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THE OUTCOME OF INTRACRANIAL SUBDURAL EMPYEMA AT STEVE BIKO ACADEMIC HOSPITAL: RETROSPECTIVE STUDY

By

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DECLARATION

I declare that the master's script, which I hereby submit for the degree Master of Medicine in Neurosurgery at the University of Pretoria, is my own work and has not previously been submitted by me for a degree at another university.

The study will also be submitted for journal publication.

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DEDICATION

I dedicate this work to my beautiful and loving wife, Doctor Sebotse Thobejane for having stood by me throughout my hurdles in life till today, your support, prayers and encouragements were second to none my love

To my handsome boys, Ofentje and Seetja Thobejane thank you for always managing to bring a smile on my face when I came home

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ABSTRACT

Objectives: Intracranial subdural empyema (ICSDE) can be a devastating condition, with a sequelae ranging from epilepsy, focal deficits to death. Factors affecting the outcome in subdural empyema range from level of consciousness, the extend of subdural pus at the time of diagnosis and the type of surgical procedure performed. Previous studies have conflicting results of unfavourable prognostic factors associated with ICSDE. The outcome of this condition at Steve Biko Academic Hospital (SBAH) is reported, as well as factors influencing the outcome.

Methods: A retrospective analysis of all the patients admitted at neurosurgery unit of SBAH during 2006 – 2010 period with confirmed subdural empyema on brain CT scan and at surgery. Data sheet was used to collect all clinical information from patients' records. Glasgow Outcome Scale and Henk W. Mauser grading were used to report on the outcome.

Results: A total of 34 patients (20 males and 14 females) with mean age of 16.1 years were admitted with a diagnosis of ICSDE. The common presenting features were headache (58.8%), fever and seizures (47.0% each). Over 61% of patients had hemiplegia at presentation. CT scan confirmed subdural collections with 70.6% over the convexity, 23.5% at the convexity and parafalx and only 5.9% had bilateral collections. Complicated paranasal sinusitis was the origin of infection in 82.3%, followed by meningitis with 8.8%. Burr hole washout was done in 52.9% of patients, while 38.2% had burr holes with drains in situ and 8.8% had craniotomy to evacuate the subdural pus. All the patients were given empiric triple antibiotic therapy. Streptococci species were the most cultured organisms in the 19 (56.0%) patients who had positive cultures, however 15 (44.0%) patients had negative cultures. Resistance to penicillin was noted in 5.0% of cases only. Sixty-five percent of patients had good outcome with no seizures nor neurological deficits. The overall mortality was 15.0% in this study, with none from patients who had craniotomy.

Conclusion: Clinical presenting features and organisms cultured seems to be the same internationally, particularly those due to complicated sinusitis. Empiric triple antibiotic therapy of 3rd generation cephalosporin plus vancomycin plus metronidazole is still relevant at SBAH. Factors associated with favourable outcome were ages between 11 and 20 years, and craniotomy as the surgical procedure of choice.

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CHAPTER 1: ORIENTATION AND GENERAL BACKGROUND

1.1 INTRODUCTION

This chapter gives the overview of the research project. It includes background of the study, the problem statement and the importance of conducting a study of this kind. The aim and objectives are defined.

1.2 BACKGROUND

Intracranial subdural empyema (ICSDE) refers to a collection of pus in the space between the dura and the arachnoid layers covering the brain[1,2,3]. It has no anatomic barriers to spread except the falx cerebri and tentorial cerebelli[2]. It is distinguished from abscesses within the brain substance with capsule around it. Incidence is higher in developing countries, with male:female ratio 2:1 to 3:1[2,3,4]. It can occur at any age group with mean of 10 – 40 years[1,2,3]. Predisposing conditions for the development of ICSDE are direct extension of local infection (contiguous spread) e.g. complicated pansinusitis in 40 – 80%, penetrating cranial trauma, post neurosurgical procedure, haematogenous spread or as a complication of meningitis[3].

Clinical features may be rapidly progressive with symptoms and signs related to either raised intracranial pressure, meningeal irritation, focal cortical inflammation or thrombophlebitis of cerebral vein and/or venous sinuses. Most patients have headache, fever and focal neurological deficits[3]. Seizures occur in up to 50% of patients[3]. Diagnosis of ICSDE should be suspected in any patient with meningeal signs and a focal neurological deficit. Imaging tools are of valuable importance and include brain CT scan and brain-MRI. Lumbar puncture carries high risk of herniation and may be sterile, particularly in patients with focal signs or raised intracranial pressure[5]. Organisms cultured depends on the source of infection, with aerobic and anaerobic streptococci common in patients with complicated sinusitis, and staphylococci and gram negative species observed in trauma/postsurgical patients. However up to 40% of cases have sterile cultures[3].

ICSDE is a surgical emergency because anti-microbial therapy alone does not reliably sterilise the empyema. Antibiotic penetration into this space is poor. Optimal surgical approach is controversial. The following has been reported as preferred surgical methods for drainage with different outcomes – craniotomy[6,7,8,9], burr hole washout[10,11] or burr holes with drain in situ[12]. The emphasis should be put on source control when dealing with ICSDE, as it carries mortality of between 6 – 35%[2].

1.3 RESEARCH PROBLEM

Subdural empyema despite being reported as rare in developed countries (reporting only 48 cases in 34 years in Europe)[11], it remains a common intracranial infection seen in South Africa (with some studies reporting 699 cases in 15 years)[8] with devastating outcome if not well managed. There has not been a baseline study evaluating the outcome of this condition at Steve Biko Academic Hospital (SBAH).

Mortality in South Africa is variable with Durban reporting as high figures as 22.3%[8] compared to 7.7% at Cape Town[7]. Previous studies have conflicting results of unfavourable prognostic factors associated with ICSDE. Hence the need to document the outcome and factors affecting the outcome of ICSDE at SBAH, as this can have positive clinical implications for the treating physicians.

1.4 AIM AND OBJECTIVES

1.4.1 Primary Objectives

To document the outcome of intracranial subdural empyema at Steve Biko Academic Hospital

To determine factors influencing the outcome of ICSDE at SBAH

1.4.2 Secondary Objective

To compare the above findings with existing world literature on subdural empyema

CHAPTER 2: LITERATURE OVERVIEW

2.1 INTRODUCTION

In this chapter, the literature is reviewed and the collected knowledge divided into manageable, sequential sections.

2.2 LITERATURE REVIEW

Several studies are available on this condition but very few reported on the factors affecting the outcome in patients with cranial subdural empyema. Overall mortality of patients with subdural empyema is reported to be between 10 and 20% but can be as high as 75% in patients who are comatose[13].

Henk W Mauser et al reviewed factors affecting the outcome in subdural empyema. They concluded that the level of consciousness and the extent of the subdural pus at the time of diagnosis have a significant bearing on the outcome[14]. Earlier on they have also reported that the delay in diagnosis and surgical treatment had a negative bearing on the outcome[11].Agrawal Amit et al reviewed subdural empyema and its management, they identified the following as unfavourable prognostic factors : encephalopathy, elderly or younger than 10 years, delay in starting antibiotics, and sterile cultures[3]- Table 1.

In an attempt to resolve the issue on the ideal surgical method in treating subdural empyema, S.A. Mat Nayan et al analysed the efficacy of these two (burr holes and craniotomy) surgical methods in terms of the outcome. They concluded that wide cranial opening (craniotomy) is the better surgical method for the treatment of intracranial subdural empyema compared to a limited procedure such as burr holes[9]. This was of course in contrast to earlier studies that reported better outcome with burholes than craniotomy by Miller et al[10].

Pasquale de Bonis et al developed treatment plan for both cranial and spinal subdural empyema (figure 1), especially after recognizing that the two surgical options both have their places in the management of patients with subdural empyema[15]. Steve Ryu et al compiled a comprehensive guide on the appropriate choice of antibiotics based on the likely source of infection, taking into consideration the possibility of multiple organisms[13] - Table 2.

TABLE 1: Prognostic Factors Associated With SDE[3]

Unfavourable prognostic factors • Encephalopathy or coma at the time of presentation • Elderly or younger than 10 years • Delay in starting antibiotics • Sterile cultures
Favourable prognostic factors • Craniotomy as surgical modality (rather than burr holes) • Early treatment (surgery and antibiotics) • Young age (10 -20 years is optimal) • Patient is alert, awake, and orientated at the time of presentation • Paranasal sinus as source of initial infection • Isolation of aerobic streptococci in the culture

FIGURE 1: Treatment Plan of SDE[15]

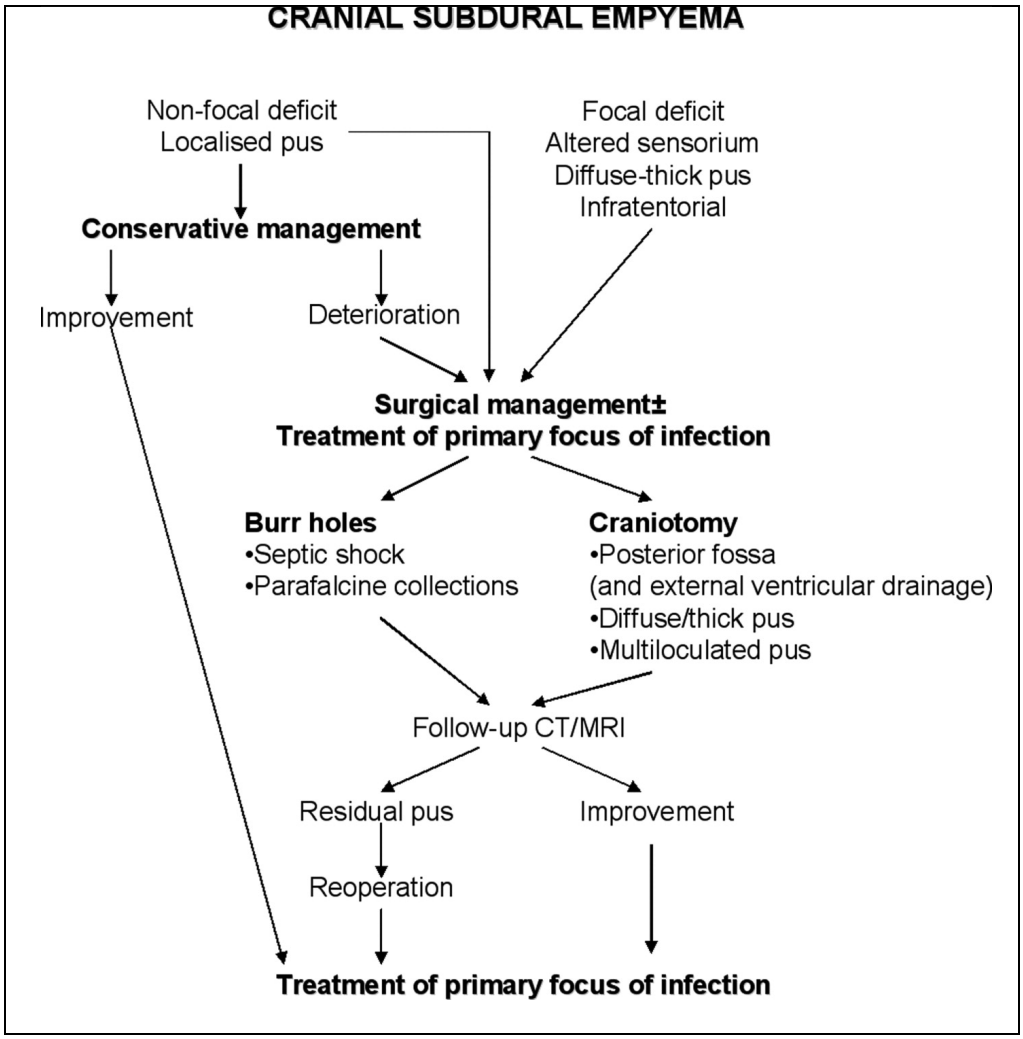


TABLE 2: Empiric Treatment Recommendations for ICSDE and EDA[13]

Presumptive Cause	Likely Pathogen	Antibiotic Therapy
Sinusitis, Otitis, Mastoiditis	Aerobic, microaerophilic, and anaerobic streptococcus, Bacteroides, S.aureus, Enterobacteriaceae, H. Influenzae, Pseudomonas aeruginosa	Vancomycin + ceftriaxone or cefepime + metronidazole
Surgery, Trauma	S. aureus, Coagulase-negative staphylococci, Clostridium, Enterobacteriaceae	Vancomycin + ceftriaxone or cefepime
Dental origin	Bacteroides, Aerobic and anaerobic streptococci, Fusobacterium	Ceftriaxone + metronidazole
In children	S. pneumonia, H. Influenzae, Neisseria meningitides	Vancomycin + ceftriaxone or cefepime
In neonates	Enterobacteriaceae, Group B streptococci, Listeria monocytogenes	Ampicillin + ceftriaxone or cefepime

Local Studies

Several studies were done locally (South Africa) at tertiary and regional hospitals to evaluate the incidence, the outcome of both surgical modes of treatments, pathogens cultured and the overall outcome of this condition at their institutions.

Arnold P.L. et al analysed 90 cases at Groote Schuur Hospital to determine the outcome looking at both surgical treatment (burr holes versus craniotomy). They concluded that burr holes were easier and safer surgical intervention for the treatment of subdural empyema compared to craniotomies. They reported 86% good recovery and a mortality of 7.7% only[7].Nathoo N. et al looked at 699 patients at Nelson R. Mandela Hospital in a retrospective study, again assessing the outcome when using burr holes or craniotomy. They concluded that craniotomy improves the outcome for cranial subdural empyema and hence their recommended surgical procedure of choice. Mortality for burr holes was 23.3% and that in craniotomy was 8.4%.[8]

Tshifularo M et al reported mortality as low as 5% on his work at Doctor George Mukhari Hospital[16].Olwoch I.P. looked at local microbiology and spectrum of sensitivity and resistance of organisms to antibiotics. This of course will assist in adapting the recommended international guidelines on empiric antibiotics for an effective and appropriate choice of antibiotic coverage based on local prevalence at Chris Hani and Charlotte Maxeke Hospitals[17].

At SBAH there is no study done to evaluate this condition or report on the outcome of intervention.

CHAPTER 3: RESEARCH METHODOLOGY

3.1 STUDY DESIGNS

This was a retrospective descriptive study over a 5 year period.

3.2 SETTINGS

This study was conducted at the Neurosurgery Unit at SBAH. Steve Biko Academic Hospital is the referring hospital for local district hospitals in Gauteng province and the Mpumalanga province.

3.3 PATIENT/RESEACH OBJECT SELECTION

3.3.1 Inclusion Criteria

All patients who were admitted at the neurosurgery unit (wards and the intensive care unit) from 2006 – 2010 with confirmed subdural empyema on CT scan and at surgery. Patient's records were reviewed from time of admission till discharge and outpatient follow-up of up to 6 months (average). Included were all the patients who presented with symptoms suggestive of intracranial pathology and were confirmed to have subdural collection(s) with contrast enhancement on Brain CT scan – figure 2, CT of the air sinuses was also included to assist in demonstrating the origin of pus. Patients were then taken to theatre to evacuate the subdural collection and it was confirmed to be pus intraoperatively. The patients underwent different surgical procedures depending on the attending neurosurgery registrar and consultant on duty's discretion. They either had multiple burr hole washout repeatedly until pus was evacuated, or burr holes leaving drains in situ to encourage on-going drainage in the ward, or just had large craniotomy washout only. All the patients received triple antibiotic therapy of ceftriaxone or meropenem plus vancomycin plus metronidazole. The specimen was send to the laboratory for microscopy, culture and sensitivity. On average those with positive cultures, the results were available within 7 days and antibiotics were changed according to the sensitivity results. The antibiotics were given intravenously for two weeks or until the pus was cleared as demonstrated by the follow-up scan (done every 4-7 days until no pus was seen on scan) then discharged on oral antibiotics (Cotrimoxazole and/or Co-amoxiclav) for another four weeks. Patients were then followed up at out-patient department for a minimum period of 6 months. All patients with deficits (physical or cognitive) received evaluation and management by appropriate specialities – physiotherapy, occupational therapy, speech and audiology.

3.3.2 Exclusion Criteria

Patients who were not operated to confirm presence of subdural pus.

Patients with brain abscesses.

3.4 MEASUREMENTS

Data was collected from patients' files. Factors such as age, sex, level of consciousness using Glasgow Coma Scale (appendix A) at the time of presentation and interventions were recorded on Data Collection Form (appendix B). Criteria for diagnosing subdural empyema : patient with fever, headache, new onset seizures/neurological deficits, this followed by CT scan imaging confirming contrast enhancing subdural collection. The treatment guidelines applied (burr holes versus craniotomy) on the management of these patients was recorded, including the culture results from microbiology and choice of antibiotics used. Neurological deficits before and after treatment, the source/cause of infection was documented. Henk W. Mauser grading system for morbidity of survivors of intracranial subdural empyema and Glasgow Outcome Scale were used to evaluate the outcome of this condition (appendices C and D respectively).

3.5 DATA ANALYSIS

The sample size consisted of all patients who were diagnosed with intracranial subdural empyema during the period 2006 to 2010. There were a total of 34 patients who met the criteria. The analytical tools that were used in order to achieve the objectives of the study firstly included descriptive statistics which mainly consist of frequency tables and graphical representation of the data. Secondly, contingency tables were used to determine proportions between the surgical procedure and mortality, Glasgow Outcome Scale and other variables such as gender, age and clinical features. Data was analysed using STATA version 11.

3.6 ETHICAL CONSIDERATIONS

This study has been approved by the Research Ethics Committee, faculty of Health Sciences, University of Pretoria – 237/2011.

All the patients who met the inclusion criteria for the study were assigned numbers to protect their identities in the research manuscripts, publication and presentations. No conflict of interest existed with all people involved in the study. The raw data will be kept for 15 years in the Department of Neurosurgery (Steve Biko Academic Hospital).

CHAPTER 4: RESEARCH FINDINGS

Data

TABLE 3: Demographics

Sex	Frequency	Percentage (%)
Male	20	58.82
Female	14	41.18
Age groups (Years)		
0 - 10	9	26.47
11 - 20	16	47.06
21 - 30	6	17.65
31 above	3	8.82

A total of 34 patients were enrolled in the study having satisfied the criteria, 20 males and 14 females. Their ages were ranging from 5 months to 43 years, with mean age of 16.1 and standard deviation of 9.4 years

TABLE 4: Infection origin

Infection Origin	Frequency	Percentage (%)
Complicated sinusitis	28	82.35
Head trauma	1	2.94
Surgical procedure	1	2.94
Meningitis	3	8.82
Pneumonia	1	2.94
TOTAL	**34**	**100.00**

Twenty eight patients (82.3%) had complicated paranasal sinusitis as the origin of the infection, followed by 3 (8.8%) with meningitis.

FIGURE 2: CT scan demonstrating left subdural and parafalx empyema

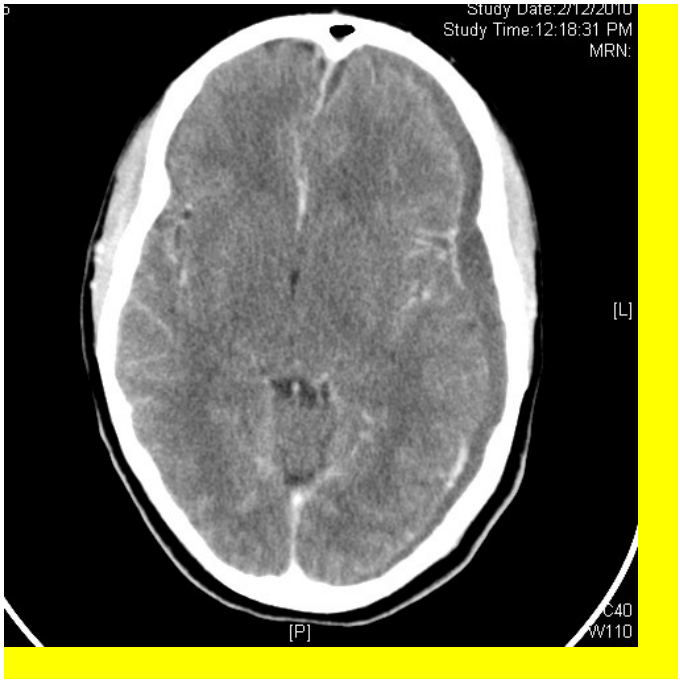
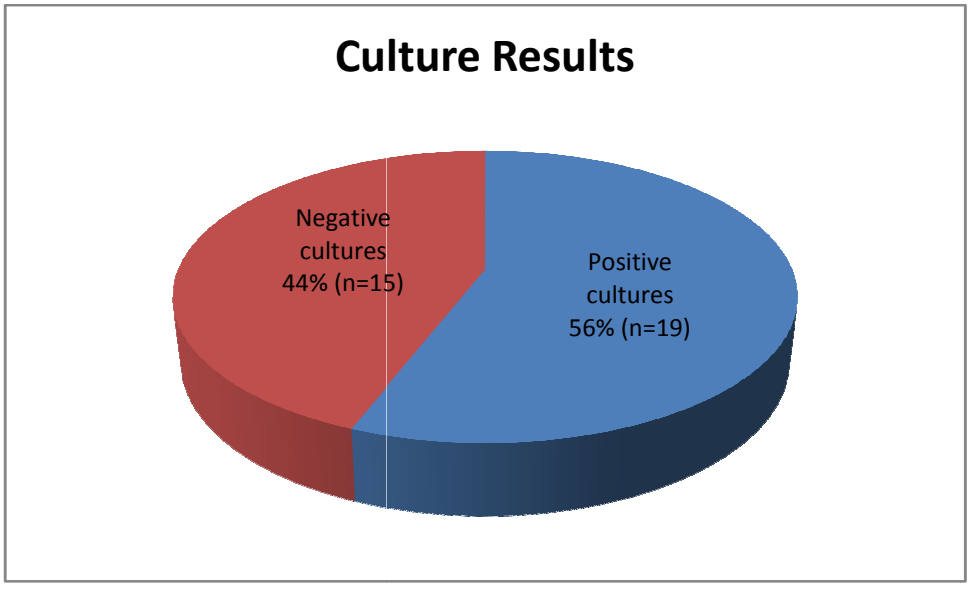
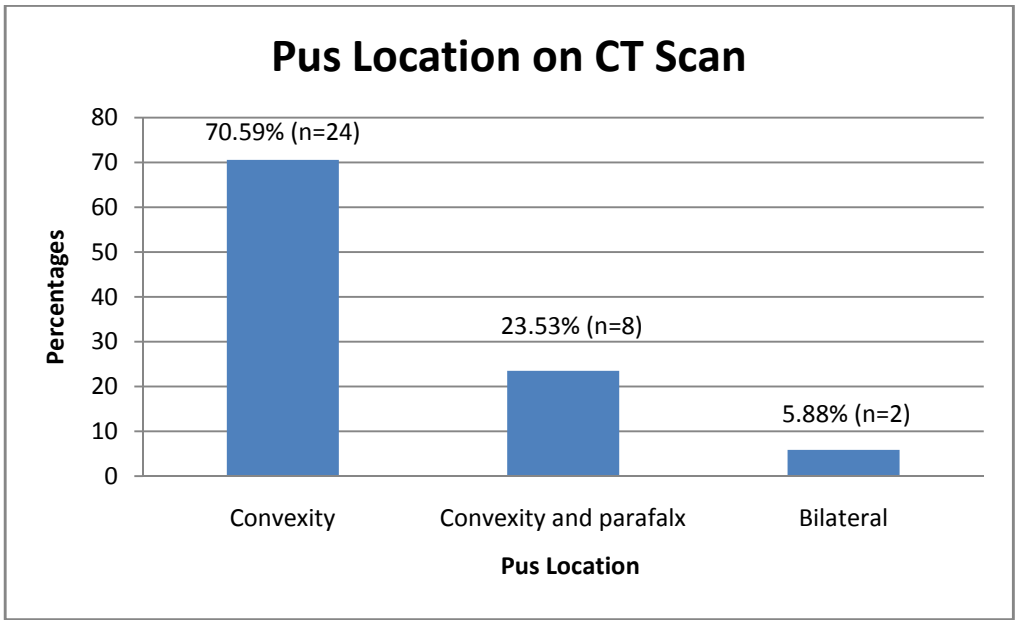


FIGURE 3: Culture Results



Pus drained was send for microscopy and sensitivity. 56% had positive cultures while 44% had negative growths.

FIGURE 4: Pus Location on Contrasted Brain CT scan



Twenty four patients had pus located on the convexity of the hemisphere involved and only 2 had pus bilaterally.

TABLE 5: Pathogens

Pathogens	Number	Sensitive (S)/Resistance (R)
1. ß - haemolytic streptococci	8	S
2. ą - haemolytic streptococci	5	S
3. Staphylococci	1	S
4. Gram negative – Klebsiella	1	S
H.Influenza	1	S
Serratia	1	S
Salmonella sp	1	S
5. Mixed	1	S

Streptococci were identified in 13 (68%) patients and gram-negative organisms identified in 4 (21%) cases.

TABLE 6: Clinical Features

Presenting Features		Number	Percentage (%)
1. Headache	Yes	20	58.82
	No	14	41.18
2. Fever	Yes	16	47.06
	No	18	52.84
3. Seizure	Yes	16	47.06
	No	18	52.84
4. Hemiplegia	Yes	21	61.76
	No	13	38.24
5. Orbital discharge	Yes	10	29.41
	No	24	70.59
6. Nausea and vomiting	Yes	7	20.59
	No	27	79.41

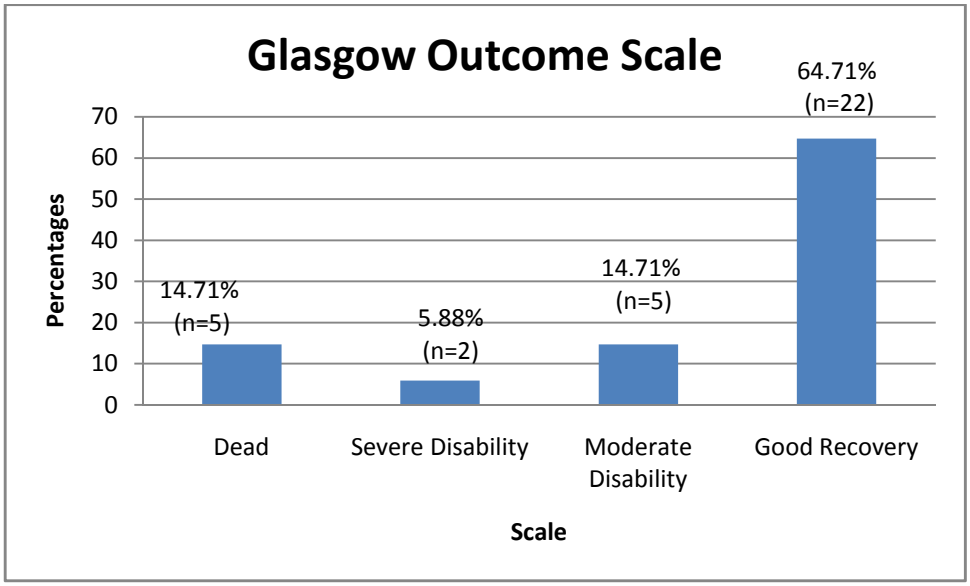
Common presenting feature was hemiplegia (62%), but patients still demonstrated the triad of headache, fever and seizures.

TABLE 7: Surgical Procedures

Procedure	Number (%)	Repeats (%)	Mortality (%)	Average Hospital Stay (Days)
Burr holes without drain	18 (52.9)	14 (77)	2 (11)	30
Burr holes with drain	13 (38.2)	4 (30)	3 (23)	29
Craniotomy	3 (8.8)	0	0	30
TOTAL	**34**			**30**

Eighteen patients had burr holes and 14 (77%) repeats. Thirteen had burr holes with drains in situ and only 4 (30%) requiring repeat surgery. Three had craniotomy done and none needed re-operation.

FIGURE 5: Glasgow Outcome Scale



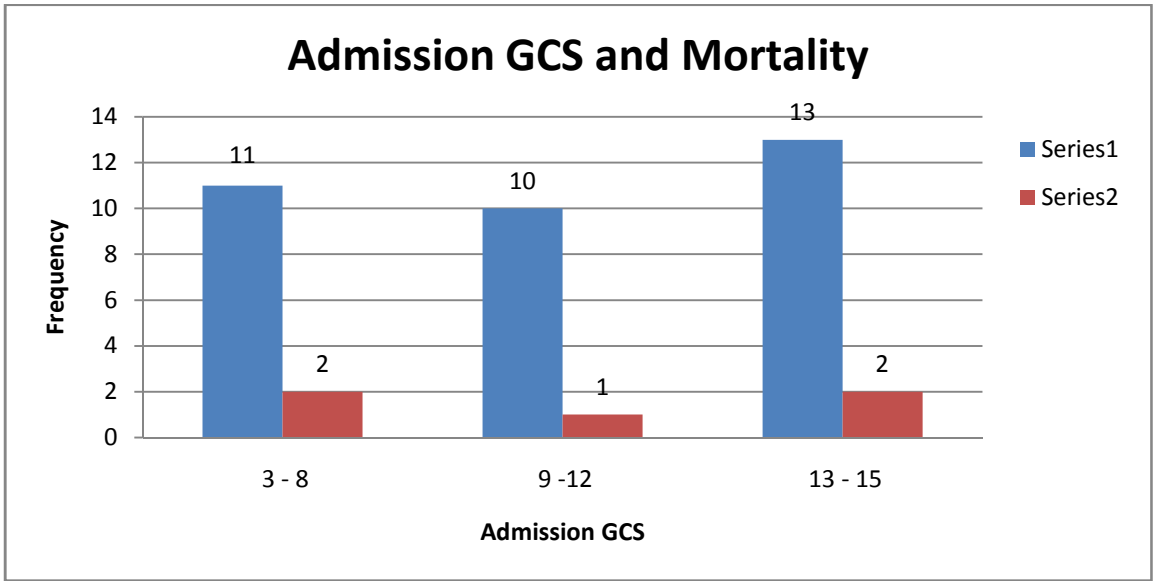
Sixty five percent of patients had good outcome, and 15% had moderate disability. Mortality was 15%.

TABLE 8: Henk W. Mauser Grading for Morbidity of Survivors of ICSDE (HWM)

HWM Grading	Frequency	Percentage (%)	Cumulative
Grade A	22	64.71	64.71
Grade B	3	8.82	73.53
Grade C	4	11.76	85.29
Grade D	5	14.71	100.00
TOTAL	**34**	**100.00**	

Twenty two patients had good recovery without seizures. Five patients died.

FIGURE 6: Admission GCS and Mortality



Graph showing mortality against admission Glasgow Coma Scale, of the 34 patients admitted (blue colour) and 5 died (brown colour) – independent of admission GCS.

TABLE 9: Contingency table of GOS and Age groups

GOS	Age Groups (years)			
	0 - 10	**11 - 20**	**21 - 30**	**31 above**
Dead	0 (0.00)	2 (12.50)	2 (33.33)	1 (33.33)
Severe Disability	0 (0.00)	0 (0.00)	1 (16.67)	1 (33.33)
Moderate Disability	3 (33.33)	1 (6.25)	0 (0.00)	1 (33.33)
Good Recovery	6 (66.67)	13 (81.25)	3 (50.00)	0 (0.00)
Total	9 (100.00)	16 (100.00)	6 (100.00)	3 (100.00)

CHAPTER 5: DISCUSSION AND CONCLUSION

5.1 DISCUSSION

There were 20 (60%) males in the study with 14 (40%) females – Table 3. This is in keeping with other international studies[2,3,7]. The reason for this male dominance remains unclear. The study also confirms what Dawodu noticed that the subdural empyema can affect any age group[2], patients' age varied from five months to 45 years. Complicated sinusitis was the main cause in 82% of patients, followed by meningitis at 8% with head trauma, surgical operations and pneumonia contributing 3% each – Table 3. Of the patients with complicated sinusitis all had paranasal sinuses as the origin of infection. None had otitis media as the origin of infection as observed by Reeves Dill.[18]

Sterile cultures were reported in 44% of cases with 56% having positive cultures – Figure 3. From the positive cultures 70% of the identified organisms were alpha and beta haemolytic streptococci – Table 5. All patients were on empiric triple antibiotic therapy consisting of 3rd generation cephalosporin/meropenem plus vancomycin plus metronidazole. The majority were de-escalated to penicillinG/ampicillin according to sensitivity results. Resistance to penicillin was not a major feature in this study, accounting for only 5% of cases as opposed 64,3% reported by Olwoch[17].Presenting features were similar to other studies[3], namely the triad of headache, fever and seizures. The most common presenting feature was hemiplegia (accounting for 60% - Table 6) as also seen by Gradidge et al[19].

It is worth noting that from this study the type of surgical procedure had no influence on the average hospital stay (Table 7).Leaving drains after burr holes reduced the likelihood for repeat surgery from 77% to 30% (Table7) as was also reported by HE et al[12]. There was no mortality associated with craniotomy in this study which then suggests craniotomy as a preferred surgical procedure of choice, as suggested by Feuerman et al[6], Bok et al[7] and Mat Nayan et al[9]. This is in contrast with what Mauser et al, who preferred burr holes to craniotomy[11].

Glasgow Outcome Scale and Henk W. Mauser grading system were used to determine outcome (Figure 5 and Table 8 respectively). Sixty-five percent of patients had good outcome with no seizures and neurological deficits at discharge. Mortality was 15% in this study, comparable to international figures. Locally this figure is higher compared to a study at Cape Town[7] and George Mukhari Hospital[16] but less when compared with the Durban study by Nathoo et al[8].None of the poor prognostic features as suggested by Agrawal et al[3], Miller et al[10] and Mauser et al[14] were found to influence mortality or morbidity in this study, e.g. admission GCS – Figure 5. Favourable outcome was associated with patients who underwent craniotomy and patients between the ages of 11 – 20 years (Table 9), this is in agreement with what Agrawal et al reported[3].

5.2 LIMITATIONS

The limitation for this study is the enrolled number of patients. A larger group might show some factors associated with poor outcome and those with good outcome.

5.3 CONCLUSION

ICSDE is still associated with high mortality if not treated early. Clinical features and organisms cultured seem to be the same internationally, particularly those from complicated sinusitis. Empiric triple antibiotic therapy of 3rd generation cephalosporin plus vancomycin plus metronidazole is still relevant at SBAH.

The type of surgical operation done has no influence on length of hospital stay. Craniotomy emerges as a procedure associated with no mortality in stable patients, multiple burr holes with drains in situ is recommended in unstable patients to avoid repeated operations. Age was another factor associated with better outcomes, particularly those between 11 and 20 years of age.

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APPENDICES

Appendix A – Glasgow Coma Scale

Eye Opening	**Verbal Response**	**Motor**
1 = no response	1 = no response	1 = no response
2 = to painful stimuli	2 = incomprehensible sounds	2 = decerebrate
3 = to verbal stimuli	3 = inappropriate words	3 = decorticate
4 = spontaneous	4 = disorientated	4 = flexion withdrawal
	5 = orientated	5 = localizes pain
		6 = obey commands

Appendix B – Data Collection Form

PATIENT DATA SHEET: THE OUTCOME OF INTRACRANIAL SUBDURAL EMPYEMA AT STEVE BIKO ACADEMIC HOSPITAL – RETROSPETIVE STUDY

PATIENT DATA

Name: _____ Age: _____

Hospital Number: _____ Sex: _____

Date of Admission: _____ Admission Diagnosis: _____

PRESENTING FEATURES

Headache: _____yes/no Fever: _____yes/no

Seizures: _____yes/no Hemiplegia: __yes/no

Others (specify): _____

Admission Glasgow Coma Scale: _____

INVESTIGATIONS

Brain CT scan – Pus Location: _____ Pus swab results: _____

Source of Infection: Complicated sinusitis _____

Penetrating head trauma ____

Other (specify) _____

TREATMENT

	Date started	Days given
1. Antibiotics		
2. Anti-epileptic		
3. Surgical procedure		
Burr holes		
Burr holes with drain		
Craniotomy		
(document repeat surgery)		

CLINICAL COURSE

GOS at discharge: _____ HWM grade: _____

Length of hospital stay: _____ Death: _____yes/no

Appendix C – Henk W. Mauser grading system

Grade	**Description**
A	Survival without or with a minor, not disabling focal deficit
B	Survival with not disabling seizures and with or without a minor focal deficit
C	Survival with severe disability
D	Death

Appendix D – Glasgow Outcome Scale

Grade	**Description**
1	Dead
2	Persistent vegetative state
3	Severe disability
4	Moderate disability
5.	Good recovery