Seasonal Variation in Spontaneous Intracerebral Hemorrhage in Iraq

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ABSTRACT:
BACKGROUND:
Spontaneous intracerebral hemorrhage is the deadliest and most disabling type of stroke. Spontaneous ICH is defined as intraparenchymal bleeding in the absence of trauma or surgery. Seasonal effect on incidence of intracerebral hemorrhage had Longley been studied with unrewarding, and conflicting results.
OBJECTIVE:
To determine whether different seasons of the year had a relationship with the rate of primary intracerebral hemorrhage,and some of the factors that may contribute for this relationship
PATIENTS AND METHODS:
A total of 315 patients diagnosed as a case of primary intracerebral hemorrhage attending AL-Imamain Medical City were taken between December 2009 and December 2011. Females were 112(35.6%) and males were 203(64.4%) aged between 18 and 93 years old with mean age group of 59.298±13.7616. The diagnosis was based on history, clinical examination and non-contrast Computed Tomography scan of brain.
RESULTS:
Of the 315 patients, the highest rate of cases during December being 13.7% and the lowest during February and October being 4.1% and 4.8% respectively.
Intracerebral hemorrhage rate among age group less than 55 years old being 42(34.71%) of 121 patients during summer. There was a significant relationship between winter season and intracerebral hemorrhage incidence among diabetic patients being 29(34.52%) of total 84 diabetic patients. 74(93.67%) of 79 patients presented during winter season had a large sized hemorrhage.
CONCLUSION:
The highest rate of intracerebral hemorrhage during December There was a seasonal variation in patient's age, incidence among diabetic patients and size of hemorrhage.
KEY WARDS: seasonal, variation, hemorrhage, Iraq.

INTRODUCTION:

Intracerebral hemorrhage (ICH) is the most devastating and disabling type of stroke. Intracerebral hemorrhage (ICH) affects >1 million people annually worldwide and is the deadliest and most disabling type of stroke. Spontaneous ICH is defined as intraparenchymal bleeding in the absence of trauma or surgery[1].

ICH is more common in men than in women[2] and the incidence increases significantly after the age of 55 years and doubles with each decade to the age of 80[3].The correlation between various types of strokes and seasonal variations have been studied in various places[4]. It is well documented that season exerts an influence in the incidence of coronary heart disease, hypertension, cerebrovascular accident and even nonvascular disorders such as pancreatitis[5-7].

Primary and secondary intracerebral hemorrhage have similar underlying pathological changes[8].Primary intracerebral hemorrhage originates from bleeding of small arteries damaged by chronic hypertension, Cerebral Amyloid Angiopathy (CAA), or other causative factors.Only 12–18% of all ICH cases are classifiable as the secondary type of ICH [9].

Hypertension is the most important risk factor for the development of intracerebral hemorrhage[10].

Some population-based studies have found a higher incidence of ICH during winter[11]whereas other studies have not found any seasonal variation[12].A recent Finnish study showed that anti-hypertensive medication reduces the peak blood pressure values in subjects exposed to cold[13].

The incidence of diabetes was found to be significantly higher in patients with ICH compared to controls [14].

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Computed Tomography (CT) was considered the imaging modality of choice for the detection of acute intracranial hemorrhage[15]. Although CT scanning is the first-line diagnostic approach, MRI with gradient echo can detect hyperacute intracerebral hemorrhage with equal sensitivity and overall accuracy[16].

The aim of study is to determine whether different seasons of the year had a relationship with the rate of primary intracerebral hemorrhage in patients admitted to the Neurological ward of Al-Imamain Medical City.

PATIENTS AND METHODS:

In this hospital based cross sectional study, 315 patients who were admitted to Neurology Department of AL-Imamain Medical City between December 2009 and December 2011 having primary ICH were ascertained.

Males were 203(64.4%) of total patients while females were 112(35.6%) with mean age group of 59.298±13.7616and ranging from 18-93 years old.

Patients were evaluated in two age groups <55 years and >55 years in relation to seasonal presentation of ICH.

Each case was diagnosed on history, clinical examination, and non-contrast CT scan brain (100% of cases) which was available in emergency department of the hospital and baseline hematoma measured and divided according to the Grading Scales[17].

In this study, we focused on primary cases of ICH.Secondary types of ICH were excluded from study such as arteriovenous malformations(AVM), trauma, tumors, drug induced, and others.

In this study, we took the commonest and accessible modifiable risk factors,including hypertension(was defined as "history of hypertension" instead of actual blood pressure readings because hemorrhagic stroke is likely to elevate blood pressure among cases, or any treatment for high BP, DM (fasting plasma glucose ≥126 mg/dL or single value ≥200 mg/dL, previous diagnosis and treatment and HBA1C).

Children was also not included in this study because of possible other causes beyond the aim of this study.

Data were collected from patients using direct interview using a validated questionnaire especially designed for this purpose.

Each year was divided into four seasons. Winter included (December, January, and February); spring included (March, April, and May); summer included (June, July, and August); and autumn included (September, October, and November).

Statistical analysis was done using statistical package for social sciences (SPSS version 16). Data were analyzed using descriptive statistics and analytical chi squared test with significant relationship defined as having p value < 0.05.

RESULTS:

Age distribution:-A total number of 315 patients attending Neurology Department of AL-Imamain Medical City were included in this study with mean age group of 59.298±13.7616 and ranging from 18-93 years.

The highest frequency of intracerebral hemorrhage patients was found to fall in patients >55 years age group being 194(61.6%) patient and only 121(38.4%) patients were ≤55 years age as shown in table 1.

Gender distribution:-The gender distribution of the sample study shows a male predominance of distribution being 203 males (64.4%) and 112 females (35.6%) of patients as shown in table 1.

Hypertension (HT):-In the sample studied, 213(67.6%) patients were hypertensive and only 102(32.4%) patients were not as shown in table 1.

Diabetes mellitus (DM):-In the sample studied, 231(73.3%) of the patients were not diabetics while only 84(26.7%) of the patients were diabetics as shown in table 1.

Size of hemorrhage:-in the sample studied, 274(87.0%) patients presented with evidence of large hematoma size being larger than 30 ml, while only 41(13.0%) patients show only a small size hemorrhage being less than 30 ml as shown in table 1.

Seasonal distribution of cases:-seasonal distribution of cases during both years of study period was shown in the figure 1 which showed a highest frequency during spring season being 85(27%) and another second peak during summer being 84(26.7%) and lowest frequency during autumn season 67 (21.3%) of total 315 patients .

Monthly distribution of cases in both years of study period:- monthly trend of cases in both years of study period with the highest percent of cases during December being 13.7% and the lowest during February and October being 4.1% and 4.8% respectively as shown in Figure 2.

Table 1: The characteristics of patients in study sample.

Age Groups	Frequency	Percent %
≥55(years)	121	38.4
<55(years)	194	61.6
Gender	Frequency	Percent %
Female	112	35.6
Male	203	64.4
HT	Frequency	Percent %
NO	102	32.4
YES	213	67.6
DM	Frequency	Percent%
NO	231	73.3
YES	84	26.7
Size of hemorrhage	Frequency	Percent %
≥30 ml	274	87.0
<30 ml	41	13.0
Total	315	100.0

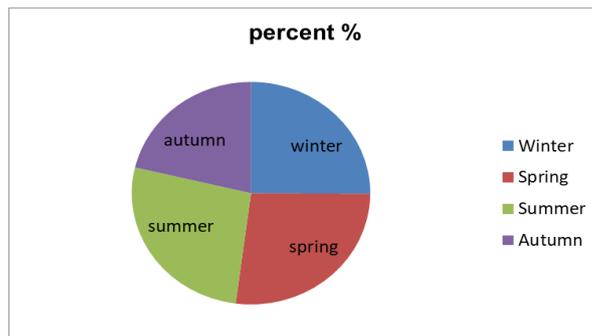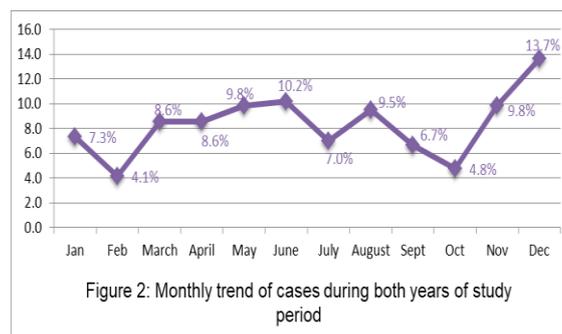**Figure 1: seasonal distribution of cases during both years of study period.**

Figure 2: Monthly trend of cases during both years of study period

Factors related to the seasonal distribution:-

Age:-there was a significant relationship(p=0.04) between patients age and season as ICH rate among age group less than 55 years old being 42(34.71%) of 121 patients during Summer while the lowest frequency was observed during autumn among patients younger than 55 years old being 20(16.52%) of 121 patients as shown in table 2 below.

Table 2: Relationship between seasons of the year and age groups of ICH patients.

Age Groups		Winter		Spring		Summer		Autumn		Total
		No.	%	No.	%	No.	%	No.	%	
≤55		26	21.48	33	27.27	42	34.71	20	16.52	121
>55		53	27.31	52	26.80	42	21.64	47	24.22	194
Total		79	25.07	85	26.98	84	26.66	67	21.26	315

X^2= 7.86 df= 3 P= 0.04

Gender:-There was no significant relationship between different seasons and gender of the patients(p=0.82) nevertheless the highest frequency of cases during spring season was among females being 33(29.46%) of 112 female patients while the lowest frequency was observed among females and during autumn being 22(19.64%) of 112 patients as shown in table 3 below.

Table 3 : Relationship between seasons and gender of ICH patients .

Gender	Winter		Spring		Summer		Autumn		Total
	No.	%	No.	%	No.	%	No.	%	
Female	26	23.21	33	29.46	31	27.67	22	19.64	112
Male	53	26.10	52	25.61	53	26.10	45	22.16	203
Total	79	25.07	85	26.98	84	26.66	67	21.26	315

X^2= 0.92 df= 3 P= 0.82

Hypertension and seasons:-There was no significant relationship between different seasons of the year and rate of ICH among hypertensive patients in study sample (p=0.63) with the highest frequency of cases was during spring season being 32(31.37%) of 102 non-hypertensive patients while the lowest frequency was observed also during autumn and among non-hypertensive patients being 19(18.62%) of 102 patients as shown in table 4 below.

Table 4: Relationship between seasons and hypertension among ICH patients.

HT		Winter		Spring		Summer		Autumn		Total
		No.	%	No.	%	No.	%	No.	%	
	NO	24	23.52	32	31.37	27	26.47	19	18.62	102
	YES	55	25.82	53	24.88	57	26.76	48	22.53	213
Total		79	25.07	85	26.98	84	26.66	67	21.26	315

X^2= 1.72 df= 3 P= 0.63

DM and seasons:-There was a significant relationship(p=0.001) between winter season and ICH incidence among diabetic patients being 29(34.52%) of total 84 diabetic patients while the lowest frequency was observed during summer season among diabetics being 14(16.66%) of 84 patients as shown in table 5.

Table 5 : Relationship between different seasons and DM in ICH patients.

DM		Winter		Spring		Summer		Autumn		Total
		No.	%	No.	%	No.	%	No.	%	
	NO	50	21.64	70	30.30	70	30.30	41	17.74	231
	YES	29	34.52	15	17.85	14	16.66	26	30.95	84
Total		79	25.07	85	26.98	84	26.66	67	21.26	315

X^2= 16.95 df= 3 P= 0.001

Size of hemorrhage and seasons:-There was a significant relationship between small sized hemorrhage and spring season(p=0.037) as the highest rate being 18(43.9%) of the 41 patients presented with a small sized hemorrhage(<30 ml), in this study while the lowest rate of patients was during winter season among patients with hemorrhage size <30 ml being 5(12.2%) of 41 patients with hemorrhage size < 30 ml the smallest portion of patients presented with small sized hemorrhage was during winter season being 5(6.32%) of 79 patients presented during winter season, while the remaining 74(93.67%) of 79 patients presented during winter season had a large sized hemorrhage as shown in table 8.

Table 6: relationship between hemorrhage size and seasons of the year.

Size		Winter		Spring		Summer		Autumn		Total
		No.	%	No.	%	No.	%	No.	%	
	>30 ml	74	27%	67	24.5%	73	26.6%	60	21.9%	274
	<30 ml	5	12.2%	18	43.9%	11	26.8%	7	17.1%	41
Total		79		85		84		67		315

X^2= 8.51 df= 3 P= 0.037

DISCUSSION:

Although some other studies showed a seasonal variation in incidence of ICH cases, data from these studies are inconsistent and conflicting. Moreover, among studies indicating seasonal occurrence of stroke, the identified season of highest occurrence has varied including winter, autumn and spring. The inconsistency of these results may be a reflection of one or more problems in the study designs. These problems include use of an inappropriate analytic model, insufficient length of time, small sample size, and focus on a single region.Finally, in some of the studies, the examination of seasonality was without respect to specific stroke type: hemorrhagic versus ischemic. Because hemorrhagic and ischemic strokes have different patho-physiological mechanisms, the relation of each stroke type to seasonality may also differ. Thus, analyses that combine all stroke types may misrepresent the effect of seasonality on specific types of stroke [18].

In this study, the highest frequency of ICH patients were at the age group> 55 years old age being 194(61.6%) patients and the remaining 121(38.4%) were ≤55 years age and these results agreed with the results found by other studies as the ICH rate was increased significantly with aging, and old age being one of the most important risk factors[19,20].

The increased rate of ICH cases among age group younger than 55 years old age during summer season agreed with the results achieved by Anlar Omer et al in Turkey[21], and Masood et al in Pakistan[22]. These data could be explained by same environmental factors experienced by patients living in the same area (Middle East) and the same diet habits rich in fish oils.

The gender distribution of cases investigated showed a predominance of ICH in male patients being 64.4% for males and 35.6% for females. These data were concordant with other studies stating the same higher frequency in men, especially those older than 55 years age[19]. Studies to date have not determined whether these can be explained entirely by equal exposure to the risk factors or whether there are additional factors, possibly genetic, which remain undiscovered [23].

There was no significant relationship(p=0.82) between different seasons of the year and rates of ICH cases among both gender groups of patients and these results agreed with the results found by other studies (Capon et al[24], Karagiannis A et al[25], Neil Anderson et al[26], and Khan FA et al[27]) although that the highest frequency of patients was during spring season and among female patients being 33(29.46%) of 112 female patients.

In this study, about 213(67.6%) of total 315 patients were hypertensive and it is the same results achieved by Togha M et al [28] in Iran. There was no significant relationship(p=0.63) between different seasons of the year and ICH cases among hypertensive patients as the highest frequency of patients was during spring season among non-hypertensive patients being 32(31.37%) of 102 non-hypertensive patients.

There was a significant relationship(p=0.001) between winter season with incidence of ICH cases among diabetic patients being 29(34.52%) of 84 diabetic patients with no identifiable cause found to explain this condition.

By Conclusion this hospital based cross sectional study discovered that summer season increased the rate of ICH cases among younger age groups (<55 years old). This study discover that cold seasons (Winter and Autumn) had a significant effect on increasing incidence ICH cases among

diabetic patients and the majority of cases admitted during winter season had a large sized hemorrhage (>30 ml).

REFERENCES:

1. Dastur CK, Yu W. Current management of spontaneous intracerebral haemorrhage. Stroke and Vascular Neurology. 2017;2:1.
2. Giroud M,Milan C,Beuriat P,et al. Incidence and survival rates during a two year period ofintracerebral and subarachnoid haemorrhages,cortical infarcts,lacunes and transient ischaemic attacks.The Stroke Registry of Dijon:1985-1989.Int J Epidemiol1991;20:892.
3. Losseff N, Adams M, Brown MM, Grieve J and Simister R. Stroke and Cerebrovascular Diseases. In: Clarke C, Howard R, Rossor M and Shorvon S. editors. Neurology: A Queen Square Textbook. 2nd ed. Wiley-Blackwell. 2016:147.
4. Wang Y, Levi CR, Attia JR, et al. Seasonal variation in stroke in the Hunter Region. Australia A 5-year hospital-based study, 1995-2000. Stroke 2003;34:1144.
5. Gallerani M, Boari B, Salmi R, et al. Seasonal variation in the onset of acute pancreatitis. World J Gastroenterology. 2004;10:3328.
6. Houck PD, Lethen JE, Riggs MW, Gantt DS, Dehmer GJ. Relation of atmospheric pressure changes and the occurrences of acute myocardial infarction and stroke. Am J Cardiol. 2005;96:45.
7. Hakan T, Kizilkilic O, Adaletli I, et al. Is there any seasonal influence in spontaneous bleeding of intracranial aneurysm and/or AVM in Istanbul? Swiss Med Wkly. 2003;133:267.
8. Steiner T, Rosand J, Diringer M. Intracerebral hemorrhage associated with oral anticoagulanttherapy: current practices and unresolved questions. Stroke. 2006;37:256.
9. Qureshi AI, Tuhrim S, Broderick JP, et al. Spontaneous intracerebral hemorrhage. N Engl J Med 2001;344:1450.
10. Zia E, Hedblad B, Pessah-Rasmussen H, et al. Blood pressure in relation to the incidence of cerebral infarction and intracerebral hemorrhage. Hypertensive hemorrhage: debated nomenclature is still relevant. Stroke 2007;38:2681.
11. Wang H, Sekine M, Chen X, et al. A study of weekly and seasonal variation of stroke onset. Int J Biometeorol 2002;47:13.
12. Khan FA, Engstrom G, Jerntorp I, et al. Seasonal patterns of incidence and case fatality of stroke in Malmo, Sweden: the STROMA study. Neuroepidemiology 2005; 24:26.
13. Komulainen S. Effect of antihypertensive drugs on blood pressure during exposure to cold. Experimental study in normotensive and hypertensive subjects. Acta Universitatis Ouluensis D Medica 949,2007.
14. Zodpey SP, Tiwari RR &Kulkarni HR. Risk factors for haemorrhagic stroke: a case-control study. Public Health 2000;114:177.
15. Lovelock CE, Anslow P, Molyneux AJ, et al. Substantial observer variability in the differentiation between primary intracerebral hemorrhage and hemorrhagic transformation of infarction on CT brain imaging. Stroke 2009; 40:3763.
16. Fiebach JB, Schellinger PD, Gass A, et al. Stroke magnetic resonance imaging is accurate in hyperacuteintracerebral hemorrhage: a multicenter study on the validity of stroke imaging. Stroke 2004; 35:502.
17. Masotti L, Lorenzini G, Pennati Paolo, et al. Clinical Grading Scales for Predicting Early Neurological Worsening in Spontaneous Intracerebral Hemorrhage.. Stroke Research & Therapy. 2016;1:1.
18. Oberg AL., Ferguson JA., McIntyre LM, et al. Incidence of Stroke and Season of the Year: Evidence of an Association. American Journal of Epidemiology,2000;152.
19. Ariesen M. J., Claus S. P., Rinkel G. J. E. et al., Riskfactors for intracerebralhaemorrhage in the general population. A systematic review, Stroke, 2003;34:2060.
20. Velkerj L., Kaufman HH, Intraparenchymal haemorrhage, New Horiz. 1997;5:342.
21. Omer A; Temel T, Ozkan U, et al. Seasonal and environmental temperature variation in the occurrence of ischemic strokes and intracerebral hemorrhages in a Turkish adult population. International journal of neuroscience, 2002;112:959.
22. Masood U, Qadri AA, Maqsood MA. Stroke; seasonal variation in etiology. Professional Med. J. 2006;13:680.
23. Stancu CC, Pleşea IE, Enache SD, et al. Morphoclinical study of intracerebral hemorrhage with subarachnoid effusion. Romanian journal of morphology and embryolog. 2011;52:263.

24. Capon A, Demeurisse G, Zheng L. Seasonal variation of cerebral hemorrhage in 236 consecutive cases in Brussels. Stroke. 1992;23:24.

25. Karagiannis A, Tziomalos K, Mikhailidis DP, et al. Seasonal variation in the occurrence of stroke in Northern Greece: a 10 year study in 8204 patients. Neurol Res. 2010;32:326.

26. Anderson N, Feigin V, Bennett D, et al. Weekly, and seasonal variations in stroke. Journal of the New Zealand Medical Association. 2004;117:1202.

27. Khan FA, Engstrom G, Jerntorp I, et al. Seasonal patterns of incidence and case fatality of stroke in Malmo, Sweden. Neuroepidemiology. 2005;24:26.

28. Togha M, Bakhtavar K. Factors associated with in-hospital mortality following intracerebral hemorrhage: a three-year study in Tehran, Iran, BMC Neurol, 2004;4:9.