

Intracerebral hemorrhage

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ABSTRACT

الأهداف: تقييم درجة انتشار النزيف الدماغي وتوزيع الحالات حسب العمر، الجنس، الأسباب، الأعراض السريرية، موقع النزيف الدماغي (ICH) على الأشعة الطبقيّة (CT) للدماغ، الوسائل العلاجية، والمحصّلة النهائية، ومقارنة هذه المعطيات مع الأبحاث المنشورة في الشرق الأوسط والدول الغربية.

الطريقة: أُجريت دراسة إستعدادية شملت 100 مريض من أصل 1498 مريض مصاب بالنزيف الدماغي التلقائي ICH، والذين تم إدخالهم إلى مستشفى الجامعة الأردنية - عمان - الأردن، خلال خمس سنوات، من يناير 2002م وحتى ديسمبر 2007م.

النتائج: كان انتشار النزيف الدماغي 6.7%. معدل العمر كان 61 سنة (71 ذكر - 29 أنثى). كان السبب الأكثر شيوعاً هو ارتفاع ضغط الدم الشرياني لوحده أو مصحوباً باستخدام الأسبيرين مع أو بدون ورفورين. كانت الأعراض السريرية الأكثر شيوعاً هي الشلل النصفي الكلي / الجزئي، اضطراب في الوعي: GCS=7.3، صداع وتقيؤ. النزيف الأكثر شيوعاً على الأشعة الطبقيّة CT للدماغ كان في مناطق الدماغ العميقة الذي حدث في 61 مريضاً. تسعة وسبعون مريضاً تلقوا العلاج الطبي، و21 مريضاً خضعوا لعمليات جراحية. توفي 42 مريض بعد حوالي 7 أيام (فترة زمنية تتراوح بين يوم واحد وستة أسابيع). كانت العوامل المؤدية للوفاة هي كبر السن (أكثر من 68 عاماً)، مقياس GCS أقل من 8، انتشار النزيف إلى طبينات الدماغ ووجود أمراض أخرى. من بين 58 مريضاً على قيد الحياة، استمر 50 منهم مصابون بإعاقة عصبية وبشكل خاص الشلل النصفي الكلي أو الجزئي في 46 مريضاً، 12 مريضاً يعانون من الصرع المزمن.

خاتمة: تظهر هذه الدراسة وجود انتشار أقل للنزيف الدماغي ICH بالمقارنة مع الدول المتقدمة، نفس توزيع الحالات حسب العمر والجنس، وعامل الخطورة الرئيسي هو ارتفاع ضغط الدم الشرياني الذي يجب أن يكون مركز اهتمام للصحة العامة في الأردن والعالم العربي.

Objectives: To study intracerebral hemorrhage (ICH) at Jordan University Hospital (JUH) with the aim of assessing prevalence, age/gender distribution, causes, clinical manifestations, and location of ICH on CT brain, treatment modalities and outcome, and to

compare these findings with those from Middle Eastern and Western literature.

Methods: Among 1498 patients with stroke seen over a 6-year-period, from January 2002 to December 2007 at JUH, Amman, Jordan, 100 patients with spontaneous ICH were studied retrospectively.

Results: The prevalence of ICH was 6.7%. The mean age was 61 years, with 71 males, and 29 females. The most common cause was hypertension, alone or combined with the use of aspirin and/or warfarin. The most common clinical manifestations were hemiparesis/plegia, impaired level of consciousness (mean Glasgow coma scale [GCS] score = 7.3) and headache/vomiting. The most common location on CT brain was in the basal ganglia (61 patients). Seventy-nine patients received medical treatment and 21 had surgery. Forty-two patients died after a mean of 7 days (ranging from one day to 6 weeks). The factors related to mortality were old age >68 years, GCS <8, intraventricular extension of ICH on CT brain and the presence of other comorbidities. Among 58 survivors, 50 were left with neurological deficit, predominantly hemiparesis/plegia in 46 patients. Twelve patients were left with chronic epilepsy.

Conclusion: This study shows a lower prevalence of ICH compared to developed countries, a similar age and gender distribution, and hypertension as the major risk factor, which should be the focus of public health in Jordan and the Arab World.

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Intracerebral hemorrhage (ICH) is a frequent and serious disease. It constitutes 10-15% of all strokes and has a higher risk of morbidity and mortality than cerebral infarction or subarachnoid hemorrhage in the Western World.^{1,2} The mortality of ICH is higher than that of ischemic stroke (34% at 3 months). Only 31%

are functionally independent at 3 months, and only 38% of the patients survive the first year.³ The ICH results from the rupture of small vessels into the brain parenchyma and accounts for 10% of all strokes in the United States (USA).⁴ It has an estimated frequency of 37,000-52,000 each year in the USA.^{5,6} Hemorrhagic stroke is uncommon in young patients.⁷ Spontaneous ICH is associated with the highest mortality of all cerebrovascular events, and most survivors never regain functional independence.⁸ The cost per year of ICH is high: 5,000 EUR for inpatient stay, 10,000 EUR for rehabilitation, 4,500 EUR for mean direct cost after discharge for the first year, and 5,500 EUR for the loss of work force of surviving patients.⁹ Controversy still exists on the management of spontaneous ICH.¹⁰ The increased incidence of ICH has not been matched with any considerable improvement in treatment.¹¹ Despite advances in the treatment of cerebral infarction and subarachnoid hemorrhage, there remains no treatment of proven benefit in improving outcome after ICH.⁵ Due to the importance of this condition and the paucity of studies from the Middle East,¹²⁻¹⁵ this retrospective study of 100 patients with ICH observed at Jordan University Hospital (JUH), Amman, Jordan, a tertiary care referral center, over a 6-year-period was carried out with the aim of assessing prevalence, age and gender distribution, causes, clinical presentation, and location of ICH on CT brain, treatment, and factors influencing outcome. Results will be compared with data from the Western and Middle Eastern literature.

Methods. The case notes of 100 consecutive patients with spontaneous ICH, (age range 17-95 years, mean=61 years; 71 males and 29 females) seen at JUH, Amman, Jordan over a 6-year-period were studied retrospectively. These were cases of spontaneous ICH who presented to the Emergency Room (ER) of JUH between January 2002 and December 2007. We excluded patients with cerebral trauma as the possible precipitating cause of ICH. The JUH is a 530-bed tertiary care referral center serving a considerable proportion of the Jordanian population. Consent and approval of the ethics committee at JUH were obtained. The ER resident examined all patients, and a neurologist confirmed their findings, and they were assessed for vital signs, especially the value of systolic BP, level of consciousness using the Glasgow Coma Scale (GCS) and the presence of convulsions and/or neurological deficit. Vascular risk factors particularly a history of hypertension (HTN), diabetes mellitus (DM) or previous stroke, as well as the prior intake of aspirin and/or warfarin was looked for. The ICH was confirmed by an urgent CT brain scan, which was read by a board-certified neuroradiologist. Most patients were admitted to the medical intensive care unit (MICU)/Neuro ICU under the care of intensivists/neurologists or neurosurgeons, while some

were admitted to the medical ward. The GCS score at the time of transfer from the ER (to ICU, operating room or hospital ward) was used as the point at which initial acute intervention would be considered. The majority (84 out of 100 patients) had very high BP in the acute phase: the mean systolic BP=184.9 mm Hg and diastolic BP=95.8 mm Hg. In case of very high BP values >180/100, BP was urgently lowered aiming at a systolic BP of 160 mm Hg. An urgent follow-up CT brain was performed in case of deterioration of GCS score to rule out an increase in the volume of the hematoma and mass effect eventually necessitating urgent surgical evacuation. Follow-up CT brain, or MRI/MRA brain, or both were performed in a few weeks in cases of suspected brain tumor/arteriovenous malformation (AVM), or to confirm the presence of complete resolution of ICH before contemplating a reinstatement of antiplatelets or anticoagulants (in cases of atrial fibrillation) to prevent future ischemic strokes. Four-vessel cerebral angiography was carried out in cases of AVM prior to embolization or surgery. Treatment was medical: namely, resuscitative measures, urgent BP lowering using diuretics, intravenous labetalol or Enalapril, antiedema agents (mannitol, dexamethasone), and anticonvulsants or surgical evacuation with or without external ventricular drainage. A few patients had embolization of AVM. None of the patients received recombinant activated factor VII. Regarding outcome, the rate and timing of mortality, as well as the factors influencing it (GCS score, age, gender, presence of intraventricular hemorrhage on CT brain) were assessed. At the last follow-up visit to the outpatient department, neurological sequelae such as motor deficit, cognitive dysfunction, and epilepsy were looked for.

Results. Among 1498 patients with stroke admitted to JUH over a 6-year-period, 100 consecutive patients with ICH were observed, thus representing 6.7% of all strokes. The age and gender distribution are shown in Table 1. There was a male to female ratio of 2.44. The mean age was 61 years (range 17-95 years), with 86%

Table 1 - Age and gender distribution.

Age (years)	Gender		Total
	Male	Female	
10-19	-	3	3
20-29	2	-	2
30-39	2	1	3
40-49	5	1	6
50-59	9	8	17
60-69	25	8	33
70-79	20	8	28
80-89	6	-	6
90-99	2	-	2
Total	71	29	100

above the age of 50 years, and 50% in the age range 50-69 years. Table 2 shows the causes and location of ICH on CT brain. Hypertension, known in 68 patients and newly found in 16, occurred in 84 patients either alone or combined with the use of aspirin and/or warfarin (mean INR=3.7, range 3-7.8). Thirty-four patients had DM, 15 smokers, 11 ischemic heart disease, 5 atrial fibrillation, and 3 end stage renal disease. Known hypertensives had poorly controlled hypertension either due to non-compliance with treatment or to inappropriate antihypertensives. The most common location on CT brain was in the basal ganglia (BG) (61 patients), 32 with and 39 without intraventricular extension (IVE), the majority (54 out of 61) were

related to hypertension. This was followed by cerebral hemispheres in 24 patients (20 due to hypertension), 11 in the posterior fossa (7 cerebellar and 4 brainstem), 2 in the thalamus related to AVM, one intraventricular hemorrhage, and one with hemorrhage at multiple intracranial sites due to leukemia. Table 3 demonstrates the clinical presentation in the ER. The prevailing clinical manifestations were hemiparesis/plegia, impaired level of consciousness (mean GCS score = 7.3; range 4-13), and headache/vomiting. Focal or generalized seizures occurred in 14 patients, among them 8 with lobar ICH, 5 BG ICH, and one intraventricular ICH. Regarding treatment, 79 patients received medical treatment (supportive measures, antiedema agents, antihypertensives, and anticonvulsants) and 21 had surgery, amongst them 10 external ventricular drainage (EVD), 4 evacuation of hematoma, 3 hematoma evacuation + EVD, 3 embolization of AVM (once with ventricular peritoneal [VP] shunt) and one VP shunt alone. Thus, surgical evacuation of the hematoma was carried out in 7 patients after a mean of 5 days (range 1-10 days), among them 5 with hemispheric ICH undergoing surgery due to deterioration of GCS score and mass effect on CT brain (3 alive and 2 dead), one with cerebellar ICH complicated by hydrocephalus, and one with BG ICH and significant mass effect on CT brain. Concerning outcome, 42 patients (30 males and 12 females) died after a mean of 7 days (range 1 day to 6 weeks), their death being either directly related to the ICH or to other comorbidities (DM in 11 patients, previous ischemic stroke in 7, ischemic heart disease with or without heart failure in 10, chronic obstructive pulmonary disease in one, end stage renal disease with acute renal failure in one, liver cirrhosis in one, and acute myeloid leukemia with severe thrombocytopenia in one). Several factors were related to mortality, among them old age >68 years in 28 out of 42 patients, impairment of level of consciousness especially deep coma (GCS <8) where mortality occurred in 34 out of 48 patients. There was also a clear relationship between IVE of ICH on CT brain and mortality: among 41 patients with IVE, 29 died (ICH located in BG in 19 patients, cerebral hemisphere in 7, and posterior fossa in 3) and 12 remained alive (ICH in BG in 10, cerebral hemisphere in one, and posterior fossa in one). However, one patient with only intraventricular hemorrhage stayed alive. There was no clear influence of prior intake of aspirin and/or warfarin on mortality: among 33 patients on aspirin (30 with hypertension), 15 died, and 18 survived; among 4 hypertensive patients on warfarin, 3 died and one survived, and among 3 hypertensive patients on both warfarin and aspirin, one died and 2 survived. Thus, only 19 patients on aspirin/warfarin died. Regarding morbidity, among the 58 patients

Table 2 - Relationship between the cause and location of ICH on CT brain.

Cause (number of patients)	Location of ICH	Number of patients
Hypertension alone (47)	Basal ganglia	30
	Cerebral hemisphere	13
	Brainstem	3
	Intraventricular	1
Hypertension + aspirin (30)	Basal ganglia	20
	Cerebral hemisphere	4
	Cerebellum	6
Hypertension + warfarin (4)	Basal ganglia	3
	Cerebral hemisphere	1
Hypertension + both aspirin and warfarin (3)	Basal ganglia	1
	Cerebral hemisphere	2
Aspirin alone (3)	Basal ganglia	3
	Thalamus	2
Arteriovenous malformation (5)	Cerebellum	1
	Brainstem	1
	Cerebral hemisphere	1
	Cerebral hemisphere	2
Amyloid angiopathy (2)	Multiple hemorrhages	1
Leukemia (1)	Basal ganglia	1
Alcoholism (1)	Basal ganglia	3
Idiopathic (4)	Basal ganglia	3
	Cerebral hemisphere	1
Total		100

ICH - intracerebral hemorrhage

Table 3 - Clinical manifestations.*

Symptom/sign	Number of occasions
Headache/vomiting	45
Hemiparesis/plegia	80
Impaired level of consciousness†	48
Dysarthria	21
Dizziness/unsteadiness	14
Aphasia	15
Seizures	
Focal	12
Generalized	2
Lateral homonymous hemianopsia	2
Hemiparesthesia/numbness	6

*All patients had more than one clinical manifestation, †confusion, drowsiness, coma: among them 34 died (mean Glasgow coma scale score = 7.3; range 4-13)

who survived, 50 were left with neurological deficit at the last follow-up after a mean of 19.8 months (range one month to 6 years), predominantly hemiparesis/plegia with or without aphasia in 46 patients, 2 with cerebellar ataxia, one with hemi-body dysesthesia, and one with lateral homonymous hemianopsia. Twelve patients were left with chronic epilepsy and are still on anticonvulsants.

Discussion. Several points emerge from this retrospective study of 100 patients with ICH seen at JUH over a 5-year-period. The prevalence of ICH in our study was 6.7% (100 out of 1498 patients with stroke), which is much less than that noted by others (10-15%).^{3,16} This is due to the fact that our study is a hospital-based series and does not reflect the real prevalence of ICH in the Jordanian population. Surprisingly, the rate of ICH was much higher in the study by Jamil¹⁷ from Saudi Arabia, where 106 patients were diagnosed with ICH during the month of July 2005 among 165 patients admitted to the ER of Arar Central Hospital in Saudi Arabia. There was a predominance of elderly men in our series, with 71 males and 29 females (M/F ratio = 2.44), 86% of patients were above the age of 50 years. This is in full accordance with Ariesen¹⁸ who noted that ICH is more common in men (risk x 3.7) and in the elderly (risk x 1.97 for each 10 years increase) as well as with others.^{16,17,19} Hypertension was the major risk factor for ICH in our patients (84 out of 100 patients). This is in accordance with other studies^{20,21} who concluded that hypertension is by far the most important and prevalent risk factor for ICH, directly accounting for approximately 60-70% of cases. Sixty-eight of our hypertensive patients had poorly controlled hypertension, and 16 were newly found to be hypertensive. Thrift²¹ mentioned that up to half of hypertensive patients who suffer an ICH are either unaware of their hypertension, non-compliant with the medication, or fail to check periodically their BP values. According to Woo,²² among hypertensive subjects, one quarter of ICH would be prevented if all hypertensive subjects received treatment.

The most common location of ICH on CT brain in our hypertensive patients was in the BG (61%). This is in full agreement with other reports.²³⁻²⁵ We found lobar hematomas in only 24 out of 100 patients (24%). This approaches the findings by Arboix²⁶ whose lobar hematomas accounted for 35.9% of cases. Twenty out of 24 of our patients with lobar ICH had HTN, which concurs with others^{23,24} who concluded that lobar hematomas in the elderly are most commonly related to cerebral amyloid angiopathy, but might also be associated with hypertension. The prevailing clinical

manifestations in our patients were hemiparesis/plegia, impaired level of consciousness and headache/vomiting. This is in full accordance with others.²⁷ Focal or generalized seizures occurred in 8 out of 14 patients with lobar ICH. This is in agreement with De Reuck's²⁸ study of 65 patients with ICH among whom only 14 had seizures and who noted that lobar hematomas occurred in 78.6% of the seizure group compared to 21.4% of the control group.²⁸

In our study surgical evacuation of ICH was carried out in 7 patients, among them 5 with lobar hematomas within a mean of 5 days, due to deterioration of GCS scores and mass effect on CT brain. This is in accordance with other studies, where a favorable outcome was found for superficial hematomas.^{29,30} Five out of the 7 patients stayed alive indicating a good surgical outcome. Despite the small number of our surgical candidates, their good outcome disagrees with the results of Mendelow,²⁹ (STICH trial), a landmark trial of 1023 ICH patients that showed that emergent surgical hematoma evacuation within 72 hours of onset does not improve outcome in comparison with a policy of initial medical management (favorable outcome in 26% of patients in the surgical group and 24% in the medical group). This might be explained by the fact that we have chosen the best surgical candidates. However, a meta analysis of all prior trials of surgical intervention for supratentorial ICH showed no benefit.³¹

The majority (84 out of 100 patients) had very high BP in the acute phase: the mean systolic BP = 184.9 mm Hg and diastolic BP = 95.8 mm Hg. All patients with BP >180/100 had intravenous antihypertensives aiming at a systolic BP of 160 mm Hg. This approach agrees with Ohwaki et al³² and with another recent study,³³ which showed that acute lowering of BP to a target systolic BP of 140 mm Hg is safe without any risk of peri hematoma ischemia. However, previous guidelines,⁵ based on expert opinion, recommended an upper threshold of BP values = 180/105 or mean BP = 130 mm Hg for initiating treatment aiming at a target systolic BP of 180 mm Hg.

Concerning outcome, 42% of our patients died after a mean of 7 days (range = one day to 6 weeks). This is totally in agreement with all other series from the Western Literature,^{2,34-37} where the 1-3 month mortality rates ranged between 33-42% despite modern ICUs and advances in our understanding of the clinical course of ICH. Surprisingly, other Middle Eastern studies,^{14,17} found a low 30-day mortality rate (17-19%) compared to our study and to those from the industrialized world, which is unexplainable. Regarding factors related to mortality, 28 out of 42 of our patients who died were above the age of 68 years indicating that

old age was a significant factor. This is in accordance with others.³⁸ However, despite that the mean age of the 96 patients observed by Jamil¹⁷ from Saudi Arabia (67.2 years), being higher than the mean age of our patients (61 years), their overall 30-day mortality was 17.7%, which is much lower than ours (42%). Also, other studies^{39,40} concluded that age had no influence on outcome of ICH. Deep coma (GCS <8) was associated with mortality in 34 out of 48 of our patients, which totally agrees with others.^{17,38} Our study showed a clear relationship between IVE of ICH on CT brain and mortality: among 41 patients with IVE, 29 died. This is in agreement with others,^{17,38,41-43} but disagrees with Huttner.⁴⁴

In our study, the intake of aspirin, and/or warfarin was associated with mortality in only 19 out of 40 patients (47%) who were taking them prior to the onset of ICH, which is not statistically significant. This is in clear contradistinction with others.^{35,45-48}

Fifty out of our 58 patients with ICH who survived were left with neurological deficit after a mean of 19.8 months, mainly hemiplegia/paresis indicating a high morbidity rate. This agrees with others.^{33,36} Twelve of our patients were left with chronic epilepsy, which is in accordance with others who noted that the risk of remote seizures appears to be high.^{28,37,49-51}

In conclusion, this study shows a lower prevalence of ICH compared with developed countries with, however, a similar age and gender distribution, and the predominance of hypertension as the major risk factor for ICH. Although, this study has the limitations associated with being a small, retrospective, hospital-based study, our results suggest that the occurrence of ICH would be greatly reduced by appropriate measures of detection and management of hypertension, especially changes in diet and lifestyle, and this should be the focus of public health in Jordan and the Arab world. Future community-based stroke registry and clinical trials in the region would further elucidate the health needs of the population.

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