



Clinical Course of Ruptured Cerebral Aneurysm at Tertiary Care Hospital in Pakistan

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Abstract

Objective: To report the clinical outcome achieved through surgical clipping of ruptured cerebral aneurysms over 7 and half years period in tertiary care hospital of Pakistan.

Methods: A retrospective study of Pakistani patients with ruptured intracranial aneurysms that were operated for clipping. The demographic details, characteristics of ruptured aneurysm, imaging of aneurysm, clinical course, progress and outcome were recorded. Fisher grading and Hunt and Hess criteria were used. Glasgow outcome scale (GOS) was used for final result. Data was recorded and analyze through SPSS version 21.

Results: 86 patients were recruited in 7 and a half year period. Mean age was 50 (SD, 14) years. There were 48 females and 38 males. There was no significant difference in the size of the ruptured aneurysms among both sexes. Two most common sites of rupture were the anterior communicating artery and middle cerebral artery. 11.6% patients had more than one aneurysm. The median door-to-treatment time with IQR was 48 hours. The majority of the patients presented with Grade II and III of Hunt and Hess criteria, while the Fischer grading was severe of Grade III and IV for most of them. The average follow-up was about 3 weeks, 39 out of 86 patients had low disability. Patients above the age of 40 had worse outcome. The mortality rate of the cross-sectional was 14% (12/86). There was no statistical significance seen in patients with GOS and H and H criteria, or GOS and Fischer grading. Post-operatively, 13 patients had hydrocephalus (13 patients), and among which 10 underwent VP shunt.

Discussion: A very low occurrence rate of aneurysm has been seen, which involve many factor, such as eligibility for surgery, financial hurdles, lack of awareness, lack of facilities, among others. The most common location for subarachnoid cerebral aneurysm in Pakistan is anterior communicating artery and second to it is middle cerebral artery. No statistical significance has been seen between Hunt and Hess grading system and outcome scale in this study, while some degree of association has been proven in other studies. Clinical outcomes have been better overall due to early intervention, if to observe factors, age and aneurysm size plays an important role with poorer results with age more than fifty as seen through Glasgow outcome scale. Other factors that matter are slow prognosis, severe clinical symptoms at time of admission and higher frequency of comorbidity. The clinical outlook shows that the most common complication of the clipping was hydrocephalus and wound infection in Pakistani population. Patients were not followed for long term outcome, hence it is a limitation of this study.

Conclusion: Despite the improvements in past two decades, there is a lack of infrastructure and awareness regarding cerebral aneurysm treatment and management in Pakistan. Moreover, alternative methods such as coiling is still not available in the majority of hospitals in Pakistan.

Keywords: Cerebral Aneurysm; Outcome; Subarachnoid Hemorrhage; Ruptured Intracranial; Aneurysm; Clipping

Abbreviations

CT: Computed Tomography; SAH: Subarachnoid Hemorrhage; MRI: Magnetic Resonance Imaging; aSAH: Aneurysmal Subarachnoid Hemorrhage; MCA: Middle Cerebral Artery; Acom: Anterior Communicating Artery; Pcom: Posterior Communicating Artery; ACA: Anterior Cerebral Artery; PICA: Posterior Inferior Cerebellar Artery; ICA: Internal Carotid Artery; BRAT: Barrow Ruptured Aneurysm Trial; ISAT: International Subarachnoid Aneurysm Trial

Introduction

Aneurysmal subarachnoid hemorrhage (SAH) is a neurological condition contributes around 5% of all cerebrovascular accidents in Pakistan and India that is 11 per 100,000 patients. Out of these 80% are due to rupture of intracranial aneurysm [1,2]. Due to this high mortality and continuing morbidity, especially when there is a ruptured aneurysm; the management of SAH has remained a challenge despite advancement in surgery and intensive medicine.

The most popular technique to treat intact or ruptured aneurysm is, either microsurgical clipping or endovascular coiling. There is a fine line between comparing coiling with clipping. Some literature shows that there is no difference in the outcome of two while others consider coiling superior [3-6]. However, coiling is still not introduced in many tertiary centers in Pakistan including ours. Moreover, our center is the only one that is operating aneurysm in our region. Neurosurgical intervention to clip is to across the neck of the aneurysm and; thus exclude it from circulation [6]. The aim of our study is to evaluate clinical outcomes of subarachnoid aneurysm undergoing clipping in patients presented at a tertiary care center in Pakistan.

In previously mentioned literature, treatment of severe cases with Hunt and Hess scale 4 or 5 managed conservatively until their symptoms get better. Although, in the early 1990s, published data depict that aggressive treatment improves results with more success from the range of 3.8% and 18% to 7% and 42.6% [7-10]. Hence, nowadays the practice is to treat the aneurysm as soon as possible. [11] The introduction of coiling in 1990 has modified the practice, but still the surgical clipping method is a gold standard treatment for cerebral aneurysms since 1960s [11,12].

Materials and Methods

The study was approved by an institutional review board of our hospital, and study was conducted in the neurosurgery department.

This was a retrospective study of Pakistani patients with ruptured intracranial aneurysms between the duration of January 2012 to September 2019, which involved admissions for SAH presented in the emergency department. These patients were admitted in Shifa International Hospital, Islamabad, Pakistan. In almost 7 years and half year period, patients that were operated for subarachnoid hemorrhage are only included in this study. Thus, 86 patients were treated with surgical clipping after evaluation.

In each case, the size and location of the ruptured aneurysm were recorded (Table 2). When multiple aneurysms were present, the one responsible for rupture and clipped was considered as the main artery. The records of all the surgical treated patients were explored to acquire patients' demographics, characteristics of the aneurysm, imaging of aneurysm, treatment outcome and complications. The size of an aneurysm on CT scan or MRI were divided as less than 5mm, 5 to 10mm and more than 10mm. The subarachnoid hemorrhage was classified on imaging for severity through Fisher grading [13]. Hunt and Hess grade was abstracted directly from the chart review [14].

Functional outcomes at follow-up were assessed using a Glasgow outcome scale (GOS), which was abstracted from hospital discharge summary and progress notes by the Neuro ICU team or Neurosurgery service. Clinical outcome at follow up was classified with GOS, which described as (1) low disability: means a resumption of normal life despite minor deficits; (2) moderate disability: means disabled, but independent that is can work in sheltered settings; (3) severe disability: means conscious, but disabled dependent on others for daily support; (4) persistent vegetative state: means minimal responsiveness; and (5) death [15]. This GOS relation was then checked with Hunt and Hess criteria and Fisher grade.

Patients were followed from the day 158 they presented at the hospital till their follow ups. Data was recorded and analyze through SPSS version 21. p-value <0.05 was considered statistically significant in subgroup analysis.

Results

Of the 86 patients included in our series, The patients in our series ranged in age from 21 to 85 years with a mean age of 50 years (standard deviation [SD], 14 years). There was a 56% (48/86) female predominance (Table 1); in women, the mean age was 49 (SD,

Sex	Age							Total
	21-30	31-40	41-50	51-60	61-70	71-80	81-90	
Male	7	3	7	9	7	4	1	38
Female	2	11	12	15	6	2	0	48
Total	9	14	19	24	13	6	1	86

Table 1: Age and sex distribution of patients with ruptured intracranial aneurysms.

12) years, whereas in the 38 men it was 51 (SD, 17) years. Males presented with ruptured intracranial aneurysms at an older mean age than females (mean age difference, 2 years; 95% confidence interval [CI], 8 years). There was no significant difference in the size of the ruptured aneurysms (t test, P = 0.467) in men (mean size, 5.3 mm) and women (mean size, 5.0 mm).

The two most common sites of rupture were the anterior communicating artery (38/86, 44.2%) and middle cerebral artery (22/86, 25.6%). The majority of the ruptured aneurysms were small. In all, 98% (84/86) of the aneurysms were 10 mm or less, whilst 65% (56/86) were 5 mm or less as seen in table 2.

Statistical analysis showed that rupture at the anterior communicating artery involved a higher proportion of aneurysms of size 5 mm or less compared to all other locations. The mean diameter of ruptured aneurysm of middle cerebral artery was 5.3 (SD, 1.8) mm,

Sex	Artery Operated	Diameter (mm)			Total
		<5	6-10	> 10	
Male	MCA	4	3	0	7
	ACoMA	12	9	1	22
	PComA	1	0	0	1
	ACA	3	2	0	5
	PICA	2	0	0	2
	ICA	0	1	0	1
Total		22	15	1	38
Female	MCA	9	6	0	15
	ACoMA	15	1	0	16
	PComA	2	2	0	4
	ACA	8	2	1	11
	ICA	0	2	0	2
	Total		34	13	1

Table 2: Sex and location of ruptured intracranial aneurysms.

anterior communicating artery was 4.8 (SD, 1.7) mm and anterior cerebral artery was 5.2 (SD, 2.5) mm.

The point prevalence of multiple aneurysms was 11.6%; 10 of the 86 patients had two or more aneurysms diagnosed (Table 3). The Z test was conducted for the proportions of small ruptured aneurysms (sized ≤5 mm) between patients having single and multiple aneurysms (Table 4), which indicated that cases with single aneurysms 184 had a larger proportion that were small. The median door-to-treatment time with IQR was 48 hours.

Sex	Single Aneurysm	Multiple Aneurysms	Total
Male	36	2	38
Female	40	8	48
Total	76	10	86

Table 3: Point prevalence of multiple aneurysms.

Size of aneurysm (mm)	Multiple aneurysm	
	Yes	No
≤5	53	3
>5	23	7

Table 4: Proportion of aneurysms (based on size) in patients with multiple and single aneurysms.

Seventy-four patients' (86%) Hunt-Hess scale was recorded, 35 (40.7%) had grade II, 29 (33.8%) had grade III, 9 (10.5%) had grade IV and 1 (1.2%) had grade V. The majority of the patients presented with Grade II and III of Hunt and Hess criteria (Table 5), while the Fischer grading was severe of Grade III and IV for most of them (Table 6). The details of other arteries are shown in for both grading systems are illustrated in tables 5 and 6. Missing values are 6 of females from Fischer grading and 8 males and 4 females from Hunt and Hess criteria.

Hunt and Hess Criteria	Age (years)							Total
	21-30	31-40	41-50	51-60	61-70	71-80	81-90	
II	5	7	4	10	7	1	1	35
III	3	3	10	7	4	2	0	29
IV	0	2	2	5	1	0	0	9
V	0	0	0	0	0	0	0	1
Total	8	10	16	17	12	3	1	74

Table 5: Shows age distribution and Hunt and Hess Criteria.

Fisher Grading	Age (years)							Total
	21-30	31-40	41-50	51-60	61-70	71-80	81-90	
I	0	3	1	4	1	2	0	11
II	0	1	3	3	1	0	0	8
III	4	3	5	7	5	0	0	24
IV	4	6	9	8	6	3	1	37
Total	8	13	18	22	13	5	1	80

Table 6: Shows age distribution and Fisher Grading.

The average follow-up was about 3 weeks, their final outcome recorded during follow up has been illustrated in table 7. 39 out of 86 patients had most favorable outcome that is low disability; however 4 ended in persistent vegetative stage. Although, patients under age of 40 were less in number and fall in criteria of low disability, as final outcome. Deaths were seen almost uniformly throughout the age groups. The mortality rate of the cross-sectional was 14%

(12/86). There was no statistical significance seen in patients with GOS and H and H criteria (Mann-Whitney-U Test, p value: 0.932) and same with GOS and Fischer grading (Mann-Whitney-U Test, p value: 0.189). Post-operative complications are shown in table 8. From which most common was hydrocephalus (13 patients), and among which 10 underwent VP shunt.

Age	Glasgow Outcome Scale					Total
	Low Disability	Moderate Disability	Severe Disability	Persistent Vegetative State	Death	
21-30	6	1	0	1	1	9
31-40	6	4	2	0	2	14
41-50	10	4	2	0	3	19
51-60	9	6	7	2	2	24
61-70	7	5	0	0	1	13
71-85	1	0	2	1	3	7
Total	39	20	11	4	12	86

Table 7: Shows association of Age groups with clinical outcome at average of 3 weeks follow up.

Post-operative Complications	Number (%)
New Sensory Deficit	2 (2.3%)
Wound Infection	3 (3.5%)
Hydrocephalus	11 (12.8%)
Transient Dysphagia	9 (10.5%)
Re-bleeding	1 (1.2%)
Seizures	3 (3.5%)
Meningitis	5 (5.8%)

Table 8: Shows percentage of patients with post-operative complications.

Discussion

This is a study of 86 patients of ruptured cerebral aneurysm over a period of around 7 and a half years in one tertiary care center, in Pakistan. A very low occurrence rate, when consider the population of Pakistan of around 197 million. Factors can be as followed: a) only included ruptured aneurysm that were eligible for surgery; b) the above data is from neurosurgical centers situated in the capital city with patients that did not have the affordability issue, excluding large proportion of rural and poor people; c) lack of awareness so prefer conservative management and not referred to neurosurgical units; d) Lack of facilities of imaging for instance CT scan and angiography in more remote areas; e) Possible role of dietary, genetic, and environmental factors in this region and f) not diagnosed properly by physicians.

The most common location for subarachnoid cerebral aneurysm in Pakistan, is anterior communicating artery, and second to it is middle cerebral artery as seen in this and other studies too [16,17]. However, Robert., *et al.* ten year BRAT study, and Andrew., *et al.* 1 year ISAT study showed most cases of anterior communicating artery followed by a posterior communicating artery, and then the middle cerebral artery [18,19]. In this study, there were 10 patients with grade 4 and 5 of Hunt and Hess criteria, and 29 with grade 3, while deaths were total 12 and patient in a persistent vegetative state were 4. Although, no statistical significance has been seen between Hunt and Hess grading system and outcome scale in this study or Robert., *et al.* 6 year BRAT study, but some degree of association has been proven in other studies [20-22].

Clinical outcomes have been better overall 227 due to early intervention, if to observe factors, age plays an important role with poorer results with age more than fifty as seen through Glasgow outcome scale [11]. Other factors that matter are slow prognosis,

severe clinical symptoms at time of admission and higher frequency of comorbidity. In H. Yang *et al.* study and Mets *et al* ISAT study shows that age and aneurysm size are the important risk factors [23]. Surgical clipping in patients above 65 years has shown a high rate of disability and mortality but proves overall to have a good outcome. Thus, to limit surgical clipping of elderly patients is not a wise idea if this option is available. It also depends on anesthesia complications and how much elders can tolerate anesthesia and craniotomy.

The clinical outlook shows that the most common complication of the clipping was hydrocephalus and wound infection. Hydrocephalus in which 2 out of 3 patients needed VP shunt. New sensory deficits, dysphagia and dysarthria were managed through physiotherapy with improvement with the passage of time. Seizures were prevented of scar epilepsy with antiepileptic drugs, though one patient reported with this. There were 12 deaths during a hospital stay; however, patients were lost to have longer follow-up so cannot interpret the result in exact mortality or how outcome changed in longer periods, and is one of the limitation of this study.

Data from other studies in Pakistani populations showed that in study Raja., *et al.* hydrocephalus and wound infection was common and second to it was meningitis and in another study of Indian population that is Sharma., *et al.* hydrocephalus was again common than meningitis [16,17].

Follow up was limited to 21 days in our study so to comment on long term follow up is not possible. Although as seen in other studies, on follow up the percentage of patients that had worse in preceding months in very little [5,23,24]. There was no significant statistical heterogeneity seen in change in clinical outcome in intermediate and long follow up of the patients. In a BRAT study with 10 year follow up after clipping procedure, retreatment was less than 1% [18].

There has been many improvements in expertise and in less invasive treatment approach have been seen in the past few decades all over the world. Although, Pakistan still has a long way to go. As mentioned earlier, from diagnosis of cerebral aneurysm to its management, advancements are necessary. For instance, details of mortality of patients without treatment is not available and only studies have been done on cerebral aneurysm in Pakistan. Furthermore, substitute procedures such as endovascular coiling is yet not accessible in the majority of hospitals of Pakistan.

Conclusion

Ruptured intracranial aneurysm in Pakistan is estimated about 8-9 per 100,000 patients. There are more females presented than males, with most frequent site to be anterior communicating artery. The mortality rate of surgically treated patient was 14% with major complication of hydrocephalus, with poor prognosis seen in patients above 50 especially above 65. Although, deaths were evenly distributed in all age groups. There is a lack of infrastructure and awareness regarding cerebral aneurysm treatment and management in Pakistan. Moreover, alternative methods such as coiling is still not available in the majority of hospitals in Pakistan.

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