



## ORIGINAL ARTICLE

## Clinical Characteristics, Predictors of Outcome of Patients Admitted with Intracerebral Hemorrhage to Benghazi Medical Center, Benghazi -Libya

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### Abstract

**Background:** Intracerebral hemorrhage (ICH) is a subtype of acute stroke and one of the leading causes of death and a major cause of morbidity worldwide. The incidence of ICH varies cross countries and ethnic groups.

**Objectives:** To study the prevalence, clinical characteristics, risk factors and outcomes of patients with ICH. Also, to evaluate clinical features that can be used as prognostic predictors of mortality in those patients.

**Methods:** *Design & setting:* an observational descriptive study at Benghazi Medical Center (BMC). *Patients and methods:* All patients with acute ICH admitted to BMC during 2017. Data were collected from patients' records. *Outcome and measures:* Age, gender, duration of hospitalization, risk factors for ICH (hypertension, diabetes mellitus, renal impairment, smoking, alcohol or drug abuse, antiplatelet or anticoagulants use), complications (cardiovascular, pulmonary, urinary tract or other infections), severity of stroke assessed by the Glasgow coma scale (GCS) and the outcome were all studied.

**Results:** The study included 110 patients. ICH represents 18% of all strokes. The mean age was 59 (12) years, 71% were male. The most encountered risk factor was hypertension, 70 (64%), reported more in older age (> 50 years), where as smoking, drug addiction and alcohol use were more common among younger age group (≤ 50 years). Hyponatremia, hyperglycemia and infections were found to be common complications; 82(75%), 28(47%) and 49(45%), respectively. The median length of hospital stay was 9(5) days, and deep venous thrombosis was associated significantly with prolonged hospitalization. In-hospital mortality was reported in 47(43%). Hyperglycemia and respiratory complications were associated with increased mortality.

**Conclusion:** Our study was comparable to regional as well as international studies. This study analyzed the difference in clinical characteristics and risk factors among older and younger age. Results concerning predictors of mortality showed some variations compared to others from different parts of the world.

### Keywords

Stroke, Intracranial hemorrhage, ICH, Predictors, Outcome

### Introduction

Intracerebral hemorrhage (ICH) is accounting for 10-20% of all strokes. The incidence of ICH varies across countries and ethnic groups, where it is much higher in low and middle income countries and more common among Asian people [1-3]. It is considered to be a catastrophic medical emergency that needs immediate actions and sometimes intervention since it has a high risk of mortality and morbidity [4,5]. Many risk factors are linked to ICH including old age, male gender, hypertension, renal failure, low lipids, smoking, alcohol, blood thinners and the use of sympathomimetic drugs like cocaine but there are many underlying different causes identified. The patients' presentation depends on the area affected by the bleeding, the size of the hematoma and if there is any extension to the ventricles [4-6]. Un-like ischemic strokes, the mortality rate for ICH is higher, reaching up to 40-60%. There are many factors that can predict the poor outcome of ICH. This includes female gender, older age, hypertension,

hyperglycemia, diabetes mellitus, chronic kidney disease, cardiovascular complications, pulmonary infections and higher stroke severity [5,7].

Studies about stroke in general and ICH in particular are scarce in Libya, the latest one being in 2014 [8]. Therefore, we intended to continuously raise-up stroke research. We selected to study patients with ICH in order to evaluate the prevalence, clinical characteristics and the different risk factors of ICH. Also to compare risk factors, clinical characteristics, and outcome between the young patients with older patients. Also to shed light on predictors of prolonged hospitalization and mortality in patients admitted with ICH.

## Patients and Methods

An observational descriptive study of all patients with acute spontaneous (non-traumatic) hemorrhagic stroke admitted to Benghazi Medical Center (BMC) during the period January through December 2017. BMC is a teaching hospital affiliated to ministry of health, provides health care to multinational population in Benghazi-Libya.

Data were collected from case records of patients admitted to the medical units including the intensive care units at BMC during 2017. All patients diagnosed with acute spontaneous ICH were included, and the diagnosis was confirmed by radiological assessment either computerized tomography scan (CT) or magnetic resonance imaging (MRI).

The data included gender, age, risk factors for ICH such as (hypertension, smoking, alcohol or drug abuse, antiplatelet or anticoagulants use), cardiovascular complications such as (arrhythmias or coronary artery disease), pulmonary, urinary tract or other infections, severity of stroke assessed using the Glasgow coma scale. All data were noted at time of presentation.

**Inclusion/Exclusion criteria:** All adults with acute non traumatic ICH were enrolled. The diagnosis of ICH has been confirmed by neuroimaging modalities either CT scan or/and MRI scan in a duration of less than 48 hours. Inclusion criteria include patients with secondary ICH such as AVM, aneurysm or tumors.

However, patients with hemorrhagic stroke of more than 48 hours or referred from other hospital were excluded due to lack of complete information.

Data were analyzed using the statistical program Statistical Package for Social Science (SPSS) version 18.0. Normality of data was determined by using the Kolmogorov-Smirnov test. Statistical significance was accepted when *P*-values < 0.05.

Numerical variables were presented by mean and standard deviations. Categorical variables were presented as numbers and percentages. For comparison of the numerical variables t-test was used. Categorical

variables were analyzed using a chi-square test. We used logistic regression in prediction of qualitative variables, and linear correlation and non-parametric regression for quantitative variables.

This study was approved by the Research Ethical Committee at Benghazi Medical Center, Benghazi, Libya.

## Results

### Clinical characteristics and risk factors of the total study population

Total number of admissions to BMC from January to December 2017 was 11299 cases, of which 606 patients admitted with strokes; 496(82%) were ischemic and 110(18%) were hemorrhagic strokes. We studied the 110 patients with ICH. There were 78(71%) male and 32(29%) female (Table 1). The age is 59(12) years, with no difference between male and female.

Hypertension was the most common risk factor for ICH and found in 70(64%) patients, where 50(71%) of them were male and 20(29%) were female. Diabetes mellitus was found in 34(31%) patients and history of renal diseases in 15(14%) patients. History of smoking, alcohol intake and drug addiction was documented in 31(28%), 7(6%), and 5(5%) patients, respectively. Aspirin use prior to ICH was found in 17(15%) patients, oral anticoagulant (warfarin) was used in 7(6%) patients, whereas the use of non-vitamin k antagonist or other antiplatelet drugs were not documented in any case. However, no risk factors were found in 21(19%) patients.

**Table 1:** Clinical characteristics of the study population.

	Total (N = 110)	≤ 50 years (N = 25)	> 50 years (N = 85)	P value
<b>Age (years)</b>	59 ± 12	41 ± 6.49	64 ± 8	
<b>Gender</b>				
Male (N,%)	78 (71%)	19 (76%)	59 (69%)	0.356
Female (N,%)	32 (29%)	6 (24%)	26 (31%)	
<b>Risk factors</b>				
Hypertension	70 (64%)	10 (40%)	60 (71%)	0.006
Diabetes	34 (31%)	7 (28%)	27 (32%)	0.462
Smoking	31 (28%)	14 (56%)	17 (20%)	0.001
Renal disease	15 (14%)	3 (12%)	12 (14%)	0.542
Alcohol	7 (6%)	5 (20%)	2 (2%)	0.006
Drug abuse	5 (5%)	4 (16%)	1(1%)	0.002
APT	17 (15%)	1 (4%)	16 (19%)	0.059
ACT	7 (6%)	0 (0%)	7 (8%)	0.155
<b>GCS</b>				
Grade I	39 (35%)	10 (40%)	29 (34%)	0.754
Grade II	29 (26%)	6 (24%)	23 (27%)	
Grade III	22 (20%)	6 (24%)	16 (18.8%)	
Grade IV	20 (18%)	3 (12%)	17 (20%)	

APC: Antiplatelet Therapy; ACP: Anticoagulants Therapy

The symptoms and signs at the time of presentation were documented as motor hemiparesis 66 (60%), headache 60 (55%), nausea and/or vomiting 45 (41%), 36 ataxia (33%), dysarthria/dysphasia/aphasia 35(32%), seizure 14(13%), disorientation 12(11%), vertigo 12(11%), visual symptoms 11(10%) and sensory symptoms 9(8%).

In addition, documented detailed description of CT findings was available only for 60/110(54.5%) patients. Out of 60, there were 40(67%) patients with non-lobar bleeding, whereas 16(27%) patients had lobar bleeds. Intraventricular extension, hydrocephalus and subarachnoid hemorrhage was seen in 22(37%), 8(13%) and 10(17%) patients, respectively.

Secondary causes of ICH were identified in 3 (3%) patients, two (2%) of them had aneurysms and one (0.9%) had arteriovenous malformations.

During their hospitalization, 44/110(40%) patients received treatment initially in the intensive care unit (ICU), whereas 66(60%) patients received treatment initially in the medical wards. The mean GCS at the time of presentation was 9(4). Further grading of GCS into 4 grades was performed and we found that 39 (35%) patients had grade 1 (GCS = 15-13), 29 (26%) patients had grade 2 (GCS = 12-9), 22(20%) patients had grade 3 (GCS = 8-4) and 20(18%) patients had grade 4 (GCS = 3). There was a statistically significant difference in the mean GCS between patients admitted initially to ICU, and those admitted initially to the medical wards (7(3) vs. 11(4);  $P = 0.000$ ). However; only 7(6%) patients had surgical interventions.

When we analyzed patients' outcome, we found that 19(17%) patients discharged with no disability, 44(40%) patients discharged with different kinds of disabilities and 47(43%) patients died.

### **Stratification of the study population according to age**

We stratified our study population according to the age into two groups;  $\leq 50$  years as young and  $> 50$  years as older age group (Table 1).

### **Clinical characteristics and risk factors among older age group ( $> 50$ years)**

There were 85(77%) patients older than 50 years, of them 59(69%) were male. The mean age among this group is 64(8) years. However; there was no significant difference in age (65(8) vs. 63(8);  $P = 0.573$ ) between male and female (Table 1).

Hypertension was the most commonly encountered risk factor and reported in 60(71%) patients, followed by diabetes mellitus in 27(32%) and history of renal diseases in 12(14%). When we looked for other risk factors, we found that 17(20%), 2(2%), and 1(1%) patients had history of smoking, alcohol intake and

drug addiction, respectively. The last three groups were male patients. Aspirin use prior to ICH was reported in 16(19%), whereas the use of oral anticoagulant (warfarin) was found in 7(8%) patients (Table 1), but non-vitamin k antagonist were not documented in any case. In this age group, risk factors for ICH were not determined in 12(11%) patients.

During their hospitalization, 33(39%) patients received treatment initially in the ICU, while 52(61%) patients received treatment initially in the medical wards. The mean GCS at the time of presentation was  $9 \pm 4$ . With further grading of GCS we found that 29(34%) patients had grade1 (GCS 15-13), 23(27%) patients had grade 2 (GCS 12-9), 16(19%) patients had grade 3 (GCS 8-4) and 17(20%) patients had grade 4 (GCS 3).

Patients' outcome among this age group was as follow, 13(15%) discharged with no disability, 35(41%) discharged with different kinds of disabilities and 37(44%) died.

### **Clinical characteristics and risk factors among young age group ( $\leq 50$ years)**

This age group includes 25(23%) patients. The mean age among this group is 41(6) years. However; there was no significant difference in the age between male and female (Table 1).

Among this age group, smoking was the most common risk factor 14(56%), followed by hypertension in 10(40%). Diabetes mellitus was found in 7(28%) and history of renal diseases in 3(12%). Alcohol intake was documented in 5(20%), and history of drug addiction was positive in 4(16%) patients. Aspirin use prior to ICH was reported in 1(4%) patient, whereas the use of oral anticoagulant (warfarin) was not documented in any case of this group. However, no risk factors were detected in 9(36%) patients (Table 1). Based on MR and/or CT angiography, we identified structural vascular lesion in 3(3%) patients; aneurysms seen in 2(2%) patients and arteriovenous malformations in 1(0.9%) patient.

During their hospitalization, 11(44%) patients received treatment initially in the ICU, whereas 14(56%) received treatment initially in the medical ward. The mean GCS at the time of presentation was  $9 \pm 4$ . On further grading we found that grade 1 (GCS 15-13) was reported in 10(40%) patients, grade 2 (GCS 12-9) in 6(24%) patients, grade 3 (GCS 8-4) in 6(24%) patients and grade 4 (GCS 3) in 3(12%) patients (Table 1).

Patients' outcome among this age group was as follow, 6(24%) patients discharged with no disability, 9(36%) discharged with different kinds of disabilities and 10(40%) died.

### **Comparison between the two age groups**

Results are shown in Table 1. There is a significant

**Table 2:** Medical complications among the study population.

	Total (N = 110)	≤ 50 years (N = 25)	> 50 years (N = 58)	p value
<b>Metabolic</b>				
Hyperglycemia*	52 (47%)	11 (44%)	41 (48%)	0.709
Hyponatremia**	82 (75%)	22 (88%)	60 (78%)	0.079
Hypernatremia***	2 (2%)	0 (0%)	2 (2%)	0.439
<b>Infections</b>				
Respiratory	37 (34%)	5 (20%)	32 (38%)	0.101
Gastrointestinal	2 (2%)	1 (4%)	1 (1%)	0.353
Urinary tract	12 (11%)	2 (8%)	10 (12%)	0.596
<b>Renal failure</b>	15 (14%)	3 (12%)	12 (14%)	0.786
<b>DVT</b>	4 (4%)	1 (4%)	3 (4%)	0.912
<b>CV</b>	11 (10%)	5 (20%)	6 (7%)	0.058

Values are expressed as numbers (%).

CV: Cardiovascular complications such as arrhythmia, heart failure and coronary artery disease, DVT: Deep Venous Thrombosis. Patients may have more than one complication

\*Hyperglycemia is defined as random plasma glucose > 140 mg/dl; \*\*Hyponatremia is defined as serum Sodium < 135 mmol/l;

\*\*\*Hypernatremia is defined as serum Sodium > 145 mmol/l

**Table 3:** The highest and lowest levels of plasma glucose, sodium, potassium, and creatinine among the study population.

Factor	Highest	Lowest
Glucose (mg/dl)	504	80
Sodium (mmol/L)	146	120
Potassium (mmol/L)	6.0	2.8
Creatinine (mg/dl)	4.1	0.3

difference in the proportion of hypertension [10(40%) vs. 60(71%);  $P = 0.005$ ] between the young and the old age groups. On the other hand; no statistical difference was found concerning diabetes mellitus.

Among other risk factors, patients in the young age group found to differ from older patients in the proportion of smoking [14(56%) vs. 17(20%);  $P = 0.000$ ], drug addiction [4(16%) vs. 1(1%);  $P = 0.002$ ] and alcohol use [5(20%) vs. 2(2.4%);  $P = 0.001$ ]. However; there was no statistical difference between the two age groups regarding aspirin or anticoagulant use. In terms of outcome, no significant difference was found between the two age groups.

### Medical complications

Different medical complications among the ICH patients are summarized in Table 2. Hyponatremia (sodium < 135 mmol/L) was the most common complication and found in 82(75%) patients, followed by hyperglycemia (blood glucose > 140 mg/dl) in 52(47%) patients. The highest and lowest levels of glucose, sodium, potassium, and creatinine documented in our study population are summarized in Table 3.

Hyperglycemia was encountered among patients older than 50 years in 41 (48%) compared to the younger

age group (≤ 50 years) in 11(44%), though the difference does not reach statistical significance ( $P = 0.709$ ). Other important complications are infections which were reported in 49(45%) patients, with respiratory tract infections being the most common and reported in 37(34%) patients. However; there was no statistical difference between the two age groups regarding pulmonary infections, hyponatremia and renal failure.

Early-onset seizure was reported in 36(33%) patients and anti-epileptic drugs (AEDs) were prescribed to 35(97%) of them.

### Predictors of mortality

The in-hospital mortality in our study was recorded in 47(43%) patients, and the median length of hospital stay was 9(5) days. Patients older than 50 years showed a tendency, though not significant, toward higher rate of mortality compared to younger patients (44% vs. 40%;  $P = 0.245$ ).

Mortality was higher among those with hyperglycemia (20(38%), OD = 0.19 (CI = 0.03-0.97);  $P = 0.047$ ), lower GCS at presentation (GCS < 8 OD = 1.9 (CI = 1.53-2.35);  $P = 0.000$ ) and those who developed respiratory tract infections during their hospitalization [34(92%), OD = 125 (CI = 20.8-756.1);  $P = 0.000$ ] (Table 4).

### Discussion

We studied the prevalence, clinical characteristics, risk factors and predictors of outcome in adult patients with acute spontaneous ICH admitted to our hospital "the BMC" during the year 2017. We further studied the differences in ICH characteristics, risk factors and outcome between two age groups. To the best of our knowledge, we are the first to execute such a

**Table 4:** Predictors of mortality

Factor	OD (95% CI)	P value
Older age (> 50 years)	0.57 (0.12-2.58)	0.474
Female gender	0.76 (0.16-3.63)	0.738
Hypertension	0.79 (0.21-2.92)	0.731
Diabetes mellitus	2.82 (0.50-15.9)	0.238
Smoking	0.32 (0.73-1.47)	0.147
Alcohol use	11 (0.12-961)	0.291
Drug addiction	3.63 (0.00-7085)	0.739
Renal failure	2.44 (0.32-18.6)	0.388
Hyperglycemia	0.19 (0.03-0.97)	0.047
Hyponatremia	0.69 (0.13-3.52)	0.662
Respiratory infection	125 (20.8-756.1)	0.000
Urinary tract infection	10.0 (0.76-132.2)	0.079
Deep venous thrombosis	0.75 (0.03-18.4)	0.861
Initial ICU admission	2.99 (0.80-11.1)	0.102
GCS < 8	1.9 (1.53-2.35)	0.000
<b>CT findings</b>		
Lobar bleed	99.6 (3.59-275)	0.007
Non-lobar bleed	0.03 (0.00-0.41)	0.008
Intra-ventricular bleed	27.2 (1.41-526)	0.029
Hydrocephalus	0.90 (0.06-12.8)	0.939

CT: Computed Tomography, GCS: Glasgowcoma Scale; OD: Odds Ratio, CI: Confidence Interval

comparison among Libyan population. We also studied different factors that can be used as predictors for mortality and/or prolonged in-hospital stay. Our results will therefore substantially improve our understanding and care of ICH in Libyan population.

The prevalence and demographic characteristics of the present study didn't differ from prevalence in previously published studies in Libya [1,9], and Egypt [10] as well as internationally [2,11].

In our study, ICH patients constitute 18% of the total stroke admission during 2017, compared to 23% in 1995 and 19% in 1984 in different previous local studies [1,9]. It is also consistent with results from similar study in Egypt where ICH found to constitute 19% and in agreement with the international numbers which are 10-30% of total strokes cases [2,10,11].

In our study, ICH was more common among male which is consistent with finding from other international studies [10,12,13]. However; some other studies showed no difference between male and female [14-17].

Gender and age distribution of our ICH patients were comparable with previous studies [12,18,19].

Hypertension was found to be the most common risk factor for ICH in our study population. This is an expected finding and is in consistent with the Egyptian study [10] and other international studies [20-22]. Furthermore, hypertension was significantly more

common among older age group, but smoking, drug addiction and alcohol were significantly more common risk factors in younger age group. Other risk factors showed no statistical difference among the two age groups. This result is attributed to the epidemiology of hypertension; as it is being more severe and common in older patients. In contrast, smoking, drug addiction and alcohol are being used more by the younger people.

Diabetes mellitus and smoking were the next most common risk factors found in our patients, which is similar to the results from the Egyptian study [10]. Although diabetes mellitus was associated with ICH in some cohorts studies, but a meta-analysis could not confirm this association [21,23,24].

We found small percentage of other risk factors for ICH such as chronic kidney disease, drinking alcohol, warfarin use, therefore, our results are not comparable to other studies in this regard [21,25,26].

In addition, there are many other risk factors for ICH mentioned in the literature such as increase in the number of childbirths, longer working hours, extended duration of strenuous work activity and long sleep duration greater than 8 hours [27-29]. We couldn't study these factors because our study was retrospective, and probably for that reason no risk factors was found in 21(19%) of our total cases.

The most common clinical presentation in our patients is hemiparesis/hemiplegia. This is expected finding and reported in previous studies [10,12,13]. In addition, more than half of the study population sustained headache. It is higher than what had been reported in other studies, probably due to the difference in study design [12].

Furthermore, deterioration in the conscious level occurred in mild degree, as more than one third of the study population presented with GCS of 13-15. This is in contrast to Baidya OP study who reported lower GCS score [13].

The diagnosis was made by brain imaging for all the cases enrolled in this study. Non contrasted CT brain was the main imaging modality in almost all of the cases, followed by MRI brain in few cases. This is supported by the previous literature in which the non-contrasted CT scan is the modality of choice in ICH [30]. In our cases, angiography was performed in few numbers of cases. Therefore, secondary causes of ICH such as aneurysms and arteriovenous malformations were less than numbers reported internationally. However; in comparison with previous results the secondary causes of ICH represent about 5% of the total ICH causes [31].

Out of the total cases, less than half were treated initially in the ICU, most probably due to their lower GCS, in comparison to the remaining patients who received treatment initially in the medical ward because of their higher GCS.

The most common medical complication was hyponatremia followed by hyperglycemia and infections. The most common site of infection was respiratory tract infections. Other studies showed hyperglycemia as the most frequent complication followed by hyponatremia. Although; other studies showed that infections were a significant complication among patients admitted with ICH specially respiratory infection which is in consistent with our findings [19].

Regarding medical complication in the two different age groups, hyperglycemia was more common among the older age group. In contrast; other complications including pulmonary infections, hyponatremia and renal failure showed no significant difference. However; in the previous literatures, renal failure was a significant medical complication among those above 50-years-old [19].

When we studied the outcome, we found that more than a third (42.7%) died and the remaining were discharged from the hospital either with no or variable degree of disability. Our finding is similar to other reports from different international studies [32-34].

Impaired consciousness upon hospital arrival measured by GCS is the most important factors linked the early mortality [35-37]. In our study, the lower GCS at time of presentation was associated with higher mortality. Other scores like NIHSS were not available. However; the use of GCS score instead of NIHSS can predicts mortality equally [38].

In the current study, other factors that were significantly associated with increased mortality include hyperglycemia and respiratory tract infection. However; previous study from Finland showed a significant association between hyperglycemia and increased mortality, but no association was found with regard to respiratory infections as predictors of the early mortality [19].

It has been reported that hypertension, diabetes mellitus, hyperglycemia and renal failure are associated with increased mortality [39,40]. In contrast, in our study these factors were not associated with significant statistical results to predict the mortality among ICH patients.

Regarding the analysis of brain imaging, detailed radiological description was available for half of the patients. However; lobar bleeds and the presence of IVH were associated with higher mortality which is consistent with the previous international results [41].

## Conclusion

Our study of ICH patients admitted to BMC during 2017 was comparable to regional as well as international studies in terms of age, gender distribution and risk factors.

As hypertension is undoubtedly a risk factor for ICH, primary prevention is the most important step in the management owing to high mortality rates in ICH patients.

Factors that can predict mortality were studied in details with variation in the results compared to other studies from different parts of the world. Utilization of different modalities of neuroimaging for ICH patients especially those with younger age groups and those with no risk factors is warranted. Further prospective studies are needed in this topic to give more details about the ICH among Libyan population in order to provide the best medical and surgical care.

## Limitations of the Study

A retrospective, single-center study. It was based on the medical records from the statistical department, so the lack of proper documentation in the files was the main problem. We could not obtain a detailed neurological assessment by the different neurological scores like NIHSS or others, and we could not retrieve detailed radiological descriptions.

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## Conflicts of Interest

None.

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