Role of Gender in the Outcome of Spontaneous Subarachnoid Hemorrhage during Subacute Stage in Patients between 40 and 60 Years-: A Single Tertiary Health Institution Experience in Imo State Nigeria

Dr. Benedict Iheanyichukwu Orji[1] Dr Francis Chiku Abeze[2],
1 , MBBS, FWACS, FICS. Consultant Neurosurgeon, Department of Surgery,
Federal University Teaching Hospital, Owerri. Imo State, Nigeria.
2 Senior Registrar Neurosurgical Unit, Department of Surgery
Federal University Teaching Hospital, Owerri. Imo State, Nigeria.

Abstract:-

- ***Introduction***

Spontaneous Subarachnoid hemorrhage (SSAH) is known to cause metabolic and pathological changes at various aging population. Factors such as rising severity of the aetiology, associated comorbidities and gender, may confound the probable outcome. There are several facts suggesting that there is significant role of each of the above factors acting independently on the outcome of SSAH, but none has elucidated the collective impact of gender and age between 41 and 60 years, on the outcome of SSAH. Thus this study wanted to see the effects of primary and attenuated secondary injuries between the ages of 40-60 years in patients with SSAH. This study aims to understand the pattern of these changes.

- ***Objectives***

To study how gender of the patients between 41 and 60 years affected their survival of spontaneous subarachnoid hemorrhage in the subacute stage.

- ***Materials and Methods***

This is a prospective study of patients with spontaneous subarachnoid hemorrhage (SSAH) managed at a tertiary hospital from January 2018 till January 2023. Twenty-two patients were studied. The patients included those with intracerebral and intraventricular hemorrhage. The study excluded patients with traumatic brain injury and patients without brain imaging. The management of these patients were uniform. The GCS on admission were checked; in the acute/subacute phase. Their age were from 41-60 years, with their corresponding outcome correlated. The outcomes were survival or mortality.

- ***Results***

Total number of patients studied was 22, male 13 (59.1%), females 9 (41.9%),

- ***Conclusion***

Older age correlated with poorer Glasgow Coma Scale (GCS) and higher mortality rate. Efforts should be intensified to tackle these factors before and during the hemorrhage to improve outcome.

I. INTRODUCTION

There exists a wide variation in the incidence of SAH. The overall incidence of SAH was approximately 9 per 100 000 person-years but varied significantly by region, with doubled rates in Japan and Finland and far lower rates in South and Central America. The incidence was higher in women and increased with age. The gender distribution varied with age. At young ages, incidence was higher in men, while after the age of 55 years, the incidence was higher in women[1].

The association of age and gender in the outcome of SSAH can be linked to the likely prevalence of some of the causative factors of SSAH in certain age groups and gender. At older age, hypertension is a prevailing cause of SSAH while ruptured aneurysm and arteriovenous malformation rupture are commonly noted in the younger age. Rates are higher in Japan and Finland and increase with age.

The preponderance of women starts only in the sixth decade. There is a dearth of data in the age and gender related incidence with respect to SSAH in the Nigerian population necessitating this study. Subarachnoid haemorrhage (SAH) from a ruptured aneurysm accounts for approximately 5% of all strokes. Because it occurs at a young age and has a high case fatality, the loss of productive life years in the general population from SAH is as large as that from cerebral infarction, the most common type of stroke[1,2,3]

In the 37 sample size study by N.K De Rooij et al, the mean age of the study population and gender distribution, mean age and proportion of women were analysed by multivariate analysis. After adjustment for age, incidence increased by a factor of 1.03 (95% CI 0.99 to 1.06) for each additional percentage point of women in the study population. Incidences were reported separately for women and men by age category in several series studied.[4,5,6,7,8,9,10] In the age group 25–45 years, incidence was significantly higher in men than in women, but in the age group 55–85 years, incidence was significantly higher in women than in men.

Gender distribution as noted in Univariate Poisson regression analysis showed that for each additional per cent of women, the incidence became 1.07 times higher (95% CI 1.04 to 1.10). The overall incidence in this subset of studies was 10.5 (95% CI 9.9 to 11.2) per 100 000 person-years; the incidence for men was 9.2 (95% CI 8.4 to 10.2) and for women was 11.5 (95% CI 10.6 to 12.6). Thus the incidence in women was 1.24 (95% CI 1.09 to 1.42) times higher than in men.

Subarachnoid hemorrhage (**SAH**) is bleeding into and within the subarachnoid space-: The area between the arachnid membrane and the Pia mater surrounding the brain.[11] Symptoms may include severe and rapid headache of sudden onset, vomiting, unconsciousness, fever, weakness, numbness and occasional seizure including neck pain and stiffnes[12]. In about a quarter of people a small bleed with resolving symptoms occurs within a month of a larger bleed.

Spontaneous SAH occurs in occasions of non-traumatic or iatrogenic intracranial bleeding conditions. The severity of SSAH is determined among other things by the volume of hemorrhage into the subarachnoid space.

In 85 percent of spontaneous cases the cause is a cerebral aneurysm—a weakness in the wall of one of the arteries in the brain that becomes enlarged. They tend to be located in the circle of Willis and its branches. While most cases are due to bleeding from small aneurysms, larger aneurysms (which are less common) are more likely to rupture.[13] Aspirin also appears to increase the risk.[14]

In 15–20 percent of cases of spontaneous SAH, no aneurysm is detected on the first angiogram.[15] About half of these are attributed to non-aneurysmal perimesencephalic hemorrhage, in which the blood is limited to the subarachnoid spaces around the midbrain (i.e. (mesencephalon). In these, the origin of the blood is uncertain.[13] The remainder are due to other disorders affecting the blood vessels like cerebral arteriovenous malformation, disorders of the blood vessels in the spinal cord, and bleeding into various tumors.[13]

There are several grading scales available for SAH. The Glasgow Coma Scale (GCS) is ubiquitously used for assessing consciousness. Its three specialized scores are used to evaluate SAH; in each, a higher number is associated with a worse outcome.[16]

The first widely used scale for neurological condition following SAH was published by Botterell and Cannell in 1956 and referred to as the Botterell Grading Scale. The World Federation of Neurosurgeons (WFNS) classification uses Glasgow coma score and focal neurological deficit to gauge severity of symptoms.[20]

Grade	GCS	Focal neurological deficit
1	15	Absent
2	13–14	Absent
3	13–14	Present
4	7–12	Present or absent
5	<7	Present or absent

A comprehensive classification scheme has been suggested by Ogilvy and Carter to predict outcome and gauge therapy. The system consists of five grades and it assigns one point for the presence or absence of each of five factors: age greater than 50; Hunt and Hess grade 4 or 5; Fisher scale 3 or 4; aneurysm size greater than 10 mm; and posterior circulation aneurysm 25 mm or more.[21]

This study tends to appreciate the effect of gender on the outcome of SSAH in patients between the ages of 40 - 60 years.

II. MATERIALS AND METHOD

This is a prospective study of patients with spontaneous subarachnoid hemorrhage (SSAH) managed at a tertiary hospital from January 2018 till January 2023. Fifty patients were studied. The patients included those with intracerebral and intraventricular hemorrhage. The study excluded patients with traumatic brain injury, brain surgery and patients without brain imaging. The GCS on admission were checked; in the acute/subacute phase. The age were stratified to fit into ages between 40 and 60 years, with their corresponding outcome correlated. The outcomes were patterned into survival or mortality.

Statistical analysis was with Statistical Package for the Social Sciences, SPSS. The imaging techniques were brain CT scan and brain MRI. The management of the patients were uniform. They were managed in the ICU and had intravenous fluids, nasogastric feeding when needed, antihypertensives, diuretics, broad-spectrum antibiotics, intranasal O2 when necessary, DVT prophylaxis. The GCS on admission were checked. The electrolytes were checked and appropriate and timely correction made on admission thus standardising the treatment of all the patients. The abnormalities were promptly corrected and followed up. Consent was administered to the patients' relative on presentation in accordance with the ethical standard of the health institution.

III. RESULTS

Tables and Charts for patients 41-60 years

Statistics

		Age	Sex	GCS	Outcome
N	Valid	22	22	22	22
	Missing	0	0	0	0
Mean		49.5000	1.4091	9.5909	1.4091
Std. Error of Mean		.94834	.10729	.76066	.10729
Median		49.0000	1.0000	9.5000	1.0000
Mode		49.00	1.00	7.00	1.00
Std. Deviation		4.44811	.50324	3.56783	.50324
Minimum		41.00	1.00	4.00	1.00
Maximum		60.00	2.00	15.00	2.00

Table 1. Statistics for age, sex GCS and Outcome for patients 41-60 years.

Age

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	41.00	1	4.5	4.5	4.5
	44.00	1	4.5	4.5	9.1
	45.00	3	13.6	13.6	22.7
	46.00	1	4.5	4.5	27.3
	47.00	1	4.5	4.5	31.8
	48.00	1	4.5	4.5	36.4
	49.00	5	22.7	22.7	59.1
	50.00	2	9.1	9.1	68.2
	53.00	3	13.6	13.6	81.8
	54.00	2	9.1	9.1	90.9
	56.00	1	4.5	4.5	95.5
	60.00	1	4.5	4.5	100.0
	Total	22	100.0	100.0	

Table 2. The age distribution of patients 41-60 years

Gender

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	13	59.1	59.1	59.1
	Female	9	40.9	40.9	100.0
	Total	22	100.0	100.0	

Table 3. The sex distribution of patients 41-60years.

GCS

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	4.00	2	9.1	9.1	9.1
	5.00	1	4.5	4.5	13.6
	6.00	1	4.5	4.5	18.2
	7.00	4	18.2	18.2	36.4
	8.00	1	4.5	4.5	40.9
	9.00	2	9.1	9.1	50.0
	10.00	3	13.6	13.6	63.6
	11.00	1	4.5	4.5	68.2
	12.00	2	9.1	9.1	77.3
	14.00	2	9.1	9.1	86.4
	15.00	3	13.6	13.6	100.0
	Total	22	100.0	100.0	

Table 4. The GCS of patients 41-60 years.

Outcome

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Survived	13	59.1	59.1	59.1
	Died	9	40.9	40.9	100.0
	Total	22	100.0	100.0	

Table 5. The Outcome for patients 41-60 years

Charts

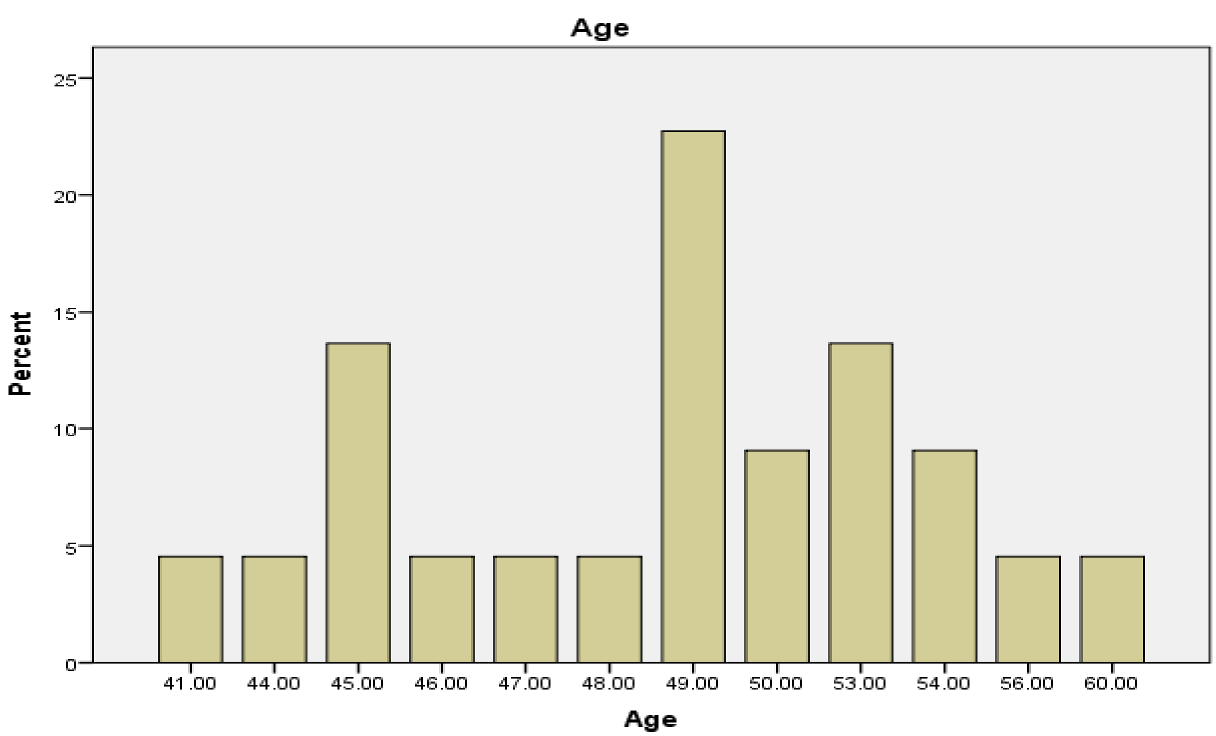

Fig 1. The Age distribution of patients 41-60

ISSN No:-2456-2165

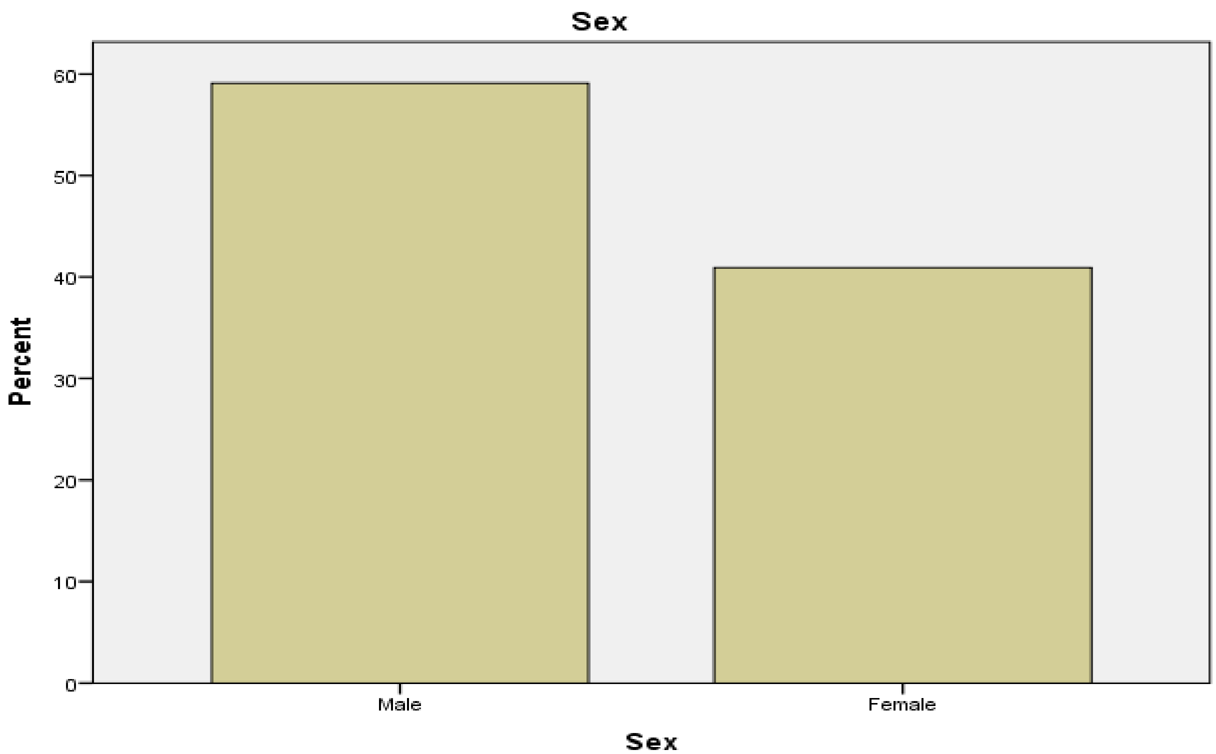

Fig 2. The Sex distribution of patients 41-60 years

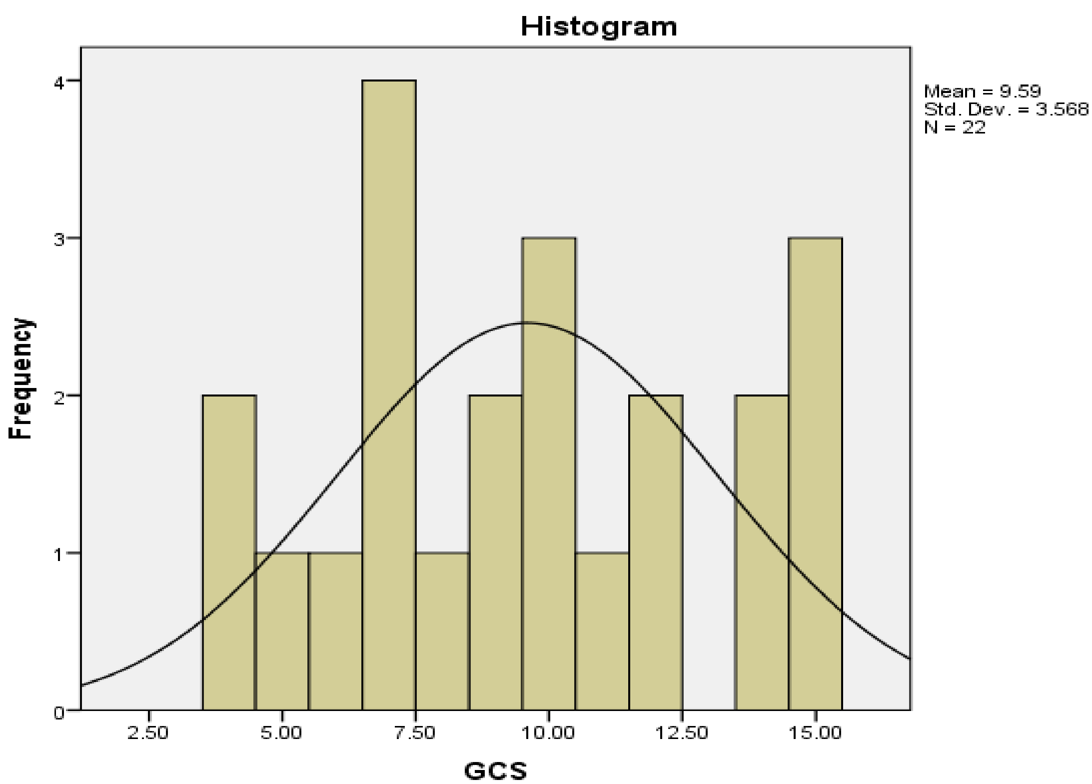

Fig 3. The Frequency of the GCS for patients 41-60 years.

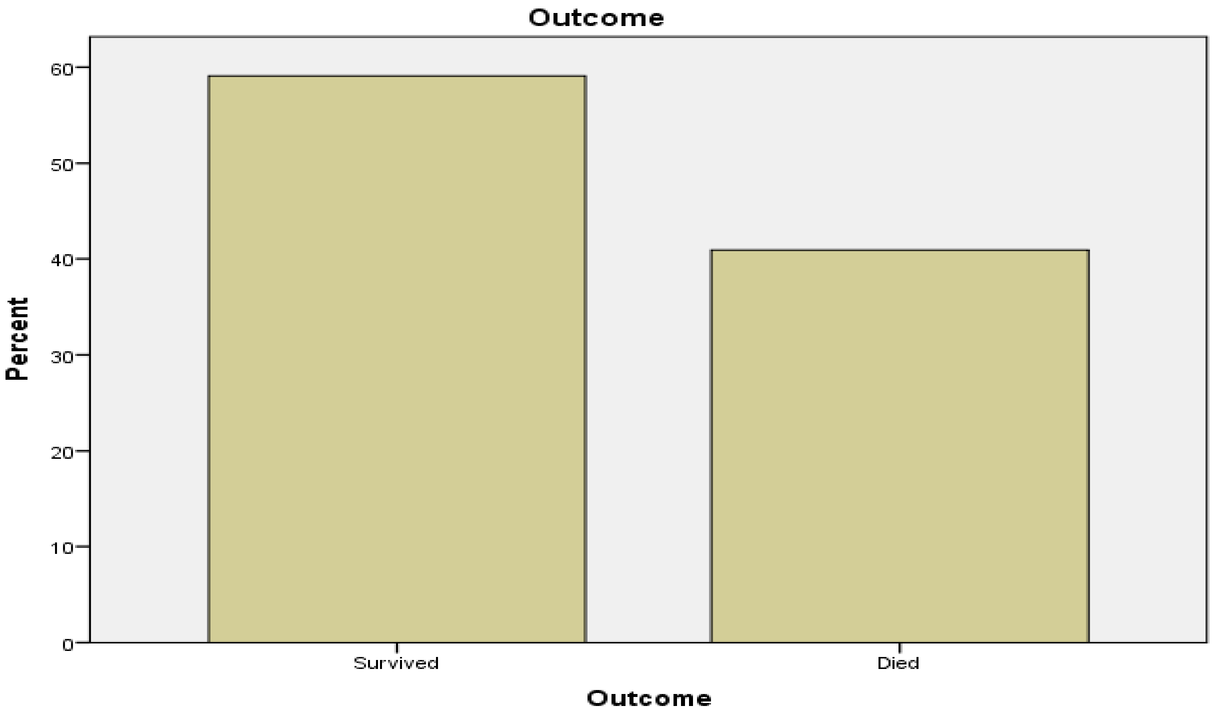

Fig 4. The Outcome for patients 41-60 years.

22 patients were studied. 13 males (59.1%) and 9 females (40.9%), Table 3. Table 1 shows the mean, median, mode, standard deviation, standard error, minimum and maximum for age, sex, GCS and outcome. Table 2 shows the age distribution. Table 3 shows the sex distribution. Table 4 shows the GCS and Table 5 shows the outcome.

The lowest GCS was 4 (9.1%) and the highest GCS was 15 13.6%, Table 4. GCS of 7 was the highest frequency 4 (18.2%), followed by 10 (13.6%) and 15 (13.6%), Table 4. 13 (59.1%) patients survived, 9(40.9%) patients died, Table 5.

More males were affected in this age group, p = 0.273. Death was less in this age group, p= 0.134. Males had fewer deaths, p = 0.128. Mortality increased with higher GCS, P=0.015, which is statistically significant.

IV. DISCUSSION

This study aims at examining the effect of gender on the outcome of SSAH in patients between the ages of 40 - 60 years.

22 patients were studied. 13 males (59.1%) and 9 females (40.9%). The mean age was 49.5, the median age was 49, the mode was 49. The mean GCS was 9.59, the median was 9.5, the mode was 7.

More males were affected in this age group. This corresponds to the findings of Charlotte H Harrison et al who stated, "we find a clear excess in men, whereas our results from the seventh decade onwards show either equal sex incidence, or a female predominance, depending on how the age categories are divided."[22]

The difference in male and female patients in the same age category could be mostly attributed to lifestyle. Yuankun Cai et al offer an explanation based on their study, "The proportion of smokers and drinkers was significantly higher in male patients than in female patients."[23]

Death was less in this age group. Mortality was less in this age group because they are relatively young and would most likely present early.

Males had fewer deaths. Males survive more than females possibly because of their genetic make up. Yuankun Cai et al has a similar finding, they stated, "our study found that the likelihood of cerebral ischemia was significantly higher in female patients with aSAH than in male patients with aSAH. This phenomenon could be because female patients with aSAH are more vulnerable to vasospasm. Studies have shown that early vasospasm predicts a higher incidence of SAH-related cerebral ischemia and a poorer prognosis. Female sex has been reported to be an independent risk factor for cerebral vasospasm after aSAH. Moreover, it has also been found that catecholamine metabolites, which reflect sympathetic excitation, have a higher level in the cerebrospinal fluid of female patients with SAH, which also suggests that they are more vulnerable to vasospasm."[23]

For male and female smokers, the risks are the same. Regarding smoking, the sex difference is reportedly smaller if not absent. [22]

Complicating the issue, sex differences in SAH incidence may interact with age, as well as with factors such as smoking and geographical region. For example, de Rooij et al found that sex differences began at age 55.[21,22]

Mortality increased with lower GCS. Low admission GCS is a poor prognostic factor. This and female sex are independent poor prognostic factors for SSAH in this age group.

Efforts should be intensified to tackle hemorrhage in the acute/subacute phase to prevent lowering the GCS which could be fatal. Most patients receive conservative treatment in this phase and if the GCS is found not to be improving urgent intervention is necessary. This would lower the raised ICP, prevent rebleed and abort their ugly sequelae. Intervention can be open, laparoscopic or cannulation with embolisation.
For prevention, we recommend regular monitoring of those at risk by CT or MR angiography. These include chronic or severe hypertensives, patients with previous bleeding episodes, patients with unruptured aneurysms, patients on blood thinners, connective tissue disorders, diabetics, etc.
This study has the limitations of available data. Many patients do not get to tertiary health centres where accurate diagnosis can be made. We suggest the pooling of data from multiple centres in our subregion, and health education to boost early referral and presentation to tertiary health institutions.

V. CONCLUSION

This study has been able to establish that age, gender and GCS have an impact on the outcome of SSAH. Patients in this age group, especially males, survive SSAH more. Low GCS is associated with increasing mortality. Efforts should be intensified to tackle the hemorrhage in the acute/subacute phase to prevent lowering the GCS which could be fatal. Routine monitoring of those at risk before and during the hemorrhage is necessary to improve outcome.

REFERENCES

[1]. N K de Rooij, F H H Linn, J A van der Plas, A Algra, G J E Rinkel. In cidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends, Neurol Neurosurg Psychiatry. 2007 Dec; 78(12): 1365–1372. Published online 2007 May 2. doi: 10.1136/jnnp.2007.117655.
[2]. Feigin V L, Lawes C M, Bennett D A.et al Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. Lancet Neurol 2003243–53. [PubMed] [Google Scholar]
[3]. Johnston S C, Selvin S, Gress D R. The burden, trends, and demographics of mortality from subarachnoid hemorrhage. Neurology 1998501413–1418. [PubMed] [Google Scholar
[4]. Thrift A G, Dewey H M, Macdonell R A.et al Incidence of the major stroke subtypes: initial findings from the North East Melbourne Stroke Incidence Study (NEMESIS). Stroke 2001321732–1738. [PubMed] [Google Scholar]
[5]. ACROSS study Epidemiology of aneurysmal subarachnoid hemorrhage in Australia and New Zealand. Stroke 2000311843–1850. [PubMed] [Google Scholar]
[6]. Lavados P M, Sacks C, Prina L.et al Incidence, 30-day case-fatality rate, and prognosis of stroke in Iquique, Chile: a 2-year community-based prospective study (PISCIS project). Lancet 20053652206–2215. [PubMed] [Google Scholar]
[7]. Kolominsky-Rabas P L, Sarti C, Heuschmann P U.et al A prospective community-based study of stroke in Germany—the Erlangen Stroke Project (ESPro): incidence and case fatality at 1, 3, and 12 months. Stroke 1998292501–2506. [PubMed] [Google Scholar]
[8]. Jakovljevic D, Sivenius J, Sarti C.et al Socioeconomic inequalities in the incidence, mortality and prognosis of subarachnoid hemorrhage: the FINMONICA Stroke Register. Cerebrovasc Dis 2001127– [PubMed] [Google Scholar]
[9]. Tsiskaridze A, Djibuti M, van Melle G.et al Stroke incidence and 30-day case-fatality in a suburb of Tbilisi. Results of the first prospective population-based study in Georgia. Stroke 2004352523–2528. [PubMed] [Google Scholar]
[10]. Vemmos K N, Bots M L, Tsibouris P K.et al Stroke incidence and case fatality in southern Greece. The Arcadia Stroke Registry. Stroke 199930363–370. [PubMed] [Google Scholar]
[11]. Abraham MK, Chang WW (November 2016). "Subarachnoid Hemorrhage". Emergency Medicine Clinics of North America. 34 (4): 901–916.
[12]. Carpenter CR, Hussain AM, Ward MJ, Zipfel GJ, Fowler S, Pines JM, Sivilotti ML (September 2016). "Spontaneous Subarachnoid Hemorrhage: A Systematic Review and Meta-analysis Describing the Diagnostic Accuracy of History, Physical Examination, Imaging, and Lumbar Puncture With an Exploration of Test Thresholds". Academic Emergency Medicine. 23 (9): 963–1003
[13]. van Gijn J, Kerr RS, Rinkel GJ (January 2007). "Subarachnoid haemorrhage". Lancet. 369 (9558): 306–18
[14]. Phan K, Moore JM, Griessenauer CJ, Ogilvy CS, Thomas AJ (May 2017). "Aspirin and Risk of Subarachnoid Hemorrhage: Systematic Review and Meta-Analysis". Stroke. 48 (5): 1210–1217. doi:10.1161/strokeaha.116.015674.

[15]. Rinkel GJ, van Gijn J, Wijdicks EF (September 1993). "Subarachnoid hemorrhage without detectable aneurysm. A review of the causes". Stroke. 24 (9): 1403–9.
[16]. Rosen DS, Macdonald RL (2005). "Subarachnoid hemorrhage grading scales: a systematic review". Neurocritical Care. 2 (2):110-8.
[17]. Hunt WE, Hess RM (January 1968). "Surgical risk as related to time of intervention in the repair of intracranial aneurysms". Journal of Neurosurgery. 28 (1): 14–20. doi:10.3171/jns.1968.28.1.0014.
[18]. Claassen J, Bernardini GL, Kreiter K, et al. (September 2001). "Effect of cisternal and ventricular blood on risk of delayed cerebral ischemia after subarachnoid hemorrhage: the Fisher scale revisited". Stroke. 32 (9): 2012–2
[19]. Teasdale GM, Drake CG, Hunt W, Kassell N, Sano K, Pertuiset B, De Villiers JC (November 1988). "A universal subarachnoid hemorrhage scale: report of a committee of the World Federation of Neurosurgical Societies". Journal of Neurology, Neurosurgery, and Psychiatry. 51 (11): 1457. doi:10.1136/jnnp.51.11.1457. PMC 1032822. PMID 3236024.
[20]. Ogilvy CS, Carter BS (May 1998). "A proposed comprehensive grading system to predict outcome for surgical management of intracranial aneurysms". Neurosurgery. 42 (5): 959–68, discussion 968–70
[21]. N K de Rooij, F H H Linn, J A van der Plas, A Algra, G J E Rinkel. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends, Neurol Neurosurg Psychiatry. 2007 Dec; 78(12): 1365–1372. Published online 2007 May 2. doi: 10.1136/jnnp.2007.117655.
[22]. Charlotte H Harrison, MRCP, Maxime Taquet, PhD, Paul J Harrison, FRCPsych, Peter J Watkinson, MD, Matthew J Rowland, PhD, “Sex and age effects on risk of non-traumatic subarachnoid hemorrhage: Retrospective cohort study of 124,234 cases using electronic health records,” Journal of Stroke and Cerebrovascular Diseases, https://www.strokejournal.org/article/S1052-3057(23)00219-7/fulltext#:~:text=Conclusions,over%2075-year%20age%20groups.
[23]. Yuankun Cai, Zheng Liu, Chenguang Jia, Jingwei Zhao, Songshan Chai, Zhengwei Li, Chengshi Xu, Tingbao Zhang, Yihui Ma, Chao Ma, Xinjun Chen, Pucha Jiang, Wenyuan Zhao, Jincao Chen* and Nanxiang Xiong, “Comparison of Sex Differences in Outcomes of Patients With Aneurysmal Subarachnoid Hemorrhage: A Single-Center Retrospective Study,” Frontiers in Neurology, 28 April 2022, Sec. Neuroepidemiology, Volume 13 - 2022 | https://doi.org/10.3389/fneur.2022.853513, https://www.frontiersin.org/articles/10.3389/fneur.2022.853513/full