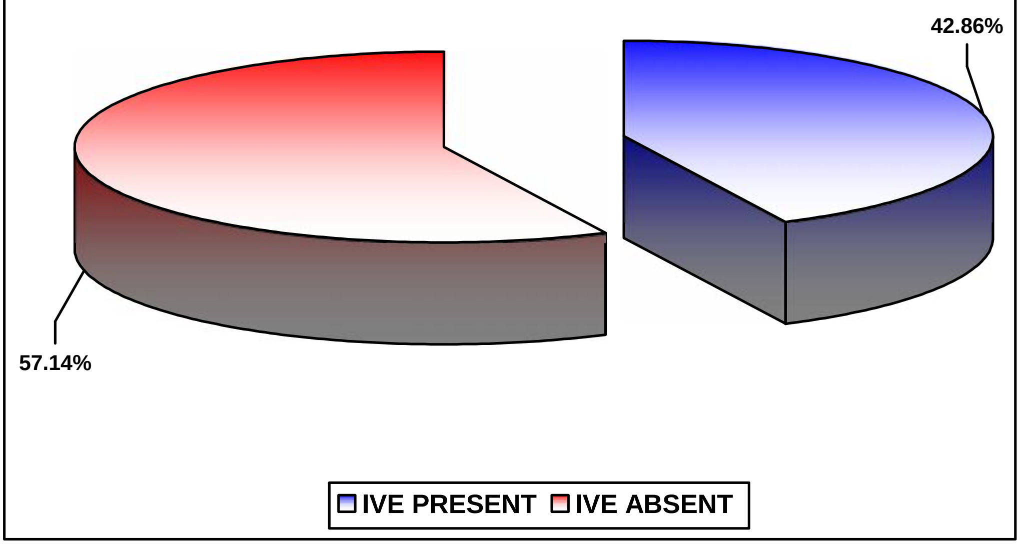


In the present study most common site of bleed was putamen (33.93%) followed by thalamus (32.14%).

Table 10. Distribution of patients according to Intraventricular extension based on CT/MRI findings

IVE	Distribution (n=56)	
	Number	**Percentage**
Present	24	42.86
Absent	32	57.14
Total	**56**	**100.00**

Graph 10. Distribution of patients according to Intraventricular extension based on CT/MRI findings

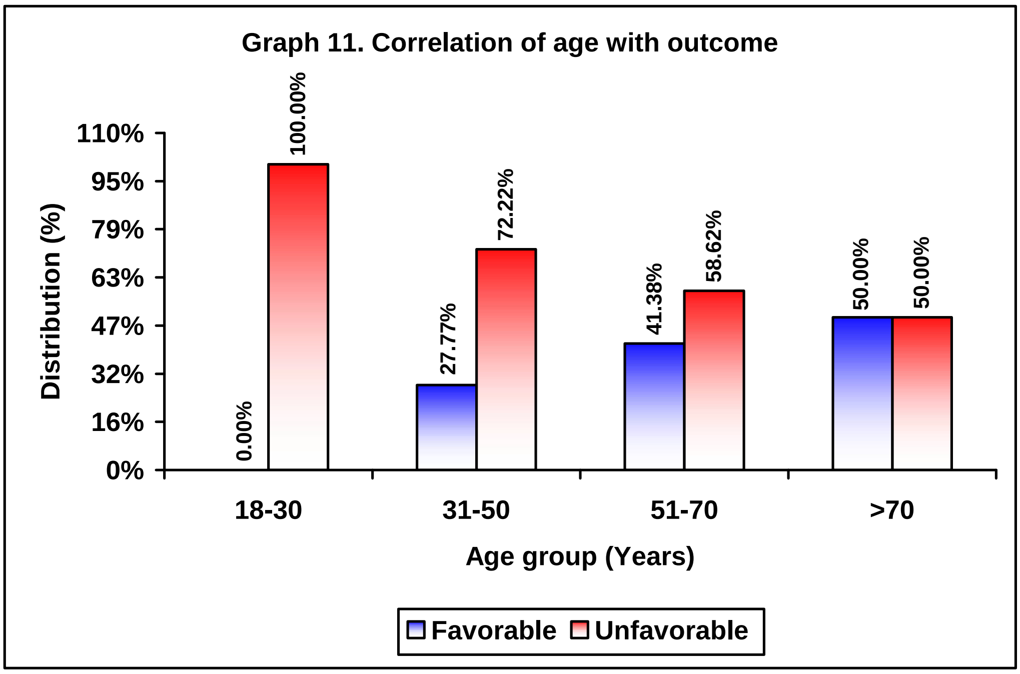


In the present study out of 56 cases, 24 patients (42.86%) had ICH with IVE and rest of the patients 32 (57.14%) didn't present with IVE of ICH.

Table 11. Correlation of age with outcome

Age groups (years)	Favorable		Unfavorable		Total	
	No	%	No.	%	No.	%
18-30	0	0.00	1	100	1	1.79
31-50	5	27.77	13	72.22	18	32.14
51-70	12	41.38	17	58.62	29	51.78
>70	4	50	4	50	8	14.28
Total	**21**	**37.50**	**35**	**62.50**	**56**	**100.00**

p=0.642

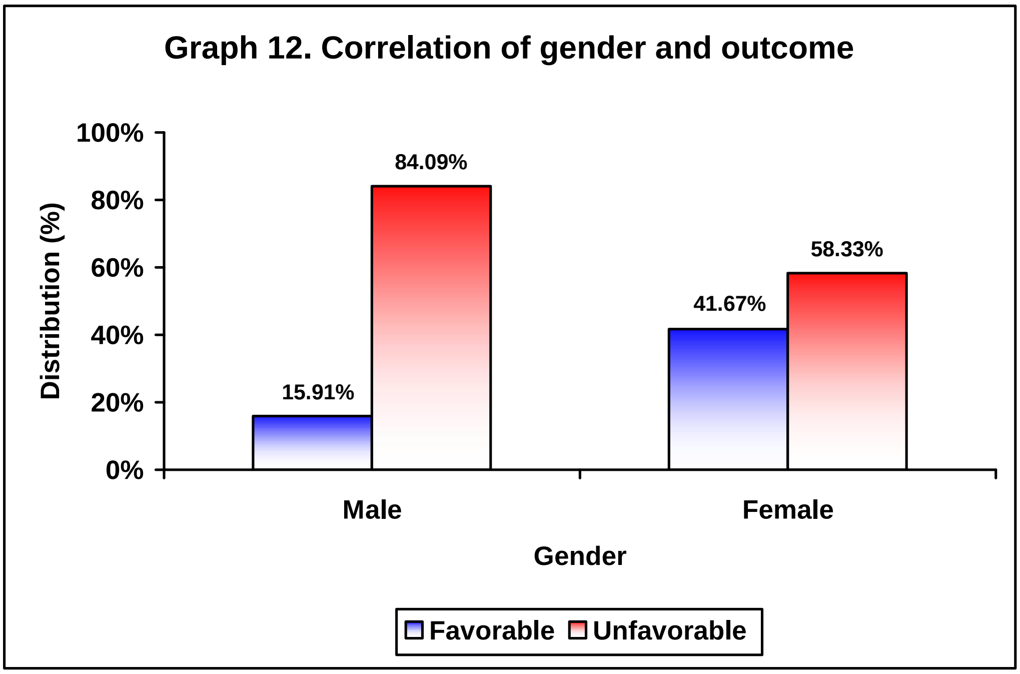


In the present study majority of the patients in the 31-50 years age group had unfavourable outcome 13 (72.22%).

Table 12. Correlation of gender and outcome

Gender	Favorable		Unfavorable		Total	
	No	%	No.	%	No	%
Male	7	15.91	37	84.09	44	78.57
Female	5	41.67	7	58.33	12	21.42
Total	**12**	**21.43**	**44**	**78.57**	**56**	**100**

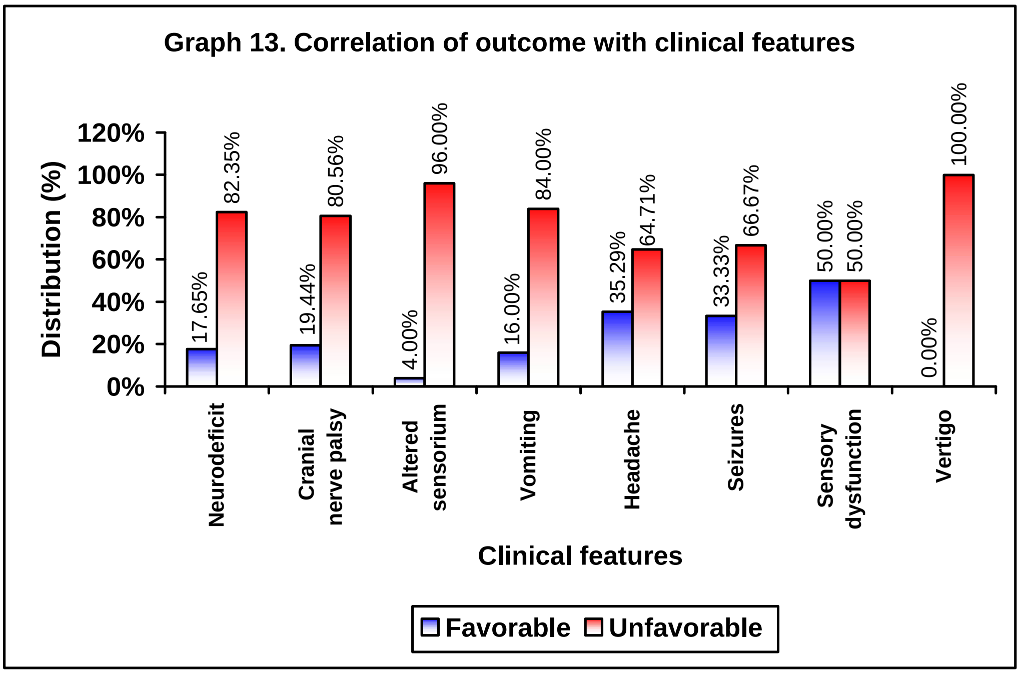
p=0.1261



In the present study outcome was unfavourable in males as compared to females but it was not statistically significant (p=0.1261).

Table 13. Correlation of outcome with clinical features

Clinical features	Favorable		Unfavorable		Total		p value
	No	%	No.	%	No	%	
Neurodeficit	9	17.65	42	82.35	51	91.07	**0.0103***
Cranial nerve palsy	7	19.44	29	80.56	36	64.29	0.8840
Altered Sensorium	1	4.00	24	96.00	25	44.64	**0.0040***
Vomiting	4	16.00	21	84.00	25	44.64	0.3742
Headache	6	35.29	11	64.71	17	30.36	0.1880
Seizures	1	33.33	2	66.67	3	5.36	0.9999
Sensory dysfunction	1	50.00	1	50.00	2	3.57	0.9000
Vertigo	0	0.00	2	100.00	2	3.57	0.9999

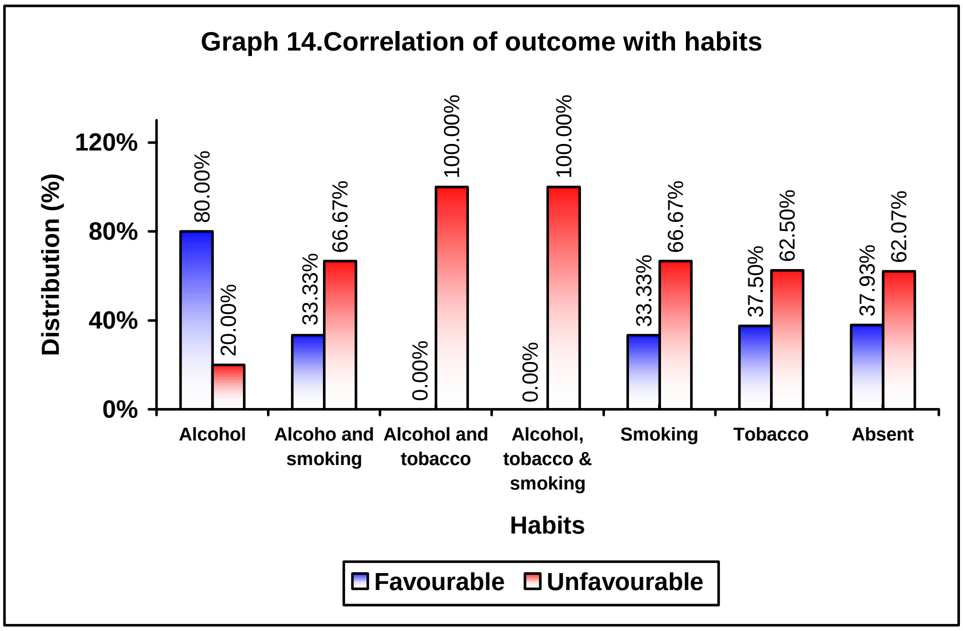


In this study patients presented with neurodeficits 42 (82.35%) and altered sensorium 24 (96%) had significantly unfavourable outcome compared to other patients.

Table 14. Correlation of outcome with habits

Habits	Favorable		Unfavorable		Total	
	No	%	No.	%	No	%
Alcohol	4	80	1	20	5	8.93
Alcohol and smoking	1	33.33	2	66.67	3	5.36
Alcohol and tobacco	0	0.00	4	100	4	7.14
Alcohol, tobacco and smoking	0	0.00	1	100	1	1.79
Smoking	2	33.33	4	66.67	6	10.71
Tobacco	3	37.5	5	62.5	8	14.29
Absent	11	37.93	18	62.07	29	51.79
Total	**21**	**37.50**	**35**	**62.50**	**56**	**100.00**

p=0.365

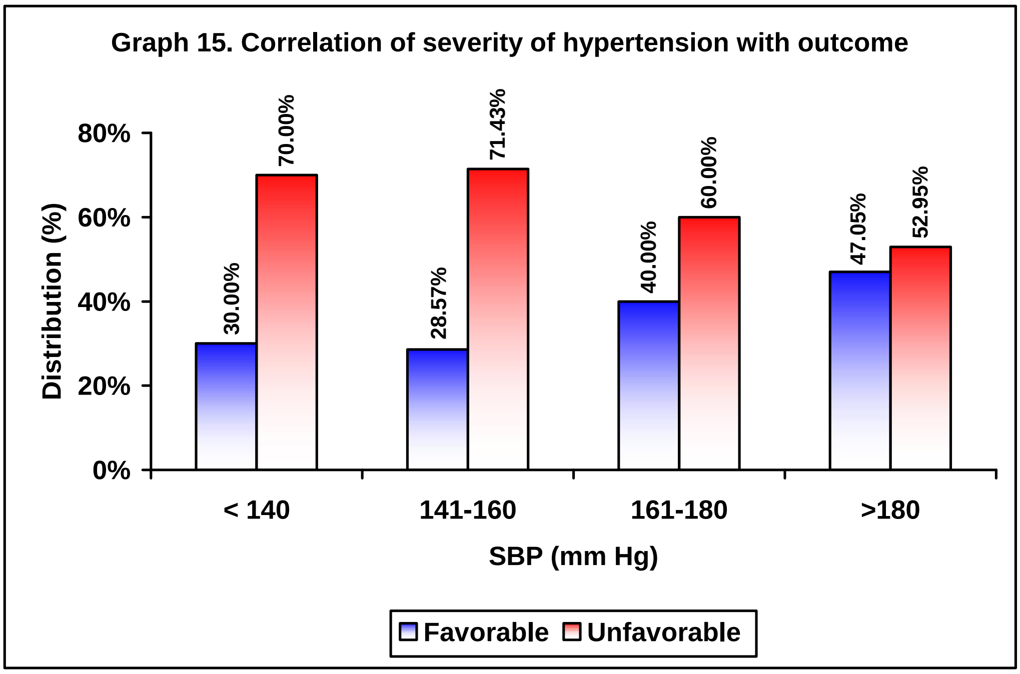


In the present study all the patients who had habit of alcohol consumption as well and tobacco 4 (100%) were found to have unfavourable outcome.

Table 15. Correlation of severity of hypertension with outcome

SBP (mm Hg)	Favorable		Unfavorable		Total	
	No	%	No.	%	No	%
< 140	3	30	7	70	10	17.86
141-160	4	28.57	10	71.43	14	25.00
161-180	6	40	9	60	15	26.79
>180	8	47.05	9	52.95	17	30.36
Total	**21**	**37.50**	**35**	**62.50**	**56**	**100.00**

p=0.701

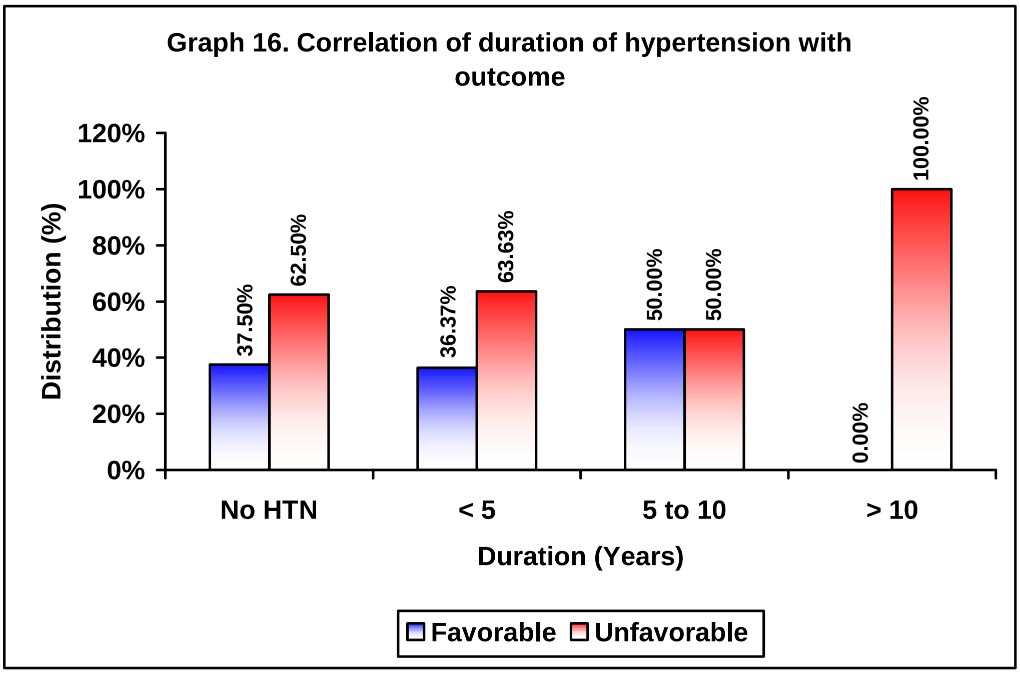


In the present study the outcome was not directly correlating with the severity of the hypertension (p=0.701)

Table 16. Correlation of duration of hypertension with outcome

Duration	Favorable		Unfavorable		Total	
	No	%	No.	%	No	%
No HTN	3	37.5	5	62.5	8	14.29
< 5	12	36.37	21	63.63	33	58.93
5 to 10	6	50	6	50	12	21.43
> 10	0	0.00	3	100	3	5.36
Total	**21**	**37.50**	**35**	**62.50**	**56**	**100.00**

p=0.454

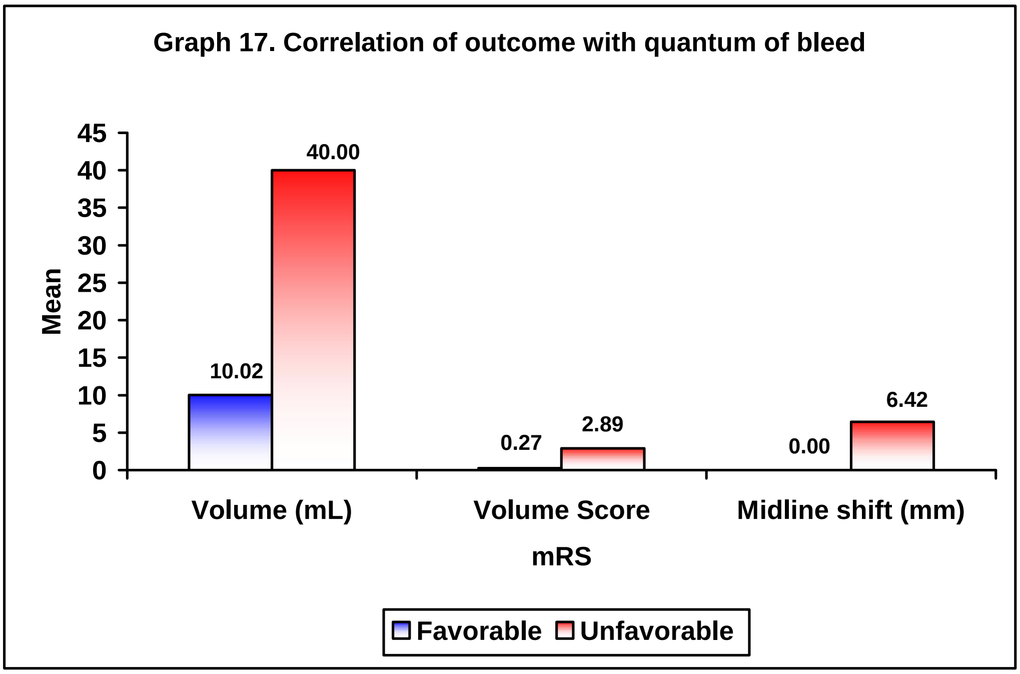


In the present study duration of hypertension was not correlating with the outcome (p=0.454).

Table 17. Correlation of outcome with quantum of bleed

mRS	Volume (mL)		Volume Score		Midline shift (mm)	
	Mean	SD	Mean	SD	Mean	SD
Favorable	10.02	6.76	0.27	0.65	0.00	0.00
Unfavorable	40.00	25.52	2.89	3.09	6.42	3.89
Total	33.57	25.93	2.36	2.97	5.39	4.29
t-value	-4.0069		-2.7721		-3.2436	
p-value	0.0002*		0.0077*		0.0036*	

***p<0.05**

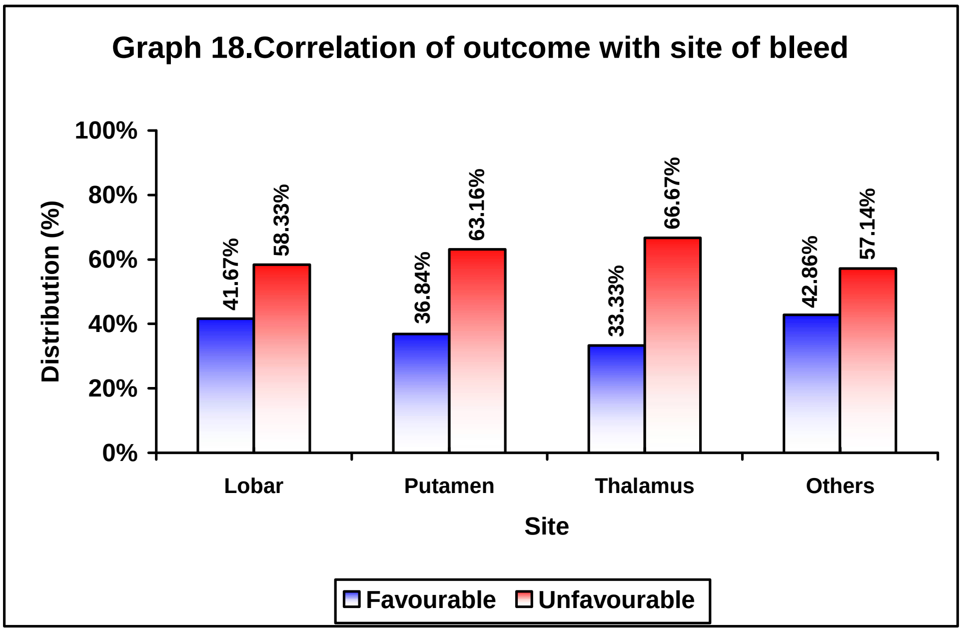


In the present study, mean volume (10.02 ± 6.76 vs 40.00 ± 25.52 mL; p=0.0002), volume score (0.27± 0.65 vs 2.89 ± 3.09 and midline shift (0.00 ± 0.00 vs 6.42 ± 3.89 mL; p=0.0036) were significantly high in patients with unfavourable outcome.

Table 18. Correlation of outcome with site of bleed

Site	Favorable		Unfavorable		Total	
	No	%	No.	%	No	%
Lobar	5	41.67	7	58.33	12	21.43
Putamen	7	36.84	12	63.16	19	33.93
Thalamus	6	33.33	12	66.67	18	32.14
Others	3	42.86	4	57.14	7	12.3

p=0.960

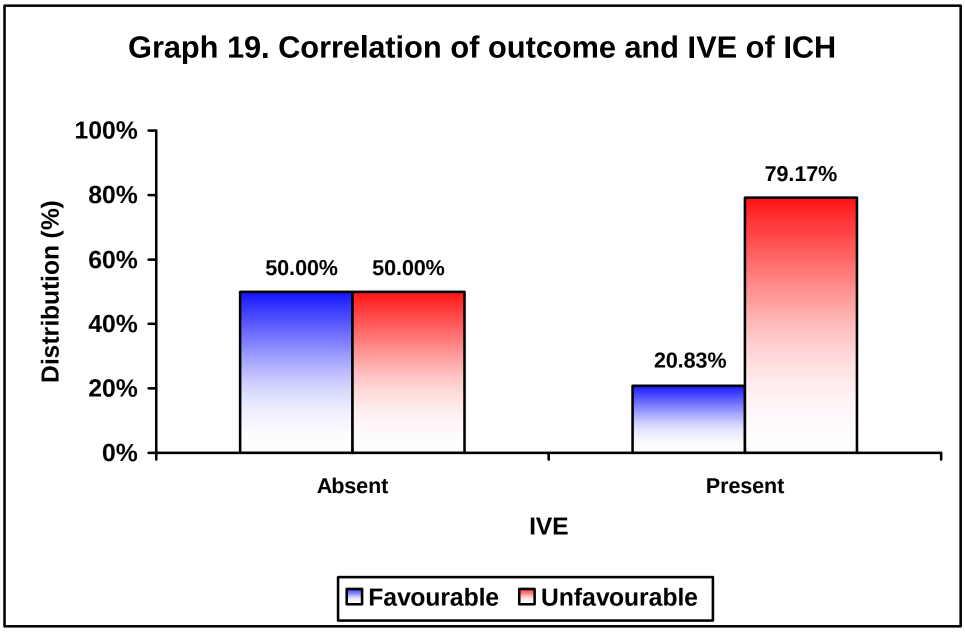


In the present study unfavourable outcome was commonly seen in patients with bleed in putamen. However association between site and outcome was not statistically significant (p=0.960).

Table 19. Correlation of outcome and IVE of ICH

IVE	Favorable		Unfavorable		Total	
	No	%	No.	%	No	%
Absent	16	50	16	50	32	57.11
Present	5	20.83	19	79.17	24	42.86
Total	**21**	**37.50**	**35**	**62.50**	**56**	**100.00**

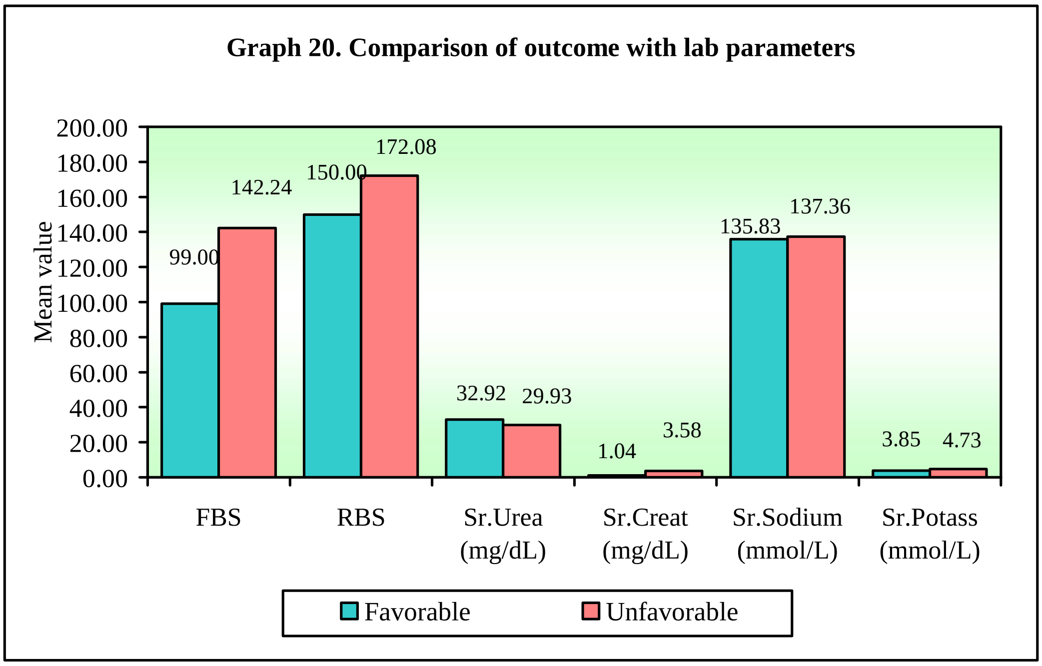
p=0.026



In the present study 79.17% of patients had unfavourable outcome who presented with IVE. The correlation between IVE of ICH with outcome was found to be statistically significant.

Table 20: Comparison of outcome with lab (mg%) parameters

Variables	Summary	Favorable	Unfavorable	Total	t-value	p-value
FBS	Mean	99.00	142.24	134.00	-1.4361	0.1672
	SD	12.81	58.77	55.59		
RBS	Mean	150.00	172.08	167.66	-0.9661	0.3389
	SD	38.26	69.31	64.59		
Bl.Urea (mg/dL)	Mean	32.92	29.93	30.57	0.4815	0.6321
	SD	25.73	16.92	18.92		
Sr.Creat (mg/dL)	Mean	1.04	3.58	3.04	-0.5851	0.5609
	SD	0.34	14.94	13.25		
Sr.Sodium (mmol/L)	Mean	135.83	137.36	137.04	-0.7468	0.4584
	SD	4.78	6.62	6.27		
Sr.Potass (mmol/L)	Mean	3.85	4.73	4.54	-0.5149	0.6087
	SD	0.42	5.93	5.26		



In the present study mean values of serum creatinine (3.58±14.94), serum sodium (137.36±6.62) and serum potassium (4.73±5.93) were higher in patients with unfavourable outcome. However values were not statistically significant.

DISCUSSION

In this cross sectional study of 56 patients with ICH with and without intraventricular extension, demographic factors, comorbid conditions, clinical presentation and CT/MRI findings affecting the outcome were evaluated.

In the present study it was observed that maximum number of patients with ICH were in the age group 51-70 years that is 29(51.78%).The youngest patient was 28yrs old and the oldest was 85yrs.This is in correlation with the study done by Ariesen et al[88] and a US[89] study.

In our study 44(78.57%) patients were males and 22(39.28%) patients were females. Male preponderance was seen with Male: Female ratio of 3.66:1.This finding is consistent with a systematic review done by Ariesen et al.[88]

In the present study common clinical presentations were neurodeficits (hemiparesis/quadriparesis) 51 (91.07%) followed by speech disorder 42(75%), cranial nerve palsy 36 (64.29%), vomiting 25 (44.64%), headache 17 (30.36%) and only 3 (5.36%) patients with seizures. This is in accordance with similar study done by Mohr et al.[52]

Hypertension was the most common comorbid condition 47(83.92%) found among patients in our study. In a pooled prospective study done by Jared et al.[89] 60% of patients with ICH had hypertension. Hypertension was found to be a significant risk factor for intracerebral haemorrhage by another systematic review by Ariesen et al.[88]

In the present study majority of patients 33 (58.92%) with ICH had hypertension for a duration <5 years. This is in contrast to another Indian study by Suthar et al [9]which showed increased morbidity and mortality in ICH patients with prolonged hypertension as evidenced by hypertensive retinopathy. This might be due to large number of newly detected hypertensive patients (21 out of 56) in our study.

The modified rankin scale (mRS) is the most practical instrument for outcome evaluation after the stroke. The mRS has zero to five point scale system where zero indicates no functional disability and five indicates severe disability requiring constant attention.[85-87]

In the present study, 2 patients (14.2%) were able to walk without assistance (Grade II), 9 patients (16.67%) were able to walk with assistance (Grade III), 19 patients (33.92%) were slightly disabled and able to look after their own affairs without assistance (Grade IV) showing improvement. Other 16 patients (28.57%) were severely disabled and bed ridden (Grade V). Longer follow-up with larger number of patients would be able to offer definitive data on the long term functional outcome in these patients.

In this study alcohol consumption was the most common habit 13(23.21%) found among patients with intracerebral hemorrhage. This correlates with the finding of a study done by Ariesen et al.[88]

In the present study most common ECG abnormality found among patients with ICH was LVH 22(39.29%). This is probably due to the underlying long standing hypertension in these patients. However to the best of our knowledge no study has directly studied the association between ICH and LVH.

In the present study most common site of intracerebral bleed was putamen19(33.9%) followed by Thalamus18(32.1%). Other sites of bleed in our study were lobar region, caudate nucleus and brainstem. Similar observations were made by an Indian study by Suthar et al,[90] most common sites of hematoma were Basal ganglia(49%),followed by lobar(21%) and Thalamus (14%). In a US study[91] most common sites of ICH were Putamen (35-50%), followed by Lobar (30%), Thalamus (10-15%), pons (5-12%), caudate nucleus (7%) and cerebellum.

In the present study mean age of the patients was 56.54.The majority of patients in 51-70yrs age group 17(58.6%) had unfavourable outcome. However in our study age didn’t correlate significantly with the outcome. A Spanish study done by Ferrete-Araujo et al.[92] showed age of the patient correlates significantly with the mortality and functional outcome at 6 months. The variation may be due to the smaller sample size in our study.

In our study outcome was unfavourable in males compared to females, but the association was not statistically significant. This is in accordance with 2 other previous studies done by Juvela et al.[93] and Ferrete-Araujo et al.[92]

The patients presented with altered sensorium and neurodeficits had significantly unfavourable outcome compared to others. This finding correlates with a study done by Juvela et al.[93]

There was no significant correlation between habits and outcome in our study. One study by Juvela et al.[93] showed poor outcome was directly associated with amount of alcohol used within last week before ICH, as well as mean corpuscular volume (MCV) suggesting that both recent drinking and long term heavy alcohol intake impair outcome.

In the present study we made an attempt to find the correlation between severity and duration of hypertension and outcome, but it was statistically insignificant. In a study done by Russel et al.[94] both duration and severity of hypertension were found to correlate with ICH.

In our study mean volume of the bleed in patients with unfavourable outcome was 40ml compared to 10ml in those with favourable outcome. The volume of ICH, ICH volume score and midline shift in CT/MRI all correlated significantly with the outcome. These findings are in accordance with the previous similar studies by Juvela et al ,[93] Ferrete-Araujo et al.[92] and Bhatia et al.[95]

We tried to find a relationship between site of bleed and outcome in our study but the relationship was statistically not significant (p=0.960).This finding corresponds to similar study done by Russel et al.[94]

In the present study 24 patients (42.86%) had intraventricular extension of bleed and out of which 19(79.17%) had unfavourable outcome. This was statistically significant and correlates with findings of previous studies by Juvela et al,[93] Ferrete-Araujo et al.[92] and Bhatia et al.[95]

Thus in the present study immediate outcome of patients with intracerebral haemorrhage correlates with clinical presentation of patients with altered sensorium/neurodeficits, quantum of bleed and intraventricular extension of bleed.

CONCLUSION

In the present study of 56 patients with or without intraventricular extension we observed significant correlation with various factors. Based on findings of the study prominent features are mentioned below.

- Among the patients presented with ICH maximum cases were in the 51-70yrs age group.
- Though males were more in number as compared to females whether gender influence the outcome is difficult to state because of small sample size.
- The common clinical presentations were hemiparesis/quadriparesis followed by speech disorder, cranial nerve palsy, vomiting and headache.
- Hypertension was a significant comorbid condition found among patients in the study. Moreover 37.5% of these cases were newly detected.
- Out of those patients who presented with ICH, majority (78.5%) had unfavourable outcome at the time of discharge according to modified rankin scale score.
- Alcoholic history didn’t have any bearing on the outcome in our study.
- The most common ECG finding among patients was LVH and it shows correlation with unfavourable outcome. This reflects the impact of longstanding hypertension on outcome.

- The clinical presentation of patient with altered sensorium/coma and neurodeficits influenced the outcome of the patients.

- The site of bleed didn’t have any influence on outcome of the patient.However quantum of bleed and midline shift were significant findings in patients with poorer outcome.

- P atients with ICH with intraventricular extension had unfavourable outcome as compared to those without intraventricular extension.

We feel it is worthy to study by adjusting comorbid conditions like hypertension, age, sex, habits and site of bleed to know whether these patients have true association .Owing to our small sample size, large sample size is required to overcome these limitations.

SUMMARY

The present study was conducted to know various demographic factors, clinical presentation, clinical and CT/MRI findings affecting the outcome in ICH patients with or with out intraventricular extension. The study was conducted on 56 patients who presented with ICH on CT/MRI to the Dept of Medicine/ Neuromedicine, KLES Dr. Prabhakar Kore hospital and MRC, Belagavi during the period Jan 2015 to Dec 2015.

- We found ICH was common in the age group 51-70 years.
- The ICH was more common in males compared to females.
- The most common clinical presentations were with neuro deficits, speech disorder and cranial nerve dysfunction.
- Hypertension was the most important risk factor found among patients.
- Most of patients with hypertension were newly detected cases.
- The duration and severity of hypertension didn't have any bearing on the study group.
- The age and gender of the patient didn't show any influence on the outcome of the patients in our study.
- The outcome of the patients were significantly affected by presentation of patients with neurodeficits/altered sensorium.
- The site of bleed was not having any bearing on the outcome.

- The volume of bleed significantly influenced the outcome of the patients.
- ICH with intraventricular extension had poorer outcome as compared to ICH without intraventricular extension.
- The patients with quantum of bleed more than 40ml and with midline shift had poorer outcome as compred to bleed quantity of 10ml with out midline shift.

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ANNEXURE I

CONSENT FOR PARTICIPATION IN RESEARCH

Mr. /Mrs.____ we are requesting you to enroll yourself in study titled “ANATOMICAL RELATIONSHIP AND CLINICAL OUTCOME OF PATIENTS WITH INTRACEREBRAL HEMORRHAGE WITH AND WITHOUT INTRAVENTRICULAR EXTENSION- A Study conducted by DR. *** ***** ******, postgraduate student in MD GENERAL MEDICINE under the guidance of DR. *** ****** ********* at J. N. Medical College, Belagavi.

You have been requested to participate in research because your profile matches with the study group. All the patients admitted with intracerebral hemorrhage can become participants of study. During the study you will be asked some questions and you are supposed to answer to the best of your knowledge.

Your participation in the research is absolutely voluntary. Your decision to participate in the study or otherwise will not affect your relationship with J.N.M.C. If you decide not participate you are free to withdraw at any time.

The purpose of research is to study anatomical relationship and clinical outcome of patients with intracerebral hemorrhage with and with out intraventricular extension.

Procedure involved

A detailed history taking, clinical examination, blood investigations and imaging investigations like CT/MRI which are not invasive procedures.

Risks and benefits

There are no risks involved and benefits are many. The study helps to identify various clinical features of the disease and identify different causative factors, avoidance of which prevents future recurrence stroke. The results deduced at the end of study will help all similar patients admitted in the hospital to assess their prognosis.

Alternatives

Even if you decline to participate, there will not be any change in the line of your management or the relationship with your doctor. You will be told about all the new information that may affect your decision to participate in the study.

Withdrawing/removal from study

You can withdraw any time from the study as you wish.you will not be penalized for such a decision.

Privacy and confidentiality

The only people to know that you are a research subject are the members of research team. No information about you or provided by you during the research will be disclosed to others without your written permission except:

In emergency to protect your rights and welfare.

If required by law.

Financial incentives for participation

You will not be paid any monetary benefits or free gifts for participation in the research. You will not be reimbursed for expenses.

Authorisation to publish results

When the results of the research are published or discussed in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

CONSENT STATEMENT

I, the undersigned, have been explained in my own vernacular language about the study and my participation in the study is voluntary. If I want I can withdraw at any time. Also I have been given enough time to clear my doubts about the study and my rights as a study participant.

In case you have any questions related to the study you can contact Dr. ****** ****** ****** (***** ******).

In case you have any questions about your rights as a study participant you can contact Dr. **** ****** (***** *****).

Signature or the left thumb impression of the participant or legally authorized representative.

Participant’s name: ______________________Signature: _________________

Witness name: _________________________ Signature: __________________

Experimenter’s name: ___________________ Signature: __________________

Guardian’s name: ______________________ Signature: ___________________

Place: ___________

Date: ____________

ANNEXURE II – PROFORMA

ANATOMICAL RELATIONSHIP AND CLINICAL OUTCOME OF PATIENT WITH INTRACEREBRAL HEMORRHAGE WITH INTRAVENTRICULAR EXTENSION –

A CROSS SECTIONAL STUDY AT K.L.E.S DR. PRABHAKAR KORE HOSPITAL AND MRC, BELAGAVI

Name of the patient :

In Patient Number :

Age :

Sex :

Date of Admission :

Date of Discharge :

Religion :

Occupation :

Address :

History of present illness

Headache :

Seizure :

Vomiting :

Vertigo / Tinnitus / Syncope :

Altered Sensorium :

Loss of consciousness :

Speech disorder :

Other symptoms :

Past history

H/o stroke :

Ht :

Dm :

Recent MI :

Any cardiac disease requiring warfarin therapy

Bleeding / coagulation disorder

Drug history

H/O Thrombolysis :

H/O Anticoagulation therapy :

Family history

H/o stroke :

Ht :

Dm :

Ihd :

Personal history

Smoking :

Alcohol intake :

General physical examination

Build & nourishment :	Vital signs
Height :	PR :
Weight :	BP :
	RR :
	Temperature :

Examination of CNS

Higher functions

Handedness :

Level of Consciousness (GCS) s :

Orientation in time, place, person :

Speech and language – :

Memory :

Intetelligence :

Delusions & hallucinations :

Cranial nerves

Right Left

1st Olfactory N– Sense of smell

2nd optic N – Acquity of vision

Field of vision :

Colour vision :

Fundoscopy :

3, 4, 6 Cranial Nerves –

Diplopia :

Squint :

Nystagmus :

Ptosis :

Right Left

Eye movements

Conjugate :

Individual eye ball movements :

Pupils :

Reflexes :

<u>5th Trigeminal N</u>

Sensory :

Motor :

Reflexes :

Corneal :

Conjunctival :

<u>7th Facial N</u>

UMN facial palsy :

LMN facial palsy :

<u>8th – Auditory .N</u>

Acquity of hearing (watch test) :

Rinner test :

Webers test :

<u>9th Glossopharyngeal .N</u>

Taste on post 1/3rd of tongue :

Pharyngeal reflex. :

<u>10th Vagues . N</u>

Patate :

Nasal regurgitation :

Nasal thong of voice :

Palatal elevation (Ah test) :

Position of uvula :

Larynx :

Hoarseness of voice :

<u>11th Accesory N</u>

Sternocleidomastoid :

Trapezius :

Right Left

<u>12th Hypoglossal .N</u>

Appearance of tongue of as in oral cavity :

Deviation of tongue on protrusion :

Power :

Motor system

Nutrition :

Tone :

Power :

<u>Shoulder joint</u>

Flexion

Extension :

Adduction :

Abduction :

<u>Elbow joint</u>

Flexors

Extensors

<u>Wrist joint</u>

Flexors

Extensors

<u>Hand grip</u>

Hip joint

Flexion

Extension

Adduction

Abduction

Knee joint

Flexion

Extension

Ankle joint

Plantar flexors

Dorsi flexors

Co-ordination

Upper limb

Lower limb

Right Left

Abnormal movements

Reflexes

Superficial	:	Corneal	:
Conjunctival	:	Palatal	:
Abdominal	:	Cremastric	:
Plantar	:	Deep	:
Awjerk	:	Iceps	:
Triceps	:	Supinator	:
Knee	:	Ankle	:
Patellar clonus	:	Ankle clonus	:

Right Left

Gait

Sensory system

Touch : Fine :

Crude : Pain :

Superficial : Deep :

Temperature : Hot :

Cold :

Post column Sensation

Vibration :

Joint position sense :

Romberg's Sign

Right Left

Cortical sensations

Cerebellar signs

Miscellaneous :

Skull & spine :

Signs of meningeal irritation :

Neurocutaneous markers :

Carotid artery pulsations :

Other system

Cardiovascular System : Respiratory System :

Per Abdomen : Modified Rankin Scale:

Investigations : Haemoglobin :

TC : DC :

ESR	:	HbA1c	:
FBS	:	PPBS	:
VLDL	:	LDL	:
HDL	:	TG's	:
Blood urea	:	S. creatinine	:
S. Na+	:	S.K+	:

ECG

Chest X-ray :

Bleeding time :

Clotting time :

CT/MRI

Volume score of IVH :

Final diagnosis

Anatomical :

Pathological :

Etiological

ANNEXURE III – KEY TO MASTER CHART

^{0}C	-	Degree centigrade
A	-	Absent
AB	-	Absent
ALD	-	Alcoholic liver disease
APTT	-	Activated prothrombin time
ARF	-	Acute renal failure
ASP	-	Aspiration
ATA	-	Ataxia
AVM	-	Arteriovenous malformation
B/L	-	Bilateral
BL	-	Bilateral
BR	-	Branch
CA	-	Cant assess
CN	-	Central
Compl	-	Compliance
CS	-	Cheye stoke breathing
CT	-	Computed tomography
CVA	-	Cedrebrovascular accident
CVS	-	Cardiovascular system
DA	-	Dysarthria
DBP	-	Diastolic Blood Pressure
DM	-	Diabetic mellitus
Dysf	-	Dysfunction

ECG	-	Electrocardiogram
EX	-	Extensor
ext	-	Extension
F	-	Female
FBS	-	Fasting blood sugar
FL	-	Flexor
GA	-	Global aphasia
Hb	-	Haemoglobin gram in percentage
HDL	-	High density lipoprotein
HPA	-	Hemiparesis
HPG	-	Hemiplegia
HT	-	Hypotonia
HTN	-	Hypertension
I.U/L	-	International units per litre
INR	-	International normalized ratio
L	-	Left
LAD	-	Left axis deviation
LDL	-	Low density lipoprotein
LGP	-	Left gaze palsy
LL	-	Lower limb
LT UMN FP	-	Left upper motor neuron facial palsy
LVH	-	Left ventricular hypertrophy
M	-	Male
M	-	Month
MA	-	Motor Aphasia

MAP	-	Mean arterial pressure
MCA	-	Middle cerebral artery
mg%	-	Milligram percentage
mg/dL	-	Milligram per deciliter
ml	-	Milliliter
mm	-	Millimeter
mmol/L	-	Millimole per litre
MRI	-	Magnetic resonance imaging
MU	-	Mute
N	-	Normal
NC	-	Non compliance
ND	-	Newly detected
NR	-	Non reactive
P UL	-	Proximal upper limb
P	-	Present
PNM	-	Pneumonia
PONS &MB	-	Pons and Mid brain
PT	-	Prothrombin time
PTRS	-	Plantar response
QDPA	-	Quadriparesis
QDPG	-	Quadriplegia
R	-	Right
RBs	-	Random blood sugar
RCTN	-	Reaction
RGP	-	Right gaze palsy

ROM	-	Range of motion
RS	-	Respiratory system
RT LL	-	Right lower limb
RT	-	Right
SA	-	Sensory aphasia
SAH	-	Sub arachnoid haemorrhage
SBP	-	Systolic Blood Pressure
SDH	-	Subdural harmorrhage
SGOT	-	Serum glutamic oxaloacetic transaminase
Sl. No.	-	Serial number
SLR	-	Sluggist reaction
SP	-	Spasticity
Sr. creat	-	Serum creatine
Sr.	-	Serum
ST	-	Sinus tachycardia
SZR	-	Seizure
TC	-	total count
TGL	-	Triglycerides
UL	-	Upper limb
UMN FP	-	Upper motor neuron facial palsy
WO	-	Worse
Y	-	Yes