

Life Events and Stroke

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ABSTRACT

Background: From the public knowledge to the scientific concepts we found that the relationship between psychological stress and risk of stroke is an old one. **Objective:** This study was designed to examine if there is a relationship between life events and occurrence of stroke (Is stress a risk factor for stroke?). And if yes which type of life events is implicated. **Subjects and methods:** Sixty patients with first ever stroke in their life time were included. Control groups consisted of 50 healthy subjects matched for age and sex with patients group and 60 subjects matched for age, sex and risk factors for stroke with the patients group, but without stroke. All patients were subjected to full history taking and neurological examination, full laboratory investigations, ECG and Echo and CT and/or MRI brain. All patients and control subjects were interviewed using *Life Events and Difficulties Schedule (LEDS)* for assessment of life events and difficulties during the six months preceding the onset of stroke (for the patients) /or the interview (for the controls). **Results:** When considering severe events and marked difficulties, patients reported much more than both control groups with highly significant difference ($P < 0.001$). Events involving humiliation and/or entrapment make the highly significant difference between patients and controls but events involving loss or danger alone showed no significant difference ($P > 0.05$). The distribution of severe life events along the 6 months before stroke (in patients group) and or before the interview (in the control groups) showed that patients have significant higher rate of reporting 1 day, 1 week, and 6 months before stroke onset than their matched controls during the same time. We also found that the lesser the load of risk factors of stroke in the patients group, the higher the rate of occurrence of severe events specially those involving humiliation and/or entrapment. **Conclusion:** These results supposed that severe events especially those involving humiliation and/or entrapment may be considered as an independent risk factor for stroke.

Key words: Stroke, Risk factors, Life events, Egypt.

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INTRODUCTION

On asking about stroke risk factor knowledge in the public, stress is the most frequently mentioned factor¹⁻². From the public knowledge to the scientific concepts we found that the relationship between

psychological stress and risk of stroke is an old one. It is dated to the early fifty's, since 1954 when Ecker stated that preceding a cerebral stroke, the patient has often suffered long standing progressive

difficulty in setting emotional problems. Immediately before stroke he may have faced an overwhelming personal threat³.

Many studies tried to examine such relationship, some studies showed that there is a relation⁴⁻⁸ and other indicating that there is none⁹. Stressful life events have been shown to precede onset of depression¹⁰, onset of psychosomatic disorders such as abdominal pain¹¹, variety of physical disorders including myocardial infarction¹²⁻¹³, breast cancer¹⁴, and relapse of multiple sclerosis¹⁵⁻¹⁶.

It was found that number of situations are the most stressful to individuals as: direct attacks on a person's self esteem, marked devaluation of self and blocked escape¹⁷. It was found that events involving humiliation or entrapment preceded the bulk of onsets of depression, loss only events were uncommon and danger only event rarely led to depression¹⁸.

As the relation between stroke and stress remains an issue of controversy this study was designed to examine if there is a relationship between life events and occurrence of stroke (Is stress a risk factor for stroke?). And if yes which type of life events is implicated.

SUBJECTS AND METHODS

It is a case control design.

Subjects include:

I-Patients group: 60 patients with first ever stroke in their lifetime. All patients were admitted to stroke unit in Ain Shams Specialized Hospital.

II-Control groups:

a: 50 healthy subjects matched for age and sex with patients group.

b: 60 subjects matched for age, sex and risk factors for stroke with the patients group, but without stroke.

Methods: All patients were subjected to

-Full history taking and neurological examination.

-Full laboratory investigations: CBC, lipid profile, fasting and post-prandial blood glucose sugar

- ECG and Echo.

- CT and /or MRI brain.

All patients and control subjects were interviewed using *Life Events and Difficulties Schedule* (LEDS) with its new version (18) for assessment of life events and difficulties during the six months preceding the onset of stroke (for the patients) or the interview (for the controls). The LEDS is a semi structured instrument assessing a wide variety of stressors.

Each event is rated according to many dimensions as long term contextual threat, type of event, focus, independence and others¹⁹.

Some definitions in the LEDS system

1-Severe event: It is the event that rated 1 or 2 on the scale of long term threat and must be subject or joint focused.

2-Marked difficulty: It is the difficulty rated 1-3 of the scale of unpleasantness.

3-New classification of severe events: (18)

-Humiliation/entrapment.

-Loss alone.

-Danger alone.

- **Humiliation:** an event rendering the person devalued in relation to others or self.

- **Entrapment:** the individual is imprisoned in a punishing situation.

Statistical Methods:

SPSS software package (V. 9.02) was used for data analysis. The methods used for statistical analysis were the following:

1. Comparison between 2 independent proportions using Z test.
2. Calculated Relative Risk Ratio (RRR). It measures how many times the risk is present among the target or diseased group relative to that of the non-diseased or control group. It is the ratio of the 2 Odd's values of the diseased and non-diseased groups.

RESULTS

1-Age: Ranged from 45-70 years old, with mean 61 ± 5.6 .

2-Sex: 43 males (71%) and 17 females (29%)

3-Type of stroke: a-ischemic stroke 51 patients (85%), b-hemorrhagic stroke: 9 patients (15%).

Ten percent of the patients had no known risk factors for stroke, 32% had one known risk factor and 58% had more than one risk factor (table 1 and 2).

Table (1): Classification of patients and control according to Risk factors

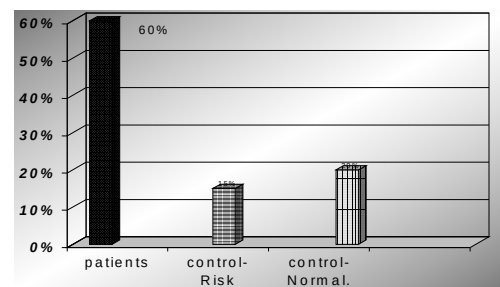
Risk factor	Patients		Control	
1 risk factor	19	32 %	22	20 %
>1 risk factor	35	58 %	38	34.5 %
No risk factor	6	10 %	50	45.5 %

Table (2): Types of risk factors in patients and controls

	Patients		Control	
Hypertension	33	(55%)	32	(53%)
DM	38	(63%)	39	(65%)
IHD	15	(25%)	16	(27%)
Smoking	27	(45%)	26	(43%)
Hypercholesterol	9	(15%)	9	(15%)
Hypertriglycerid	6	(10%)	6	(10%)

Both patients and controls (2 control groups) reported life events and difficulties (even controls reported more than patients), but when considering only severe events and marked difficulties, the patients reported much more than both control groups with highly significant difference (table 3 and 4, and fig.1).

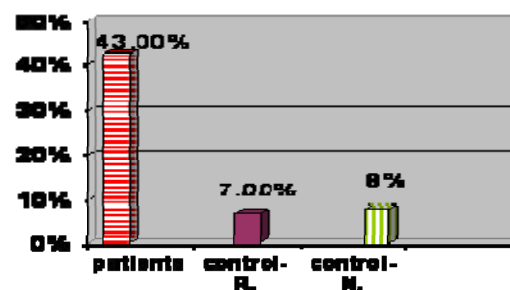
Figure (1) Rate of severe events among patients and controls.



$P < 0.001$, Highly Significant

Comparison between patients group and both control groups regarding the new classification of severe events (table 5 and 6, and fig. 2) showed that events involving humiliation and/or entrapment make the highly significant difference between patients and controls but events involving loss or danger alone showed no significant difference.

Figure (2) Rate of reporting humiliation/ entrapment among patients & controls



The distribution of severe life events along the 6 months before stroke (in patients group) and or before the interview (in the control groups) showed that patients have significant higher rate of reporting 1 day ,1 week, and 6 months before stroke onset than their matched controls during the same timing.(table 7 and fig. 3).

In the same context, hemorrhagic stroke patients reported all their events (100%) just before onset (1 day and 1 week), in comparison to lesser percentage (33.3%) in ischemic patients (table 8). No significant relation was found between and of the known risk factors for stroke and severe life events (table 9).

Fig (3): Distribution of severe life events along the 6 months before stroke onset or interview in patients and controls.

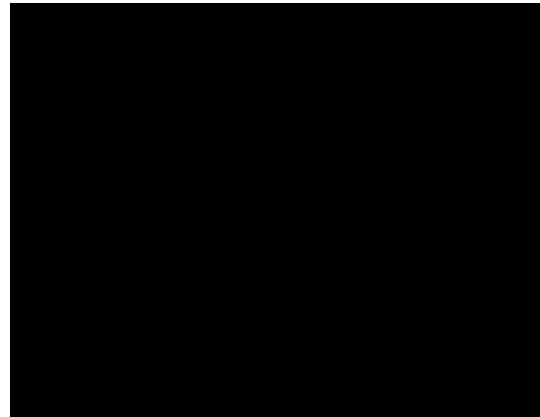


Table (3): Comparison between stroke patients & control group with risk factors regarding presence of life events & difficulties before onset of stroke or date of interview

Parameter	Stroke patients No=60	%	Control with Risk F. No=60	%	P-value	Sign if.
At least 1 event	46	76.6	40	66.6	0.05 >	NS
At least 1 difficulty	37	61.6	31	51.6	> 0.05	NS
Severe events	36	60	9	15	<0.001	HS
Marked difficulty	28	46.6	10	16.6	< 0.001	HS

NS=non significant, HS =highly significant

Table (4): Comparison between stroke patients & normal control group with no risk factors regarding presence of life events & difficulties before onset of stroke or date of interview

Parameter	Stroke patients No.=60	%	Control with no Risk F. No.=50	%	P-value	Sig .
At least 1 event	46	76.6	41	82	0.05 >	NS
At least 1 difficulty	37	61.6	32	64	> 0.05	NS
Severe events	36	60	10	20	<.001	HS
Marked difficulty	28	46.6	11	22	< 0.001	HS

Table (5): Comparison between stroke patients and control group with risk factors regarding types of severe events

Parameter	Stroke Patients No.=60	%	Control group with Risk F. No.=60	%	P-value	Sig.
Humiliation	26	43.3	4	6.6	<0.001	HS
Loss	7	11.6	3	5.0	> 0.05	NS
Danger	3	5.0	2	3.3	> 0.05	NS

Table (6): Comparison between stroke patients and normal-control group regarding types of severe events

Parameter	StrokePatients N=60	%	Control group with no risk F. N=50	%	P	Sig.
Humiliation	26	43.3	4	8.0	<0.001	HS
Loss	7	11.6	5	10.0	> 0.05	NS
Danger	3	5.0	1	2.0	> 0.05	NS

Table (7): Distribution of severe life events along the 6 months before stroke onset or interview in patients and controls .

	Patients	Controls	OR	CI
1 Day	9 (25%)	1 (5.2%)	6	1.1-51.5
1 week	7 (19.4%)	3 (15.7%)	1.2	1.2- 5.6
One month	4 (11.1%)	7 (36.8%)	0.2	0.05-0.8
3 months	6 (16.6%)	4 (21%)	0.7	0.1- 3.0
6 months	10 (27.7%)	4 (21%)	1.4	1.3- 5.4

Table (8): Comparison between hemorrhagic stroke patients and ischemic stroke patients regarding timing of severe events.

	Hge. Patients with severe events	Infarct. Pat. With severe events	P-value	S
1 Day	5 (83.3%)	4 (13.3%)	< 0.001	HS
1 Week	1 (16.7%)	6 (20%)		

HS: highly significant.

Table (9): Comparison between patients with various risk factors for stroke and patients without regarding occurrence of severe events .

Parameter	group	Severe events	P	Sign.
HTN	+ve (33)	22 (67%)	> 0.05	NS
	-ve (27)	14 (52%)		
DM	+ve (38)	24 (63%)	>0.05	NS
	-ve (22)	12 (55%)		
IHD	+ve (15)	11 (73 %)	>0.05	NS
	-ve (45)	25 (56%)		
Smoking	+ve (27)	19 (70 %)	>0.05	NS
	-ve (33)	17 (52%)		
High.chol.	+ve (9)	7 (78%)	>0.05	NS
	-ve (51)	29 (57%)		
High.trigly.	+ve (6)	4 (67 %)	>0.05	NS
	-ve (54)	32 (59%)		

NS: non significant.

Table (10): Comparison between different groups of stroke patients and control groups regarding rate of reporting humiliating severe events.

Parameter	Stroke patients	Stroke patients with humiliating event	Control groups	Control groups with humiliating severe events	P-value	Sig.
One risk factor	19	13 (68%)	22	3 (13.6%)	<0.001	HS
More than 1 risk factor	35	8 (22.8%)	38	1 (2.6%)	<0.001	HS
No risk factors	6	5 (83.3%)	50	4 (8%)	<0.001	HS
Total	60	26	110	8		

HS: highly significant .

On classifying the patients according to numbers of risk factors and comparing them with their corresponding control groups as regards severe events involving humiliation and/or entrapment, the difference was highly significant (table 10).

Also we found that the lesser load of risk factors, the higher the rate of occurrence of severe events specially those involving humiliation and/or entrapment (table 11).

Table (11): Relation between humiliation/entrapment events and load of risk factors among patients.

	Humiliation /entrapment events	P-value	Sig .
Patients with no risk factors (6)	5 (83%)	<0.001	HS
Patients with 1 risk factor (19)	13 (68%)		
Patients with >1 risk factors (35)	8 (23%)		

HS: highly significant.

DISCUSSION

Life events are inevitable and are encountered by almost every individual. When considering life events and difficulties in general, there was no significant difference between patients and controls. But regarding severe events and

marked difficulties there was highly significant difference between the 2 groups.

These results support the public knowledge about cause of stroke. Our results are in agreement with other studies^{5, 7-8}. Other studies failed to find such difference⁹. This may be due to sample differences, (small sample size, 37 patients in Macho study, and only ischemic stroke). Also methodological differences as they used checklist method which carry lot of biases.

When classifying severe events according to the new classification of humiliation /entrapment, stroke patients experienced those events with much higher percent than the 2 groups with highly significant statistical difference ($P < 0.001$).

Severe events involving humiliation or entrapment preceded the bulk of onset of depression as such events are the most stressful events exceeding by far the loss alone or danger events¹⁸. We reached to the same result with our stroke patients, but we did not find study examined this point in stroke patients. The relationship between life events and stroke onset was further examined using other parameter which is timing of severe events.

Both patients and controls reporting severe events all over the period of 6 months (not restricted to the period near to the interview) and this observation ruled out the recall bias which is one of the most

prevalent bias when measuring stressful life events.

The patients have significant higher rate of reporting severe events 1 day and 1 week (immediately before onset) and 6 months (long time before onset).

There are different possible mechanisms by which psychological stress may increase risk of stroke. These mechanisms may be chronic (explained by stress occurred many months before stroke) or may be acute (explained by stress occurred immediately before onset of stroke). Stress produce rapid sympathetic activation and increased catecholamine release which translate into changes in systemic haemodynamic factors. It causes increased heart rate and elevated blood pressure²⁰. Repetition of this response may lead to sustained elevation of the blood pressure²¹.

Psychological stress plays an important role in the development of atherosclerosis²² and has also been associated with progression of atherosclerotic changes of the carotid artery²³. Catecholamine secreted by stress activate platelets directly because platelet membranes contain α_2 adrenergic receptors²⁴. Repeated platelet activation with secretion of platelet-derived growth factor may enhance arterial smooth muscle proliferation in developing atheromas²⁵⁻²⁶. Also stress increases plasma concentrations of several prothrombotic factors together with enhanced platelet function which may be the mechanism by which psychological stress promotes plaque formation²⁷⁻²⁸.

Brief episodes of stress can elicit transient endothelial dysfunction. Severe and frequent stress may lead to prolonged periods of endothelial dysfunction which constitute a further link between stress and atherosclerosis²³. During platelets

activation in response to stress, they secrete platelet proteins as platelet factor 4 (PF4) and B-thromboglobulin (BTG).

The activated platelets that have secreted their proteins have an altered plasma membrane surface that facilitates platelet-platelet and platelet-vessel wall interactions. So platelets activation may enhance accumulation of platelets in the turbulent blood flow at sites of arterial damage and partial obstruction and this could trigger acute ischemia²⁸.

All severe events occurred to hemorrhagic stroke patients were immediately before stroke onset, (one day or week before). All severe events involving humiliation or entrapment occurred immediately in the day before stroke onset. This may be explained by increase in the blood pressure associated with such severe stress and this was in contrast to ischemic stroke patients where only 10 (33%) of the severe events occurred immediately before stroke (may be explained by the mechanism causing acute ischemia), while the majority 20 (67%) occurred months before stroke onset (which may be explained by the chronic mechanism).

The study of the relationship between the presence of severe event before stroke onset and risk factors of stroke revealed no statistically significant relation between any of these risk factors and the presence of severe events. These results come in contrast to the results of House et al. who found that severe events precede stroke onset with statistically significant higher rate in non hypertensive patients than hypertensive patients. This difference in results may be explained by the small sample size in our study. Also Hypertensive and smoker stroke patients recorded significantly higher scores of stressful life

events than non hypertensive and non smoker patients⁵. In addition, stressed subjects had a more unfavorable risk factor profile than subjects reporting stress⁸. These differences may be due to methodological issues since these studies used checklist measures which differ from interview measures.

When comparing patients with no risk factors, one risk factor and more than one risk factor for stroke with their corresponding controls, we found that patients of the three groups reported having severe events involving humiliation or entrapment by much higher percent than their control groups (higher statistically significant difference, $P < 0.001$).

When comparing the 3 groups with each other, we found higher significant association between severe events involving humiliation or entrapment and absence or less risk factor for stroke. From these results we are asking if severe events especially those involving humiliation or entrapment could be considered as a risk factor for stroke independent from other known risk factors.

Before we jump to such conclusion the results need to replicate on larger sample. To reach to such conclusion is worthy as this will be a modifiable risk factor with possibility of preventive actions via improving coping skills and social support.

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أحداث الحياة و السكتة الدماغية

عند سؤال العامة عن معلوماتهم عن أهم مسببات السكتة الدماغية يأتي الضغط النفسي من أكثر الأسباب ذكرا ، وقد حاولت دراسات عديدة دراسة هذه العلاقة ، فظهرت بعض الدراسات وجود علاقة بينما أظهرت دراسات أخرى عدم وجود علاقة بين أحداث الحياة وحدوث السكتة الدماغية ، وقد كان هدف هذا البحث هو دراسة ما إذا كانت هناك علاقة أم لا ، وإذا كانت إيجابية بنعم ، فما هو نوع الأحداث التي يمكن أن تسبب ذلك ، تم فحص ٦٠ مريض مصابون بالسكتة الدماغية لأول مرة في حياتهم من قسم الأوعية الدماغية بمستشفى عين شمس التخصصي وتكونت العينة الضابطة من مجموعتين : المجموعة الأولى تكونت من ٥٠ شخص متماثلون في السن و الجنس ولا يعانون من أى من العوامل الخطرة الشائعة للسكتات الدماغية ، والمجموعة الثانية تتكون من ٦٠ مريض يعانون من العوامل الخطرة للسكتات الدماغية ولكن لا يعانون منها ، وقد تم فحص المرضى إكلينيكيًا وبالأشعة المقطعية أو بالرنين المغناطيسي و تم عمل رسم قلب وموجات فوق صوتية على القلب و تحاليل معملية كاملة ، و تمت مقابلة المرضى والعينة الضابطة باستخدام مقياس أحداث الحياة والصعوبات بالإصدار الجديد (عام ١٩٩٥) لتقييم أحداث الحياة والصعوبات في فترة الستة أشهر التي سبقت السكتة الدماغية للمرضى والتي سبقت المقابلة بالنسبة للمجموعة الضابطة ، وقد أظهرت نتائج البحث أن المرضى يذكرون حدوث أحداث شديدة وصعوبات بالغة أكثر من العينة الضابطة بدرجة مهمة إحصائياً ، وقد وجدت الأحداث التي تتضمن الإهانة (الإذلال) و/أو عدم القدرة على إيجاد الحل بنسبة أكبر في المرضى عن المجموعة الضابطة عكس الأحداث التي تتضمن الفقد أو الخطورة فقط ، أما بالنسبة لتوزيع أحداث الحياة على مدار فترة الستة أشهر التي تسبق السكتة الدماغية فقد أظهرت الدراسة وجود معدلات عالية من أحداث الحياة في فترات يوم وأسبوع و ستة أشهر ما قبل السكتة الدماغية مقارنة بالعينة الضابطة خلال نفس الفترات ، وقد وجد في عينة المرضى أنه كلما قلت العوامل الخطرة أو انعدمت كلما زادت نسبة وجود أحداث الحياة الشديدة وخاصة المتضمنة إهانة أو عدم القدرة على إيجاد الحل ، وقد نستنتج من هذا البحث أن الأحداث الشديدة وخاصة التي تتضمن الإهانة (الإذلال) و/أو عدم القدرة على إيجاد الحل يمكن اعتبارها كعامل من العوامل الخطرة لحدوث السكتة الدماغية بمفردها وغير معتمدة على عوامل أخرى ، وننصح بتكرار الدراسة على عدد أكبر من المرضى للتأكد من هذه النتيجة المهمة حيث أن الضغط النفسي سيعتبر من العوامل الخطرة التي يمكن التحكم فيها عن طريق زيادة المساندة الاجتماعية ومهارات التكيف لمنع حدوث السكتة الدماغية.