

Association between Hemorrhagic Stroke and Diabetes Mellitus; A Hospital-Based Case-Control Study

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ABSTRACT

Introduction: Stroke is the third leading cause of death in the world. Numerous studies show that diabetes mellitus is one of the risk factors for stroke. In general, stroke is divided into two types: hemorrhagic & ischemic, and approximately 15-25% of strokes are the hemorrhagic type.

Objective: As it is claimed that diabetes mellitus is an important risk factor for hemorrhagic stroke, this study attempts to explain the association between diabetes and hemorrhagic stroke.

Method and Data Collection: According to Epi Info statistic software; 102 participants who were $40 \geq$ years old, and had a hemorrhagic stroke in their brain CT scan or MRI, were selected as cases, and 255 Participants without having a hemorrhagic stroke, including as controls. The proportional distribution of cases and controls in terms of sex and age was considered. Data has been obtained primarily through the design of a questionnaire from admitted patients in the neurosurgery and neurology wards of Aliabad university hospital.

Results: Out of 357 participants, 181 (50.7%) participants were female and 176 (49.3%) were male. The study found that 25.5% of the participants in the case group, and 13.3% of the participants in the control group, were exposed to diabetes mellitus.

Considering (P-Value = 0.006) and Odds ratio (OR=2.224; 95% CI = 1.253 – 3.945), the association between hemorrhagic Stroke and diabetes mellitus is suggested to be significant.

Conclusion: As a result of the study, we can claim that among other risk factors, Diabetes Mellitus can also be considered a possible predisposing factor for Hemorrhagic Stroke and there is a significant association between Hemorrhagic stroke and Diabetes mellitus.

Keywords- Blood Sugar, Diabetes Mellitus, and Hemorrhagic Stroke.

I. INTRODUCTION

Stroke is the third leading cause of death in Western countries, and numerous studies show that diabetes mellitus is one of the risk factors for stroke [1]. It is estimated that 15 million people have a stroke every year, and in general, strokes are divided into two types: hemorrhagic and ischemic, and approximately 15-25 percent of strokes are the hemorrhagic type, which causes bleeding inside the cranium. Among the various risk

factors for stroke, one of them is diabetes [2]. Intracranial bleeding can be diagnosed by CT scan and MRI.

Diabetes mellitus is one of the chronic and progressive diseases and it is predicted that by 2040, it will affect 642 million people in the world. Diabetes is a known risk factor for cerebrovascular diseases [3]. Diabetes is a group of common metabolic disorders characterized by hyperglycemia and refers to those whose fasting plasma glucose level is equal to or greater than 126 mg/dL (FPG \geq 126 mg/dL) or the average percentage of

glucose in hemoglobin should be equal to or more than 6.5%. (HbA1C \geq 6.6%), [4].

Considering the above points, diabetes is one of the important risk factors for hemorrhagic stroke, which has been explained in many international studies. In a cohort study in Japan, among 4875 patients with type 2 diabetes, with an average age of 65.4 years and 57% male, and 43% female; after five years, it was found that 5% of diabetic patients had a hemorrhagic stroke and 24.3% had an ischemic stroke, and the control of glucose level was emphasized in these patients [5]. Another study in Iran Indicates that 20% of Hemorrhagic stroke patients have a history of diabetes mellitus and there is a significant relationship between them (P = 0.041) [6]. Out of 36 participants, it was found that 50% of hemorrhagic stroke patients have diabetes mellitus [7]. In a meta-analysis, It was found that 26% of hemorrhagic stroke patients had diabetes [3]. In the same way, another meta-analysis shows that 10.6% of hemorrhagic stroke patients have diabetes [2].

It is clear that Diabetes is one of the known risk factors for stroke, and the incidence of stroke is higher in people with diabetes compared to people without diabetes. Similarly, out of 4083 patients, 149 patients had diabetes, including 30% of them had a hemorrhagic stroke and 70% of them had an ischemic stroke [8]. Glucose levels in diabetic patients with hemorrhagic stroke compared to non-diabetic patients, exposed to hemorrhagic stroke, are higher and this raises the risk of death in hemorrhagic stroke patients [9]. A case-control study (120 cases and 135 controls), shows that diabetes mellitus was present in 33.1 % of intracerebral hemorrhage (case group) and 22.2 % in the control group(P=0.054), therefore was no significant relationship between diabetes mellitus and hemorrhagic stroke was found [10]. A review of scientific literature has shown that the relationship between diabetes and hemorrhagic stroke remains controversial [11].

II. OBJECTIVE

It is claimed that diabetes mellitus is an important risk factor for hemorrhagic stroke, and numerous studies report the existence of an association between diabetes and the formation of hemorrhagic stroke; therefore, in this study, an attempt is made to explain the association between diabetes and hemorrhagic stroke.

III. STUDY QUESTION

Is there an association between diabetes mellitus and hemorrhagic stroke?

IV. RESEARCH METHOD

A Hospital-based Case-Control Study.

Study Site: Neurosurgery and Neurology wards of Aliabad University Hospital.

Sampling Method and Sample Size: Sampling is Convenience and has two types of criteria:

1- Inclusion criteria: According to Epi Info statistic software based on previous studies and considering a 95% confidence interval, and 90% power; 102 participants who were 40 years old or older, have a hemorrhagic stroke in their brain CT scan or MRI, without a history of trauma, selected as case and 255 participants that efforts to match individuals in terms of age and sex, without having a hemorrhagic stroke in their brain CT scan or MRI, as control included in this study.

Unmatched Case-Control Study (Comparison of ILL and NOT ILL)

Two-sided confidence level: 95%

Power: 90%

Ratio of controls to cases: 2.5

Percent of controls exposed: 15%

Odds ratio: 2.5

Percent of cases with exposure: 30.6%

	Kelsey	Fleiss	Fleiss w/ CC
Cases	95	102	111
Controls	237	255	277
Total	332	357	388

2- Exclusion criteria: Participants who were exposed to intracranial hematoma due to trauma or whose blood coagulation disorder has been proven, are excluded from the study.

Sours of Data and Analysis: Data has obtained primarily through the design of a questionnaire from admitted patients in the neurosurgery and neurology wards of Aliabad university hospital from September 2022 - May 2023. As many as 102 participants who have a hemorrhage in their brain CT scan or MRI, were selected as Case, and 255 participants, efforts to match in terms of age and sex, without having a hemorrhagic stroke, were chosen as Control. The criteria for having diabetes are; taking sugar medication or proving sugar in the blood test, as blood plasma glucose level was equal to or greater than 126 mg/dL in the fasting state (FPG \geq 126 mg/dL) or based on the average percentage of glucose in hemoglobin, equal or more than 6.5 percent (HbA1C \geq 6.6%) [4]. The obtained data were analyzed with the software of SPSS version 24.

The main variables of the study: Hemorrhagic stroke and diabetes; taking into account age, sex, duration of diabetes, and the types of oral or injectable treatment.

Facilities: Sufficient number of patients with necessary imaging and laboratory examinations are available in Aliabad University Hospital.

Limitations: sometimes in the history of the patients, the reason for intracranial bleeding, whether it is hemorrhagic stroke or bleeding caused by trauma, is not clear; In this case, these participants were not included in the research.

Ethical issues: Whit an official letter, the proposal of this study was approved by IRB of the Kabul University of

Medical Science research center. Before applying this study, the purpose and significance of the study were explained to each participant. During the data collection informed consent was collected from all participants (cases & controls). Participants' involvement was only on a voluntary basis. We had never written the participants' names, and the confidentiality of the data has kept at all levels of the study.

Despite all this, the study is non-interventional, so there are not any ethical barriers.

V. RESULTS

All 357 participants (cases and control), is almost equal in terms of gender (181 females and 176 male) (Table 1). 102 participants who have a

hemorrhagic stroke in their brain CT scan or MRI; are selected as cases, and 255 participants without Hemorrhagic Stroke, were selected as control (Table 2). The proportional distribution of case and control in terms of sex and age was considered (Tables 6 & 7). Out of all, 60 participants were exposed to diabetes (Table 3). The most exposure duration (diabetes mellitus) is between 1-5 years (Table 4). The patients who have diabetes mellitus most of them used oral drugs (Table 5). The study found that 25.5% of the participants in the case group, and 13.3% of the participants in the control group, were exposed to diabetes mellitus. Considering (P-Value = 0.006) and Odds ratio (OR=2.224; 95% CI = 1.253 – 3.945), the association between hemorrhagic Stroke and diabetes mellitus is suggested to be significant (Table 8).

The data were analyzed in the SPSS version 24, and the following results were obtained:

Table 1: Participants' Gender.

	Frequency	Percent	Valid Percent	Cumulative Percent
Female	181	50.7	50.7	50.7
Male	176	49.3	49.3	100.0
Total	357	100.0	100.0	

As the table shows that the number of participants included in this study, is almost equal in terms of gender.

Table 2: Groups of Case and Control.

	Frequency	Percent	Valid Percent	Cumulative Percent
Case = Hemorrhagic Stroke	102	28.6	28.6	28.6
Control = Not Hemorrhagic Stroke	255	71.4	71.4	100.0
Total	357	100.0	100.0	

As the Table shows, the number of the control group is 2.5 times more than the case group.

Table 3: Exposure (Diabetes Mellitus)

	Frequency	Percent	Valid Percent	Cumulative Percent
Exposed to DM	60	16.8	16.8	16.8
Not Exposed to DM	297	83.2	83.2	100.0
Total	357	100.0	100.0	

As the table shows, 60 (16.8%) participants are exposed to Diabetes Mellitus.

Table 4: Diabetes Mellitus Duration (Duration of exposure).

	Frequency	Percent	Valid Percent	Cumulative Percent
1-5 Years	40	11.2	66.7	66.7
6-10 Years	8	2.2	13.3	80.0
11-15 Years	7	2.0	11.7	91.7
16 => Years	5	1.4	8.3	100.0
Total	60	16.8	100.0	

Based on the table, most of the patients have been suffering from Diabetes for 1-5 years.

Table 5: Kinds of Treatments for Diabetes Mellitus

	Frequency	Percent	Valid Percent	Cumulative Percent
Oral Treatment	54	15.1	90.0	90.0
Oral and Injection	6	1.7	10.0	100.0
Total	60	16.8	100.0	

Based on this table, most patients who suffered from diabetes, have used oral treatment.

Table 6: Participant Sex with Case and Control Cross tabulation

		Case: (HI)	Control: (not HI)	Total
Female	Count	55	126	181
	% within Participants' Gender	30.4%	69.6%	100.0%
	% within Case and Control	53.9%	49.4%	50.7%
Male	Count	47	129	176
	% within Participants' Gender	26.7%	73.4%	100.0%
	% within Case and Control	46.1%	50.6%	49.3%
Total	Count	102	255	357
	% within Participants' Gender	28.6	71.4	100.0%
	% within Case and Control	100.0%	100.0%	100.0%

As the table shows, the proportional distribution of people included in groups of case and control, in terms of sex is almost equal.

Table 7: Participant Age.

	Frequency	Percent	Valid Percent	Cumulative Percent
40-49 Years	74	20.7	20.7	20.7
50-59 Years	79	22.1	22.1	42.9
60-69 Years	118	33.1	33.1	75.9
70 years older	86	24.1	24.1	100.0
Total	357	100.0	100.0	

According to this table, the number of people included in the study, from different groups of age, are almost close to each other.

Table 8: Association of Case and Control with Exposure (Diabetes Mellitus)

		Expose to Diabetes Mellitus	Not Expose to Diabetes Mellitus	Odds	total
Case: Hemorrhagic Stroke	Count	26	76	0.342	102
	% within Case and Control	25.5%	74.5%		100.0%
Control: Not Hemorrhagic Stroke	Count	34	221	0.154	255
	% within Case and Control	13.3%	86.7%		100.0%
Total	Count	60	297		357
	% within Case and Control	16.8%	83.2%		100.0%

Chi-Square Tests:

Pearson Chi-Square: Value: 7.701 - Degree of Freedom: 1 - P-Value: 0.006

Odds Ratio for case and Control with 95 % confidence interval:

Lower: 1.253 Upper: 3.945 Value: 2.224

As the table shows, compared to the control group, a higher percentage of participants in the case group (25.5% vs 13.3%) were exposed to diabetes mellitus. (P-value= 0.006) and Odds ratio (OR=2.224; 95% CI = 1.253 – 3.945).

VI. DISCUSSION

In this study, 102 participants who had a hemorrhagic stroke in their brain CT scan or MRI; were selected as the case group, and 255 participants without Hemorrhagic Stroke, were selected as the control group (Table 2). The proportional distribution of cases and

controls in terms of sex and age was considered (Table 6 & Table 7). The number of females in this study was slightly more than males which the reason may be the lack of women's access to healthcare services and cultural restrictions on women in Afghanistan, therefore when their health status becomes worse and more complicated they are allowed to attend in hospital (Table 1). Out of the

357 participants included in the study, 60 were exposed to diabetes (**Table 3**). Patients who suffered from diabetes mellitus have taken anti-diabetes drugs, and most of them (54 participants) have used oral treatment, and 6 patients have used both oral and injection (insulin) for their treatment, but because of the poor economic situation, and cultural beliefs in Afghanistan they may do not use their medication regularly, therefore it may cause to predispose them to hemorrhagic stroke (**Table 5**). The study found that 25.5% of the participants in the case group, and 13.3% of the participants in the control group, were exposed to diabetes. Considering (P-Value = 0.006) and (OR=2.224; 95% CI = 1.253 – 3.945), the association between hemorrhagic Stroke and diabetes mellitus is suggested to be significant (**Table 8**).

By comparing the results of this study with other international references, it is indicated that Glucose levels in diabetic patients with hemorrhagic stroke compared to non-diabetic patients, exposed to hemorrhagic stroke, are higher and this raises the risk of death in hemorrhagic stroke patients [9]. In a meta-analysis research, It was found that 26% of hemorrhagic stroke patients had diabetes [3]. As a result of research conducted by Mr. Hagg, out of 4083 patients, 149 patients had diabetes, including 30% of them had a hemorrhagic stroke. [8]. The results of these studies are close to our study and show a significant association between hemorrhagic stroke and diabetes mellitus.

But among 4875 patients in Japan with type 2 diabetes mellitus, with an average age of 65.4 years and 57% male, and 43% female, just 5 % of diabetic patients had a hemorrhagic stroke [5]. The reason for this variation may lie in the diet, exercise, and the geographical difference. In the International Journal of Stroke in 2017, it was found that 50% of hemorrhagic stroke patients have diabetes mellitus [7]. In 2018 the Journal of Tropical Medicine in Sub-Saharan Africa; shows that 10.6% of hemorrhagic stroke patients have diabetes mellitus [2]. Other studies show that there is no significant relationship between diabetes mellitus and hemorrhagic stroke, and the association between them remains controversial [10][11]. The result of these studies is not the same as our findings, there is no specific reason for this difference, but racial or climatic reasons can be considered.

VII. STRENGTHS OF THE STUDY

This study used primary data with the standard method (Case-Control study) in one of the prestigious Neurosciences centers of Afghanistan (Aliabad University Hospital). The admitted patients were included and their laboratory and imaging examinations were available.

VIII. WEAKNESSES OF THE STUDY

While collecting data; It was seen that a number of Hemorrhagic Stroke patients; Only one year passed

since their diabetes mellitus was diagnosed, which can probably deny the destructive effect of diabetes on the brain vessels.

IX. CONCLUSION

As a result of the study, we can claim that among other risk factors, Diabetes Mellitus can also be considered a possible predisposing factor for Hemorrhagic Stroke and there is a significant association between Hemorrhagic stroke and Diabetes mellitus.

**(P-Value = 0.006, Odd Ratio = OR=2.224;
95% CI = 1.253 – 3.945)**

SUGGESTION

With all these findings, arguments, and differences, it is necessary to conduct cohort research with a larger sample size in order to reach a more specific conclusion about the association between hemorrhagic stroke and diabetes mellitus.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest related to the subject matter or materials discussed in this article.

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