

A 5-year study on the Epidemiology and Outcome of patients with Non-Traumatic Subarachnoid Hemorrhage in Malta

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Abstract:

Objective: The aim of this study was to measure the incidence, treatment and outcome of non-traumatic Subarachnoid Haemorrhage (SAH) cases occurring in Malta during the five-year period between January 2011 and December 2015, in order to determine whether the lack of a local neurovascular service is associated with a poor outcome.

Method: A retrospective analysis of adult patients (above the age of 16) diagnosed with non-traumatic SAH was carried out. The data collected included a five-year period from January 1st 2011 till December 31st 2015.

Results: The incidence of SAH was estimated at 4.04 cases per 100,000 population per year. An underlying aneurysm was found to be the cause of the SAH in 69.1 % of cases investigated with CT angiography or Cerebral Angiography. In these patients, definitive management in the form of coiling or clipping of the aneurysm was carried out, within the period between January 1st 2011 and December 31st 2015, in the United Kingdom as part of an agreement between the two countries. The outcome of these patients measured at 6 months using the Modified Rankin Scale (MRS) was found to be excellent.

Conclusion: Despite our geographical and logistical limitations, outcomes of those patients with initial low Hunt and Hess (H+H) scores have not been affected by the lack of a local neurovascular service. Results are comparable to those of other international centres. Further studies looking into feasibility of expanding our local services are being carried out.

Keywords

Subarachnoid haemorrhage, aneurysm, incidence, Modified Rankin Scale

Abbreviations:

- Subarachnoid Haemorrhage (SAH)
- Computerized Tomography (CT)
- Computerized Tomography Angiography (CTA)
- Magnetic Resonance Angiogram (MRA)
- Modified Rankin Scale (MRS)
- Hunt and Hess (H+H)
- Arterio-venous malformation (AVM)
- United Kingdom (UK)
- Mater Dei Hospital (MDH).
- Anterior communicating artery (ACA)
- Glasgow Coma Scale (GCS)
- Intensive Treatment Unit (ITU)
- Lower Urinary Tract Infection (LUTI)
- External Ventricular Drain (EVD)
- Cerebrospinal Fluid (CSF)
- Medical Out-patients (MOP)

Introduction

Subarachnoid Haemorrhage (SAH) refers to the extravasation of blood into the subarachnoid space between the pial and arachnoid membranes causing a haemorrhagic stroke.¹ It has an overall global incidence of 9/100,000 per year.² It may occur in a wide variety of clinical contexts including head trauma. Non-traumatic or spontaneous SAH is most commonly caused by a

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ruptured cerebral aneurysm and to a lesser extent due to arterio-venous malformation (AVM).

Mortality due to SAH has been shown to be significant at 50% with 10-15% dying prior to arrival at hospital.³

In January 2017, the population of Malta was reported as 420,869.⁴ Currently, there is only one study which describes the incidence and outcomes of non-traumatic SAH cases in the Maltese population. This was carried out over the 2-year period 2009-2010.⁵ The purpose of our study is to re-evaluate the incidence and outcome of non-traumatic SAH during the five-year period between January 2011 and December 2015. The study was also aimed at determining whether the lack of a local neurovascular service, and hence the transport of patients to the UK for definitive treatment, is associated with a poor outcome.

Study Methods

All patients in the Maltese Islands who present with symptoms suggestive of a SAH are managed at the main public hospital, Mater Dei Hospital (MDH). They are admitted under the care of one of our four Consultant Neurologists. Patients who are seen at private clinics are quickly transferred to the general hospital MDH for further investigation and treatment since there are no other facilities on the island equipped to treat this condition.

Data of adult patients (≥ 16 years of age), with a clinical diagnosis of SAH from January 1st 2011 till December 31st 2015, was collected and analysed from 4 separate sources:

1. Patients who were referred abroad for treatment of ruptured aneurysms were obtained from the Treatment Abroad Committee;
2. Patients whose cause of death on the death certificate was listed as "Subarachnoid Haemorrhage" from the Death Register;
3. Patients who were discharged from Mater Dei Hospital with a diagnosis of SAH were identified from the hospital activity analysis, using ICD9 coding system;
4. Patients who were diagnosed with SAH on CT Brain were collected using the hospital computer system RIS Centricity Web.

All patients who were diagnosed with a traumatic SAH were excluded.

The patients who died out of hospital were identified solely from the Death Register. All other patients were identified from more than one of the above mentioned sources, therefore ensuring that the data collection was thorough and complete. This method guaranteed that there were no missed SAH cases that were admitted to hospital.

Results

The total number of patients with definitive spontaneous non-traumatic SAH over the five-year period was 85. Therefore, the incidence rate of SAH in the Maltese population is calculated to be 4.04 per 100,000 population per year. There was a significant increase from the previous study which calculated the incidence to be 3.16 per 100,000 population per year.

a) Patient characteristics

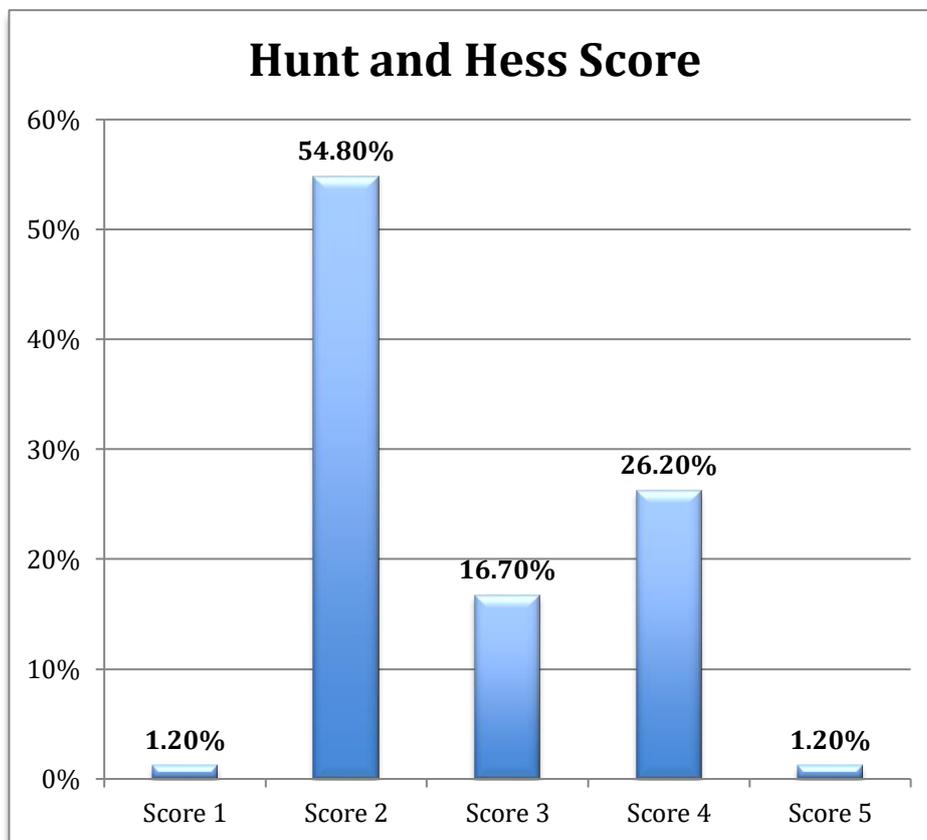
Of the 85 patients admitted with non-traumatic SAH over the study period, 49 (58%) were female and 36 (42%) were male. The mean age of presentation was 55 (range between ages 17 to 89). One patient died before arrival to hospital and before receiving medical attention. This patient was certified dead due to SAH according to their death certificate confirmed by post-mortem examination. The death of this patient was not analyzed further since the death happened outside of hospital and there were no available medical notes.

b) Clinical presentation

Almost all patients presented with sudden onset, severe, thunderclap headache, usually associated with photophobia, nausea and vomiting. 21 patients presented with loss of consciousness, 9 presented to hospital in an unresponsive state and 3 presented with confusion. One patient presented with a generalized tonic-clonic seizure, whilst another 5 patients presented with cardiac arrest needing resuscitation. Other commonly described symptoms included dizziness, neck pain, inappropriate/slurred speech and visual disturbances such as blurred or double vision. Tables 1 and Figure 1 seen below demonstrate the H+H Scores on admission.

Table 1: Hunt and Hess Scores on admission

Hunt and Hess Score	Percentage for total of 84 patients
1	1.2%
2	54.8%
3	16.7%
4	26.2%
5	1.2%

Figure 1: Hunt and Hess Scores on admission - percentage for total of 84 patients**c) Risk factor profile**

The main risk factors described in our cohort of patients were: hypertension in 14 patients, smoking in 19 patients, hyperlipidemia in 4 patients and diabetes mellitus in another 4 patients. Other pre-existing conditions included: 1 patient with Systemic Lupus Erythematosus, 1 patient with Chronic Lymphocytic Leukaemia, 1 patient with glucose-6-phosphatase deficiency and 1 patient who was diagnosed with Hepatitis C.

d) Investigations

All patients, excluding the patient who died out-of-hospital, had a non-contrast CT scan of the brain. SAH was confirmed in all patients on CT scan except for two patients. One of these presented 7 days after onset of severe headache. This patient had an unremarkable CT scan, however a subsequent MRI of the brain confirmed a SAH and a right-sided anterior communicating artery (ACA) aneurysm. The other patient whose CT scan was reported as normal presented with an occipital

thunderclap headache radiating to the frontal area. A follow-up CT angiogram reported the presence of basilar artery spasm.

A lumbar puncture was only carried out on one patient and xanthochromia was confirmed with an opening pressure of 35 mmH₂O, confirming the diagnosis of SAH.

Following a diagnosis of SAH on CT of the brain, 15 patients with a low Glasgow Coma Scale (GCS) and multiple co-morbidities were deemed unfit for angiography. They were not investigated with further imaging modalities and were treated conservatively. Of these, 14 patients passed away within the first few days of admission. The remaining patient had a 6-month post-diagnosis MRS score of 5 and was being managed at the rehabilitation hospital.

The other 69 patients were investigated for the possibility of underlying aneurysm with further

imaging modalities including CT cerebral angiogram (CTA) or magnetic resonance angiography (MRA). 49 of them were found to have one or more aneurysm (71% of all those patients who received angiography). 40 of these patients were referred to the United Kingdom (UK) for definitive treatment of the aneurysm and 9 were not. Of these 9 patients who remained at MDH, 8 patients passed away during the admission and 1 survived to the 6-month follow-up visit. The 20 patients who were investigated with further imaging modalities but did not have any cerebral arteriovenous malformations or cerebral aneurysms detected were managed symptomatically at MDH. This is summarised in Figure 2 and detailed in Table 2 below.

Figure 2: Summary of investigation and patient flow between 2011 and 2015.

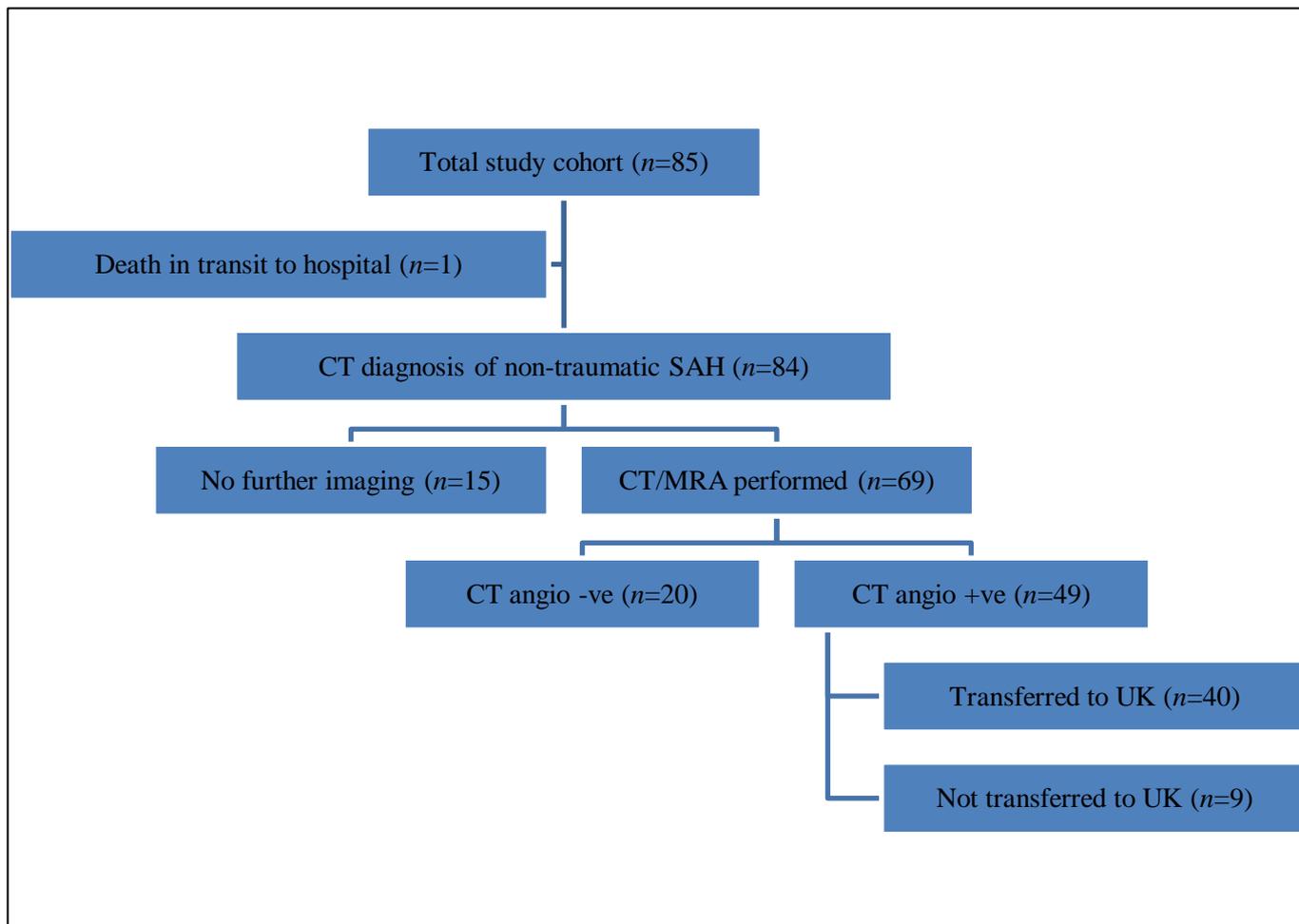


Table 2: Details of investigation and patient flow in each of the 5 years of the study.

	2011	2012	2013	2014	2015	Total
CT diagnosis of non-traumatic SAH	16	15	19	15	19	84
No further imaging	7	0	4	3	1	15
CT angio -ve	4	6	4	2	4	20
CT angio +ve and transferred	5	8	9	8	10	40
CT angio +ve and not transferred	0	1	2	2	4	9

Table 3: List of post-op complications reported in 16 patients treated abroad

Patient	Complications
1	Frontal lobe ischemia rendering him aphasic, global weakness 3/5, apathetic; LUTI E.Coli
2	Cerebral salt wasting syndrome
3	Staphylococcal sepsis; fluctuating symptoms of aggression and visual hallucinations; severe postural hypotension
4	Cataracts; right eye ptosis
5	Vasospasm; drop in GCS
6	Seizures
7	Puncture site hematoma/pseudoaneurysm
8	UTI
9	Intracerebral bleeding; Bilateral ischemic infarcts
10	Frontotemporal stroke; Right hemiparesis
11	Neurogenic pulmonary oedema; Nosocomial chest infection
12	Vasospasm
13	Long QTc intervals on ECG
14	Re-bleed from aneurysm
15	Ventriculitis with coagulase-negative streptococcus, followed by CSF leak from his EVD site
16	Hydrocephalus, extreme agitation; multisystemic pathology including Klebsiella Pneumoniae chest infection.

Table 4: Modified Rankin Scale (MRS)

	MRS								<i>Total</i>
	0	1	2	3	4	5	6	Lost to f/u	
Number of patients with no angiography	0	0	0	0	0	1	13	1	<i>15</i>
Number of patients transferred to UK	17	8	1	1	1	2	1	9	<i>40</i>
Number of patients with +ve CTA but not transferred	0	0	0	0	1	0	8	0	<i>9</i>
Number of patients with -ve CTA and not transferred	16	2	0	0	0	0	2	0	<i>20</i>
<i>Total</i>	<i>33</i>	<i>10</i>	<i>1</i>	<i>1</i>	<i>2</i>	<i>3</i>	<i>24</i>	<i>10</i>	<i>84</i>

e) Management

Most patients were admitted to Neuro-Medical Ward, however the patients with a low GCS on admission were managed directly in Intensive Care. Upon diagnosis of SAH, treatment with Nimodipine, lactulose and analgesia was immediately initiated.

f) Length of Stay

Of the 39 patients that were transferred to the UK for further treatment, 31 of them had an average stay in Malta of 2.84 days before being flown abroad. 5 patients required an extended stay at ITU in view of initial low GCS, averaging 26 days. 2 patients had missing information in their medical file and 1 patient was flown to his home country with no further input regarding management.

The average stay of 27 patients that received treatment abroad was that of 19 days. This has to take into consideration their post-op care and any complications that arose. 11 patients did not have the official discharge letter in their medical file, hindering us from obtaining official dates and any procedures done. One patient spent 10 days in hospital; however, no treatment was eventually given.

g) Outcome of SAH

Patients in general had a good long-term outcome from their coiling or clipping procedure. However, a number of complications were reported post-op, as indicated in Table 3.

h) Complications occurring in patients with SAH who did not undergo coiling or clipping

One patient who was managed conservatively suffered a small area of infarction left frontal region, including severe headaches (repeat CT Brain showed no hydrocephalus but resolution of SAH) and high blood pressure.

i) Post-treatment follow-up

Patients were advised to have repeat imaging between 4 to 6 months after the procedure in Malta. This ranged from CT scans, an MRA or a cerebral angiogram, depending on the patient's case. Every patient was followed up at MOP to assess for any residual symptoms and to ensure that the aneurysm/AVM was successfully treated with no evidence of a recurrence of bleeding.

Two patients who were referred to the UK for definitive treatment were not of Maltese nationality. They did not return to Malta after transfer abroad and were lost to follow-up. The remaining patients

who underwent coiling or clipping and returned from the UK, were followed up at Neurology Outpatients for at least 6 months.

j) Mortality

Out of the total of 85 patients diagnosed with non-traumatic SAH, 25 patients passed away during the admission at MDH or at the rehabilitation hospital before the 6-month follow-up. (29% mortality). All deaths occurred within an average of 5.41 days. Out of the total 40 patients who were transferred to the UK for definitive treatment, 39 of them survived past the 6 month follow-up. The remaining patient who was transferred, passed away after 30 days in the UK post-coiling. Eight out of nine patients who were diagnosed with an aneurysm on CTA and not transferred abroad succumbed to their illness. The 6-month mortality of patients transferred to the UK was therefore 2% while that of the patients who were not transferred was 88.9%. The majority of the deaths occurred in patients with a H+H score of >3 on admission and in patients who were deemed unfit to undergo further investigations during the admission and not stable enough for transfer abroad.

It must be noted that two of the patients who were transferred for treatment abroad were lost to follow-up since they returned to their respective home countries after definitive treatment.

This left 7 patients from the transferred abroad group who were lost to follow-up or did not attend the 6 month post treatment review.

Table 4 shows the Modified Rankin Score at 6 months after the initial presentation for the patients who were followed-up.

Discussion

All patients diagnosed with a SAH are ultimately referred and managed at MDH, the main acute hospital in Malta and the only hospital offering the services of a critical care unit. In our study, the data was compiled in such a way so as to represent all cases of non-traumatic SAH which occurred in Malta during the study period chosen. The incidence of 4.04 per 100,000 population per year is on the lower side of average incidence data however it has shown a rise when compared to the previous incidence of 3.16 per 100,000 population measured during the period between 2009-2010. The worldwide incidence of non traumatic SAH has been shown to be about 10.5 per 100,000 person

years.¹⁰

Patient who are diagnosed with a ruptured aneurysmal SAH, should ideally receive definitive treatment as early as possible. Every effort is made from our end in order to minimize delays in transfer of patients abroad, however certain logistical limitations may be inevitable; such as when the patient remains unfit for air transfer and requires stabilization. Our audit shows that the mean number of days from initial presentation to definitive treatment in the UK was 2.84 days.

The average hospital volume estimated from our results adds up to a value of 17 cases per year. The association between outcomes for patients with SAH and hospital treatment volume has been described in multiple studies.⁶⁻⁸ It has been shown that hospitals which treat more cases of SAH, have substantially lower rates of in-hospital mortalities, when compared to low-volume hospitals.⁶ Better outcomes at high-volume hospitals may be attributed to the specialized services and staff expertise. The definition of high-volume hospitals described in the literature varies. It ranges from cut-points between 5 cases per year⁷ and up to 45 cases per year.⁸ For ruptured aneurysms, it has been shown that an institution using coil embolization would be expected to have fewer in-patient deaths when compared to an institution which never used this technique.⁸

Selection bias giving rise to confounding factors occurs since certain high-risk and unstable patients with ruptured aneurysms are not considered for coil embolization and physicians are reluctant to transfer such cases with a poor prognosis.⁸

The literature shows that patients who are acutely ill with high Hunt and Hess grades after SAH can however undergo successful coil embolization despite their poor medical condition and a high frequency of vasospasm. In one series, 27 patients with 29 aneurysms were all H+H grade 4 or 5 (poor grade) and were treated within 72 hours after ictus. Sixteen patients (59%) died within 30 days of SAH, whereas 11 (41%) survived. Eight patients (30%) had a favorable outcome (MRS ≤ 2). Therefore, these results were similar to what was seen in aggressively treated surgical patients. Many of these patients have a good clinical outcome, although there still remain high rates of morbidity and mortality with this disease.⁹ Such a consideration would therefore justify ongoing efforts at introducing a neurovascular service

locally.

The main limitation of this audit is the small population size, giving our study a low power.

Conclusion

Our study has shown that the incidence of non-traumatic SAH in Malta remains on the low-incidence range, when compared to other countries. CTA and MRA were successful in diagnosing at least one aneurysm in each of the 71% patients with a positive CT brain. Despite the low incidence and the logistical limitations for delivering patients to centres in the UK for definitive treatment of aneurysmal bleeds, our standard of care and survival rates are not below those of other centres. The 6-month mortality of patients transferred to the UK was 2% while that of the patients who were not transferred was 88.9%.

However current efforts at introducing a specialised neurovascular service locally could still result in the added benefits of avoiding logistical problems in transfer of patients, reducing costs, and in the possibility of treatment of the high-risk patients who would otherwise not receive definitive coiling of the aneurysm. Further studies would then be required in order to assess such a service and the outcome of both the low- and high-risk patients with non-traumatic SAH receiving treatment.

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