CLINICAL PATTERNS OF FOCAL INTRACRANIAL SUPPURATION, AND COMMON CAUSATIVE ORGANISMS, AS SEEN AT THE KENYATTA NATIONAL HOSPITAL ; A PROSPECTIVE STUDY.

A PROJECT FOR A DISSERTATION IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE IN NEUROSURGERY, FROM THE UNIVERSITY OF NAIROBI.

BY

DR. M.A. MAGOHA,

MB, Ch.B. (NAIROBI)

H58/66701/11.

PRINCIPAL INVESTIGATOR:

DR. MICHAEL A. MAGOHA,

RESIDENT, NEUROSURGERY, DEPARTMENT OF SURGERY, UNIVERSITY OF NAIROBI.

SIGNED……

…….

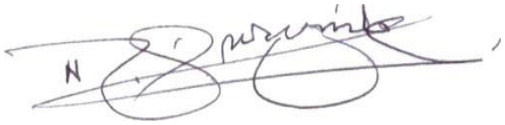
SUPERVISORS

PROFESSOR N.J. MWANG'OMBE,

ASSOCIATE PROFESSOR, DIVISION OF NEUROSURGERY,

DEPARTMENT OF SURGERY,

UNIVERSITY OF NAIROBI.



SIGNED……

……

DR. C.K. MUSAU,

LECTURER, NEUROSURGERY,

DEPARTMENT OF SURGERY

UNIVERSITY OF NAIROBI.

SIGNED……

……

DR ANNE MAINA,

MEDICAL MICROBIOLOGIST
LECTURER DEPARTMENT OF MICROBIOLOGY
UNIVERSITY OF NAIROBI

SIGNED……
…….

STUDY OUTLINE:

LIST OF ABBREVIATIONS:

A/E - Accident and emergency.

BA -Brain abscess.

BBA - Bacterial Brain abscess.

PV - Purulent ventriculitis.

CT -Computerised tomography.

FIS - Focal intracranial suppuration.

GAR -Gross attendance ratio

HIV - Human immunodeficiency virus.

ICU -Intensive care unit.

ICSD - Intracranial suppurative disorders.

KNH -Kenyatta national hospital.

MRI -Magnetic resonance imaging.

SBE -Subdural empyema.

SP - Species

IVRBA - Intraventricular rupture of a brain abscess

LIST OF TABLES

LIST OF FIGURES

LIST OF IMAGES

SUMMARY

BACKGROUND: Focal intracranial suppuration continues (FIS) to be serious life threatening condition in developing nations due to lack of widespread availability of computerized tomography, and in the background of immunosuppression secondary to Human Immunodeficiency Virus (HIV) infection. A previous local study at Kenyatta national hospital revealed a 1 in 3 chance of mortality in patients presenting with FIS.

STUDY OBJECTIVE: This study aimed to identify the current demographics, clinical presentations, Location, risk factors and microbiologic profile of patient presenting to KNH with FIS.

STUDY DESIGN AND SITE: This was a prospective descriptive cross sectional study carried out at the Kenyatta National Hospital.

STUDY PARTICIPANTS: All patients with FIS meeting inclusion criteria.

EXPECTED MAIN OUTCOME AND MEASURES: 42 Patients were enrolled in the study. 87% were males. 33% of patients were between the ages of 26-45. 62% were referrals from satellite facilities, 50% of which were in Nairobi. The mean duration of symptoms was between 8-14 days. With the commonest symptoms being headache and hemipsaresis. Most were post traumatic(42.9%). 69% of the abscess' were sterile. The commonest pattern of FIS was intraparenchymal abscess with subdural extension. (50%). The commonest location was frontal.(31%)

INTRODUCTION

Focal intracranial suppurations (FIS) are localized infections of the intracranial compartment and also refer to local collections of pus within the cranium. The condition which is also known as intra cranial suppurative diseases (ICSDS). Is reported to exhibit a variety of patterns from epidural abscess, subdural empyema, brain abscess, and purulent ventriculitis (1,2).

Indeed of all the FIS the most widely studied and feared are brain abscess'. A brain abscess is an intraparenchymal collection of pus. The incidence of brain abscesses is approximately 8% of intra-cranial masses in developing countries and 1–2% in the western countries (3,4). They begin as localized areas of cerebritis in the parenchyma and evolve into collections of pus enclosed by a well vascularized capsule. It is noted that with large brain abscess' and in situations of capsule rupture, a previously "Localised" brain abscess may progress into any other singular unspecified FIS or a combination. Of note is Intraventricular rupture of a brain abscess (IVRBA) remains a catastrophic and fatal complication of bacterial brain abscesses (BBA), (5,6,7). This is regardless of the progression or development of Purulent Ventriculitis (PV). Tsung-Han et al in a Taiwanese retrospective study over a 20 year period (1986-2005) identified 62 patients with IVRBA and concluded the following predictive factors of IVRBA ; whether the abscess is deep seated, multiloculated and close to the ventricle wall, a reduction of 1 mm in the distance between the ventricle and brain abscesses increases the rupture rate by 10%. (8).

Focal intracranial suppurations commonly occur as sequelae of otogenic and dentogenic infections, para nasal sinusitis and other infections of cranial or systemic

origin (2). FIS has also been reported in leukemia patients (9) and following viral infections such as in immunosuppressed patients with HIV (10). Intracranial abscess associated with Halo ring treatment of unstable cervical spine injuries due to pin loosening and pin site infections are unusual, but have been previously reported in the literature (11). Sometimes however, it is not possible to identify the primary source of infection. Even though there has been a gradual decline in the incidence worldwide, Focal Intracranial Suppurations continue to pose considerable diagnostic and therapeutic challenges to the practice of neurosurgery. This is particularly so in developing countries including Africa, where modern facilities for diagnosis and treatment as well as availability of appropriately qualified manpower are relatively inadequate (1,2).

Focal intracranial suppurations are relatively rare but the consequences of missed or delayed diagnosis are significant (12). The clinician is urged to consider the diagnosis of Focal Intracranial Suppurations in patients with headache and focal neurological symptoms. Historically the condition was considered almost always fatal with a pre antibiotic era mortality rate of 100% (13). However over the past three decades outside Africa, the incidence and mortality of FIS is reported to be decreasing with a reported incidence ranging from 0.4-0.6/100,000 (14). Helweg- Larsen et al in a fifteen year retrospective survey of pyogenic brain abscesses involving one hundred and two patients confirmed that clinical signs of brain abscess are non specific. This was because the majority of these patients presented without clear signs of infection, and diagnosis and treatment was often delayed (14).

The reported reduction in incidence and mortality of FIS was largely attributed to the rise and availability of modern diagnostic modalities such as Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI) over the last three decades. Computerized Tomography in particular provided more accurate diagnosis and localization of the abscesses, and aided rapid detection of postoperative recurrence and complications that accounted for some of the deaths in the pre CT scanning era. Serial CT studies provide a reliable means to optimize the timing of surgical intervention and plan appropriate medical antibiotic therapy (15). Despite the advances in medical imaging techniques, laboratory diagnostics, surgical interventions and antibacterial treatment, brain abscess which can be caused by bacteria, mycobacteria, fungi, parasites, and more recently immunosuppression, remains a challenging clinical problem in neurosurgery with substantial morbidity and mortality (16).

In some select centers in Africa, there has been reasonable increase in the use of computerized tomography scans as the most dependable diagnostic tool in brain abscesses resulting in some decreased morbidity and mortality. Emejulu et al reported only 9% mortality while some 72.8 % of the patients fully recovered to their pre-morbid activities and duties with no residual neurological deficit (17). However data from within the African continent, and other developing countries is minimal and disjointed and therefore unable to provide an objective and holistic picture of the true impact of the advent of computerized tomography and magnetic resonance imaging in the management of focal intracranial suppurations. The exception here is within the many emerging university and other specialized hospitals within urban areas in many African countries that are much better equipped with these facilities in addition to an

increasing number of well trained neurosurgical personnel that support the treatment process.

In Africa, focal intracranial suppurations were reported by Adeloye in Ibadan Nigeria to comprise about 2-5% of all intracranial space occupying lesions (18). Subdural empyema due to Streptococci and Staphylococci was however reported to be relatively of frequent occurrence in Africans in Rhodesia the present day Zimbabwe. This was in a retrospective study which was carried out involving patients more than half of whom had history of an infection process outside the central nervous system. Treatment was effected through multiple burr holes, irrigation and antibiotics (19).

Mwangombe in a study carried out at Kenyatta National Hospital, Nairobi lnvolving 65 surgically treated patients reported the commonest cause cause of brain abcess in this locality to be trauma, and the most common organisms isolated included Staphylococci, Streptococci, Klebsiella, and Haemohylus Influenza *sp* with an overall mortality of 30.7 %. (20). Trauma was also recently reported as the commonest cause of brain abscess in Africans by Anwary in a study carried out at Umtata general hospital and the Nelson Mandela academic hospital in the Eastern Cape South Africa (21). Sichizya et al in another study involving 121 surgically treated patients with brain abscess at Groote Schuur hospital in Cape Town, South Africa reported an improved mortality of 13% (22)

As a whole several aspects of management of Focal Intracranial Suppurations remain controversial including the need for and when to institute surgery, the optimal surgical

approaches, the type and length of antibiotic treatment, and the need for monitoring during and after treatment (14).

LITERATURE REVIEW

HISTORY

Focal intracranial suppuration has historically been considered almost always fatal, with Brain abscess' being the captain of death with a near 100% mortality (13). Many famous figures have succumbed to this illness throughout history. Perhaps the one of the most infamous sporting injuries in history in the death of King Henry II in June 1599 from a jousting accident that resulted in intra-orbital splinters that caused intra-orbital cellulitis. Within 11 days this complicated with a left inter-hemispheric subdural empyema and a subcortical collection of pus (brain abscess). This was regrettably confirmed by his physician, Andreas Vesalius at autopsy. (23) This illustrates that even then FIS is a disease in continuum, if left to progress without intervention.

Sir Percivall Pott (1714-1788) an astute and prolific mid-eighteenth century English surgeon with a strong interest in head injury is attributed as probably the first to recognize and document that infections elsewhere in the body could spread and cause BA. (24).

The first successful operation for a brain abscess recorded is by the French Surgeon F.S Morand in 1768 on a Supratentorial abscess (25). After the advent of contemporary anaestetic and surgical techniques Dr. Cemil Topuzlu in 1891 reported a successful operation for BA, the first in the Ottaman empire, heralding a change in the localization and management of FIS using clinical features only in this pre imaging era (26). During this same period Dr Mc Ewan of Glasgow published a seminal monograph, entitled "Pyogenic Infective Disease of the Brain and Spinal

Cord," This described the results of a case series of 19 BA patients in which decalcified chicken bones had been used to drain the pus, with only a 5.3% of mortality.

Dr Macewen's diagnosis just like Topzulu was based on clinical findings impeccably illustrated by his three clinical stages of BA development. Indeed his clinical observations are still very relevant today as when he described them 100 years ago. Macewen recorded 25 cases of brain abscess. Nineteen of these patients came to his attention in time to undergo surgery, resulting in 18 recoveries. All five of his patients with extradural abscess recovered. These results were achieved in the era known as "the most glorious period in British surgery." Noted by many Neurosurgeons including Dr Harvey Cushing. Neurosurgery was in its infancy; nevertheless, even as the 20th century closes, Macewen's results still have not been surpassed.(25)

Over the past three decades, in the developed and western countries and specifically outside Africa, the incidence and mortality of brain abscess has been reported to be rapidly decreasing with incidence of 0.4-0.6 per 100,000 (14). This reported reduction in morbidity and mortality is largely attributed to the rise and availability of modern diagnostic techniques in neuroimaging such as computer tomography (CT) and magnetic resonance imaging (MRI). The University of California San Francisco in 1978 famously reported a 0% mortality in management of FIS in a case series of 20 patients since the commencement of routine diagnostic CT at the institution. Despite the recent advances in microbiological isolation and neuroimaging techniques, neuroanaesthesia, antimicrobial and antifungal treatment, and neurosurgical techniques including technology assisted and precise neurosurgical interventions, brain abscess continues to remain a very challenging clinical problem to

neurosurgeons globally, with significant morbidity and mortality, still leading to some case fatalities (15,27).

Within the African continent, neurosurgical services in were still mostly lacking, or very poor when available due to lack of medical infrastructure, qualified neurosurgical personnel and relevant equipment necessary for the effective investigation, localization and management of brain abscess. One of the first neurosurgical units to be established in sub Sahara Africa was at the university of Ibadan in Nigeria in 1965, from where brain abscess in Africans was later reported by Adeloye to comprise 2-5% of the intracranial space occupying lesions (27, 18). Currently in some select well equipped African centers with well trained neurosurgical personnel, there has been increased utilization of computerized tomography scanning as the most dependable diagnostic tool in the management of brain abscesses resulting in some reduction in morbidity and mortality (2,17,22).

Unfortunately data from within the African continent and other developing countries is minimal and often disjointed and therefore mostly unable to provide a complete objective and holistic picture of the true impact of the advent of computerized tomography and magnetic resonance imaging in the management of brain abscesses in the continent. The exception here is with the many emerging university and other specialized hospitals in many African urban centers that are much better equipped with these facilities in addition having increasing numbers of well trained neurosurgical personnel to adequately support the treatment process. An example of this is the Kenyatta National Hospital and the University of Nairobi with over 90% of the Kenyan population relying on its Neurosurgical services (28).

AETIOLOGY

Focal intracranial suppurations can be caused by bacteria, fungi, or parasites which include helminthes, Protozoa, and viruses. The aetiological causative agent of the FIS cannot be identified in a significant number of cases. It may result from traumatic brain injury, prior neurosurgical procedure, contiguous infective spread from a local source such as mastoiditis, paranasal sinusitis, or dental infection, or haematogenous spread from of a systemic infection such as endocarditis or bacteremia. Bacteria enter the brain through contiguous spread in about half of the cases, and through haematogenous dissemination in about one third of the cases with unknown mechanisms accounting for the rest. In most cases, FIS results from several predisposing factors such as infection with human immunodeficiency virus (HIV), history of treatment with immunosuppressive drugs like in organ transplant patients (27). HIV infection is associated with brain abscess caused by Toxoplasma gondii and in some cases mycobacterium tuberculosis (29,30). Patients who have received solid organ transplant are at risk of norcardial and fungal brain abscess by aspergillus or candida species (31).

The causative organisms in brain abscess varies according to the age and immunological status of the patient. In adults aerobic, macroaerophilic and anaerobic streptococci are found in 60-70% of cases and are common in abscesses from dentogenic infection and sinusitis. Anaerobic Bacteroides species and enteric bacteria including E. Coli, Proteus, and Pseudomonas are present in 10-15% of cases, and are the most common isolates in brain abscesses arising from penetrating cranial trauma such as gun shot injuries to the head or neurosurgical procedures (27,32). The cause of infection in FIS is identifiable in many cases but the source of infection still

remains unidentifiable in approximately 25% of cases even, after thorough investigations have been carried out to identify the isolates (32-34). Multiple organisms have been isolated in approximately 18% of cases (32). FIS in neonates is a frequent complication of meningitis with the most frequently

EPIDEMIOLOGY

Intracranial abscesses are rare but deadly disease in developed countries. Various studies have reported incidences of approximately 4 per million population, and others ranging from 0.3-1.3/100,000 and accounts for 1 in 100,000 in multiple series hospital admissions (14;32). This accounts for approximately 1% of intracranial space occupying lesions. In contrast intracranial abscesses remains a very serious and significant clinical problem in developing countries where it accounts for approximately 8% of intracranial space occupying lesions (35). Predisposing factors vary in different parts of the world (32).

It occurs at any age but is more common in the third decade of life. Abscesses due to paranasal infections are most common between the ages of ten and thirty years. Otogenic abscesses are most common in childhood and after forty years of age. Predisposing factors in particular sinusitis, otitis, mastoiditis, head trauma or surgery are present in about 80% of affected children (36).

Mathisen and Johnson in a study carried out in 1997, reported that in at least 15% of cases no source can be identified (20). Bacterial meningitis is the main predisposing factor in young children. The decrease in bacterial meningitis due Haemophilus

Influenzae as a result of the development of Haemophilus Influenzae vaccine has resulted to reduction of prevalence in young children. (2,32,39).

In most clinical studies it has been reported that intracranial abscesses are more common in males compared to females (40,41).

As noted prior, the introduction of antibiotics and the increasing availability of computer tomography and magnetic resonance imaging, the mortality rate in brain abscess has decreased to 5-15%. However very high mortality rates of up to 80% are still associated with rupture as reported by (42).The prognosis however depends upon the speed with which diagnosis is established and the commencement which may involve antibiotics and surgery. New and emerging pathogens especially those in immunosuppressed individuals have renewed the necessity of early diagnosis and treatment. (43).

In Africa and other developing countries, mortality and morbidity has remained high compared to the rest of the world, as reported in various studies with Mwangombe reporting a mortality of 30.7% in Nairobi, Kenya (20), and Malik et al in a study carried out in Bombay India reported a mortality of 44.7% (41). However some improvement has been reported by Shokunbi and Malomo in working at the University College hospital, Ibadan Nigeria who reported a mortality of 11% (2), and Sichizya et al who reported a mortality of 13% at the University of Cape Town in South Africa (22).

Major advances such as newer and more efficient imaging techniques enabling early diagnosis, stereotactic neurosurgical procedures, and the discovery of newer and more

effective antibiotics which cross the blood brain barrier more effectively have in general lead to a substantial reduction in mortality (35, 44,45).Despite these advances however, brain abscess remains a potentially fatal clinical condition in the developing world (35, 44, 46).

Despite the differences between the developing and developed world, demographic details of brain abscess remain similar regardless of geographic location of the patients.

PATHOPHYSIOLOGY

Intracranial abscesses are located in the fronto-temporal, fronto-parietal, parietal, cerebellar, and occipital lobes of the brain in descending order (47).

In at least 15% of cases, the source of infection remains unknown or cryptogenic (14). Focal intracranial suppuration involves a three step process namely: Inoculation, propagation and manifestation.

The suppuration may be free or encapsulated within the cranium or brain parenchyma. Abscesses may vary in size from a microscopic focus of inflammatory cells to a large encapsulated area of necrosis occupying a major part of the cerebral hemisphere. They may be single or multiple. The depth of the Inoculation determines the location of Propagation i.e:

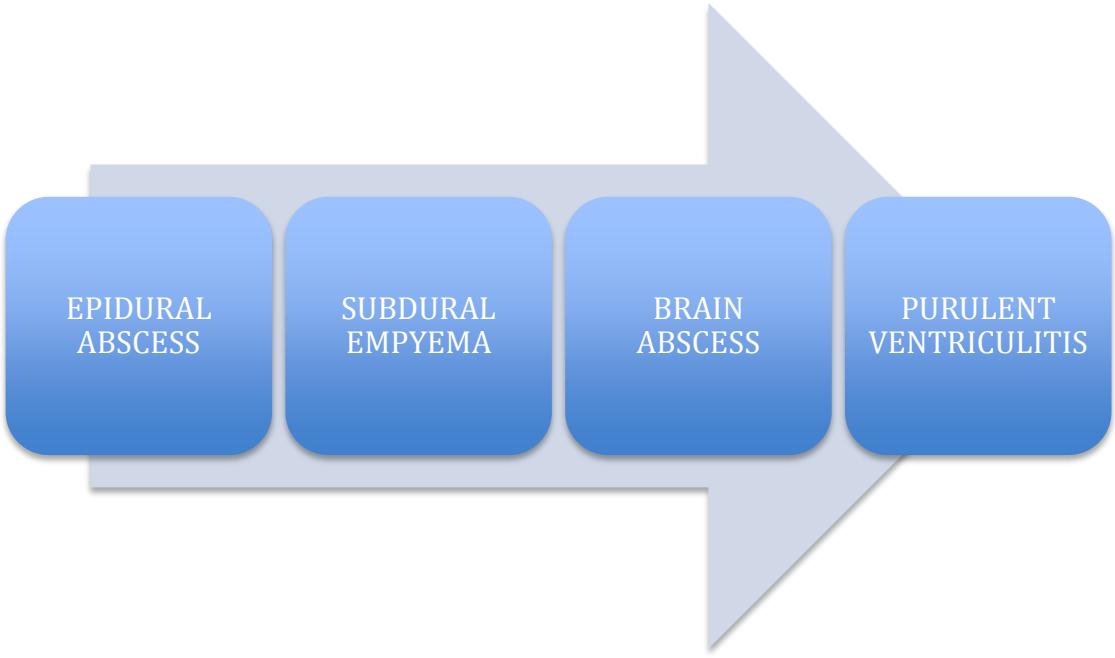


Figure 1. Figure illustrating unchecked propagation of suppuration

MODES OF INNOCULATION

INTRACRANIAL TRAUMA

Breach of neuro-protective barrier, via penetrating or neurosurgical intervention has been identified in numerous series as an independent pathogenic mechanism that may result in abscess formation in 2-37% of the cases. Trauma that causes open skull fracture enables organisms to seed directly in the brain. Brain abscess can also result as a direct complication of intracranial surgery, foreign bodies such as bullets or shrapnel and trauma to the face (42,48). In these cases, infection is often caused skin colonizing bacteria such as staphylococcus aureus or staphylococcus epidermidis, or gram-negative bacilli (49).

CONTIGUOUS SPREAD

Focal intracranial Suppuration may be to contiguous spread from parameningeal foci of infection. Pathogens may originate from adjacent bone, teeth, sinus mucosa, internal auditory canal or cochlear structures and travel into the intracranial vault via venous drainage or valveless emissary veins, thus inoculating the intracranial compartment (50). Direct extension usually causes a single brain abscess and may occur from necrotic areas of osteomyelitis in the posterior wall of frontal sinus, the sphenoidal and ethmoidal sinuses, mandibular dental infections as well as subacute and chronic otitis media and mastoiditis (51,52).

The causative agents of intracranial abscess vary according to age and immunological status of the patient. ICSD secondary to contiguous spread are frequently caused by streptococcus species, but staphylococcal and poly-microbial abscesses including those caused by anaerobes and gram negative bacilli also occur (53). Specifically in adults, aerobic, microaerophilic and anaerobic streptococci are common in abscesses from sinusitis and dental infections. Anaerobic bactericides species and enteric bacteria including E.Coli, proteus, and pseudomonas sp are also present in a significant number of cases (27,32,38, 54).

Staphylococcus aureus present in 10-15% of cases and is the most common cause in abscess associated with penetrating trauma and neurosurgical procedures (32).

Multiple causative organisms have been reported in approximately 18% of brain abscesses most frequently associated with sinusitis or otitis (32, 37).

HAEMATOGENOUS SPREAD

Brain abscess most frequently arise from haematogenous dissemination of organisms from distant sites of infection. The most commonly associated systemic infection are chronic lung infections such bronchiectasis and lung abscess, and acute bacterial endocarditis (32, 40).

Haematogenous spread of bacteria may also be associated congenital cyanotic heart disease, right to left cardiac shunts which allows organisms to move directly from the venous circulation into the left sided systemic circulation (17,55). Brain abscess of haematogenous origin are most common in the distribution of the middle cerebral artery followed by the interior cerebral and posterior cerebral circulation. Staphylococcus and streptococcus species are often identified in brain abscesses after haematogenous spread (17, 32).

PROPAGATION

Pathogenic mechanisms of infection (i.e. inoculation and propagation) are dependent on predisposing conditions, severe immune compromise resulting from HIV infection (29), or from immunosuppressive therapy in patients who have undergone solid organ or haematopoetic stem cell transplantation (56) or often associated with tuberculosis or non-bacterial causes of infection such as fungi or parasite. HIV infection is associated with brain abscess caused by mycobacterium tuberculosis (30), but HIV infection also predisposes patients to infection with Toxoplasma Gondii (29, 30), patients who have received solid organ transplants are at risk not only for non cardial brain abscesses (e.g. resulting from infection. With aspergillus or candida species.

Fungi are responsible for up to 90% of cerebral abscesses among recipients of solid-organ transplants. (56,57).

MANIFESTATION

The clinical manifestation of ICSDs, range from indolent to fulminant. The presentation is dependent on multiplicity of factors, including the location, size and age of the lesion, and mode of inoculation. The microbiology of the infection and the host's immune status all contribute to the presentation.

The most frequent clinical manifestation of FIS is reported as headache, fever and altered level of consciousness /neurologic deficit. These are however frequently absent as reported by Brower et al 2014b, (38) in a meta-analysis with a classic triad being reported in less than 20% of cases (58). Fever appears to be the only constant presentation in 50-75% of cases (42, 48).

DIAGNOSIS

The clinical trial of intracranial abscess of fever, headache, and focal neurological signs occurs only in a minority of patients. In most cases, intracranial abscesses present as a rapidly or subacutely developing space-occupying lesions and other signs of active infection may be absent. Diagnosis may also be difficult in a patient who presents with a clinical picture of encephalopathy without focal neurologic signs. Slowly developing intracranial abscesses may be mistaken for metastatic brain tumours (27,32,38,52). About one third of patients present with seizures that are frequently generalized and associated with frontal lobe abscesses (39).

Magnetic Resonance Imaging (MRI) with use of gadolinium enhancement is the diagnostic procedure of choice in cases of suspected brain abscess (38,27,59). Diffusion-weighted MRI or MR spectroscopy allows differentiation between brain abscess and brain tumor with central necrosis and may also help differentiate between bacterial, tuberculous, and fungal abscesses (60,61).

Contrast enhanced CT scans may fail to detect lesions that are easily identifiable on MRI. The sensitivity of the contrast enhanced CT scan may be increased if the scan is repeated some 30-60 minutes after the contrast infusion (63).Contrast enhanced CT should be used if MRI is not readily available (62).

MANAGEMENT

The management of intracranial abscesses involves early diagnosis, followed by prompt administration of appropriate antibiotics, surgical drainage or excision and the control of cerebral edema. Many abscesses contain multiple organisms requiring combination therapy of two or more antibiotics covering both aerobic and anaerobic organisms (27,38,64).

Initial therapy where the source of infection is unknown should include combination therapy involving the administration of vancomycin or oxacillin plus ceftriaxone and metronidazole for anaerobic organisms (65).

The availability of CT and MRI has made it possible in selected cases to treat intracranial abscesses with antibiotics alone (66).

Surgical management of intracranial abscesses may involve aspiration or excision. Aspiration particularly under stereotactic CT or MRI guidance is becoming extremely popular because it is less traumatic to the central nervous system than surgical excision, and carries a much lower risk of subsequent seizures (14, 67).

Aspiration removes the purulent Centre of an abscess, rendering the abscess more amenable to effective antibiotic therapy and often effectively reducing intracranial pressure (68). However no controlled trial of aspiration versus excision has been reported to date. Excision should therefore be effected in large or multi-loculated abscesses that do not respond to aspiration and in cases where ventricular rupture is imminent (69).

STUDY JUSTIFICATION

Focal intracranial suppuration is a severe life-threatening condition. The limited resources in developing countries and lack of widespread availability of imaging modalities namely computerized tomography and magnetic resonance imaging tend to delay diagnosis and prompt referral to facilities with neurosurgical personnel.

A previous 5 year retrospective study at Kenyatta national hospital from 1989-1993 revealed a 30.7% chance of mortality in patients with Brain abscess' alone (Mwangombe 2000). This is a significant mortality rate and it does not include the other forms of FIS. The management of FIS includes, prompt identification, imaging diagnosis and Neurosurgical intervention either by burr hole drainage, craniotomy or stereotactic aspiration. Since 1993 Kenyatta National hospital and its catchment population, being an urban referral hospital have made great strides in diagnosis and

treatment. At present there is no recent data regarding the current picture of FIS seen at KNH.

The current study aims to address this lack of current data and to provide a platform for improvement of patient care.

RESEARCH QUESTION

What is the pattern of Focal intracranial Suppuration as seen at the Kenyatta National hospital? (An urban referral hospital)

STUDY OBJECTIVES

BROAD OBJECTIVE

To establish the pattern of Focal intracranial Suppuration, as seen at the Kenyatta National hospital.

SPECIFIC OBJECTIVES

1. To determine the pattern and location of FIS.
2. To determine the clinical characteristics of patients with FIS.
3. To determine the common bacterial organisms of FIS.

METHODOLOGY

STUDY SITE:

Kenyatta National Hospital.

This is a national teaching and referral hospital with fully established departments for various specialties including neurosurgery, otolaryngology and neurology, under the respective departments of surgery and medicine.

These patients were studied from the ward 4C and/or ICU in where they were b admitted and managed.

STUDY POPULATION

This study involved all patients with FIS, who gave an informed consent to the study in KNH.

STUDY DESIGN

This was a descriptive prospective cross sectional study.

CASE DEFINITION / IDENTIFICATION OF PATIENTS WITH FIS

- Neuroradiological findings suggesting FIS on computerised tomography and Magnetic resonance imaging plus radiological and clinical response to antimicrobial therapy.
- A positive culture of intracranial pus despite alternative diagnosis prior (e.g: tumour or haematoma);

INCLUSION CRITERIA

All patients regardless of age, or gender with FIS confirmed as per case definition above.

EXCLUSION CRITERIA

1. Patients with diagnoses of abscess changed post intervention despite classic image characteristics.

2. Patients who shall willfully decline to participate in the study or withdraw from an on going study.

SAMPLING METHOD

All consecutive sampling of FIS patients who meet the criteria for inclusion in the study.

LABORATORY PROCEDURES:

A) SAMPLE COLLECTION AND TRANSPORTATION.

The pus will be aspirated during the operative procedure and placed in a sterile bottle, which will be place in the transport kit and labeled with identification number, date and time of collection and source of specimen.

The specimen will be immediately transported to the lab within one hour of collection.

B) ISOLATION AND IDENTIFICATION OF MICROORGANISMS

Samples will be inoculated on plated chocolate blood agar and blood agar for gram positive bacteria and Mac Conkey agar for gram negative bacteria. The plates will be incubated and bacteria identified using standard laboratory Identification methods.

CULTURE AND IDENTIFICATION TESTS

.Chocolate blood and Mac Conkey agar will be inoculated by streaking the specimen as soon as it is received in the lab. The pus sample via a swab is rolled over a small portion of the agar surface and streaked for isolation.

These are incubated in 5-10% carbon dioxide at 35-37 degrees for 24-48 hours.

Colonies were then be identified by their morphology with the assistance of the microbiologist.

GRAM STAIN PROCEDURE

Colonies are spread evenly on a slide to form a thin smear.

The smear will be heat fixed by passing it two to three times through a flame. The slides will be stained as follows:

They are then flooded with crystal violet then gently rinsed off with tap water.

They are flooded with iodine and left for at least three seconds. The iodine is be rinsed off with tap water.

They are then decolorized by adding acetone or 50% alcohol to the smear for 30 seconds while holding the slide at an angle to allow the decolorizer to drain.

The excess decolorizer is gently rinsed off for 30 seconds with tap water.

The smear is flooded with neutral red counterstain for 30 seconds and then gently rinsed off with tap water.

The slide is allowed to dry and then examined under a microscope for gram negative and positive rods and cocci.

C) ANTIMICROBIAL SUSCEPTIBILITY

Testing to selected drugs will be done by the disc diffusion method on Mueller Hinton agar.

Gram positive isolates will be tested for Penicillin, Ampicillin, Levofloxacin, Erythromycin, Vancomycin and Teicoplanin.

Gram negatives will be tested for Amikacin, Doxycycline, Gentamycin, Ceftazidime, Cefuroxime, Piperacillin/Tazobactam and Meropenem.

Gram positive organisms will be tested for methicillin resistant staphylococcus using cefoxitin disc screen test and gram negative bacteria tested for extended spectrum beta lactamase on muller hinton agar and using disc diffusion with Cefotaxime and ceftriaxone.

Culture and sensitivity method

1st DAY

Using a sterile wire loop, 3-5 well-isolated colonies will be emulsified in 3-4 ml of sterile physiological saline. In a good light the turbidity of the bacterial suspension is matched to the turbidity of to 0.5 McFarland standard (the standard is mixed immediately before use). When comparing turbidities it is easier to view against a printed card or sheet of paper. Using a sterile swab, Mueller Hinton and blood agar, agar plates are inoculated for gram negative bacteria and gram positive bacteria respectively. Excess fluid is removed by pressing and rotating the swab against the side of the tube above the level of the suspension. The swabs are streaked evenly over the surface of the medium four to six times, rotating the plate approximately 60° to ensure even distribution. With the Petri dish lid in place, the Petri dishes were allowed 3-5 minutes *(no longer than* 15 *minutes)* for surface of the agar to dry. Using sterile forceps, the appropriate antimicrobial discs are placed and evenly distributed in the inoculated plate.

Within 30 minutes of applying the discs, the plates are inverted and incubated aerobically at 37°C for sixteen to eighteen hours.

2nd DAY:

After overnight incubation, agar plates are examined to ensure that the growth was confluent or near confluent.

Using a ruler or caliper on the under of the plate, the diameter of each zone of inhibition was measured in mm. The endpoint of inhibition will be where growth starts.

EXPECTED RESULTS

Interpretation of zone sizes Using the Interpretative Chart the zone size of each antimicrobial was interpreted by reporting the organism as 'Resistant' and 'Sensitive (Susceptible)'.

Resistant: A pathogen reported as 'resistant' implied that the infection it had caused was not responding to treatment with the drug to which it is resistant irrespective dose or site of infection.

Sensitive (susceptible): A pathogen reported as sensitive suggested that the infection it has caused was likely to respond to treatment when the drug to which it is susceptible was used in normal recommended doses and administered by an appropriate route.

QUALITY ASSURANCE OF PROCEDURES

Specimen collection and inoculation onto media were carried out aseptically All the laboratory procedures were carried out with the assistance of qualified personnel. Quality control measures were carried out at each step of the specimen processing. Standard operating procedures were adhered to for all procedures

Reagents and stains. The date of preparation for each batch of reagents and stains were indicated. The gram stain reagents were properly stored and were tested with the control strains ATCC 25923 for gram positive and ATCC 25922 for gram- negative organisms were used.

Culture media Media was prepared as per manufacturer's instructions and the date of preparation indicated on each batch. Control strains were cultured to assess media quality. To assess for media sterility 2% of plates from each batch were incubated overnight at 370C and checked for contamination. Where contamination was suspected the entire batch was incubated for upto 18 hours at 370C and those that were contaminated were discarded. To assess whether the culture media could support growth of microorganisms 2% of the plates were inoculated with an appropriate control strain. If growth was not supported the particular media was discarded and fresh media prepared. Media was kept at 4-8% for a maximum of three weeks.

SAMPLE SIZE DETERMINATION

The sample size was determined by use of the Fisher formula.

$$n = \frac{z^2 \hat{p}(1-\hat{p})}{m^2}$$

Where:

p = expected prevalence or proportion or estimated proportion of Mortality among patients with FIS.

m= degree of precision or a tolerance error margin or width of the Confidence interval (CI) (a measure precision of the estimate).

z= Z statistic for a level of confidence or is the normal distribution critical value for a probability of $\alpha/2$ in each tail. For a 95% CI, z=1.96. That Z is the standard Normal distribution value for which the probability of falling above the value is α. For $Z_{0.025}$=1.96

For this study, the level of confidence is 95%, an error margin of ±10% as being considered acceptable and from a past study, Honda et al 2009, expected prevalence of FIS at about 10%. (8-14%).

Using this information in the sample size formula above we estimated a sample of 35, thus,

$$n = \frac{z^2}{m^2}\hat{p}(1-\hat{p}) = \frac{1.96^2}{0.1^2} \times 0.1 \times 0.9 = 35 .$$

Note: n will be the minimum sample size.

SCREENING AND RECRUITMENT

The principal investigator reviewed files of all FIS patients who have been admitted and/ or managed at the KNH. The files of patients who met the criteria shall be selected and sampled for the study. The patients were given all the relevant information pertaining the study and those that gave consent were recruited. A questionnaire was administered, a thorough history and physical examination was also conducted for each patient.

DATA MANAGEMENT AND ANALYSIS

DATA ENTRY AND MANAGEMENT

Data was entered into the questionnaire by the principal investigator and study assistant after which the forms were reviewed by the principal investigator to ensure they have been entered appropriately. Errors found were corrected and those that could not be corrected discontinued from study.

The data will then be entered and analyzed using the Statistical Package for Social Scientists (SPSS USA Inc) Version 20.0.

DATA ANALYSIS

Descriptive statistics such as frequencies, proportions, measures of central location and variation (mean, mode, ranges and standard deviation) were used for most variables (Age, Gender, among others).

The above data shall be presented in tables, pie charts or bar graphs. The student t-test will be used to obtain the mean. The Mann-Whitney test will be used to obtain the median for the continuous variables with extreme values. The chi-square test will be used for reporting proportions for categorical variables.

STUDY FEASIBILITY

The KNH is a national teaching and referral hospital receiving patients from the whole country as well as from the neighboring countries. Previous studies at KNH revealed approximately 16 patients per year of FIS A/E department of KNH. These admissions will provide sufficient sample size for the study.

STUDY LIMITATIONS.

1. Being a hospital based study the results cannot be generalized to population.
2. The study focuses mainly on in-patients therefore leaving out-patients.
3. Due to the design of the study one can only determine outcomes but not establish cause and effect

MITIGATIONS

1. Kenyatta National hospital is a National referral hospital with a large catchment population as a majority of referrals from the nation present at this institution.
2. The nature of the FIS requires admission and in patient management.

ETHICAL CONSIDERATIONS

1. Permission to carry out the study will be sought from the Kenyatta National Hospital Scientific and Ethical Review Committee.
2. Patients will be enrolled into the study only after giving informed consent.
3. The usual care and evaluation of procedures will be facilitated.
4. Results of the investigations will be communicated to the primary health care providers in the respective units where the patient/s will be admitted.
5. Those that decline to give consent will not be discriminated.
6. Confidentiality with each client shall be maintained.
7. The benefits for the patients who participate in the study is that they will have thorough assessment (history taking and physical examination), those found to have other illnesses without adequate treatment shall be referred to their primary care giver.
8. There's no harm for patients who participate in this study.

RESULTS

DEMOGRAPHIC DATA

During the study period 47 patients presented to KNH with FIS. However 3 declined to participate in the study and two died shortly after presentation to the hospital resulting in 42 patients being enrolled into the study. Of these patients a vast majority (83.3%) of them were male versus the low (16.7%) female patients.

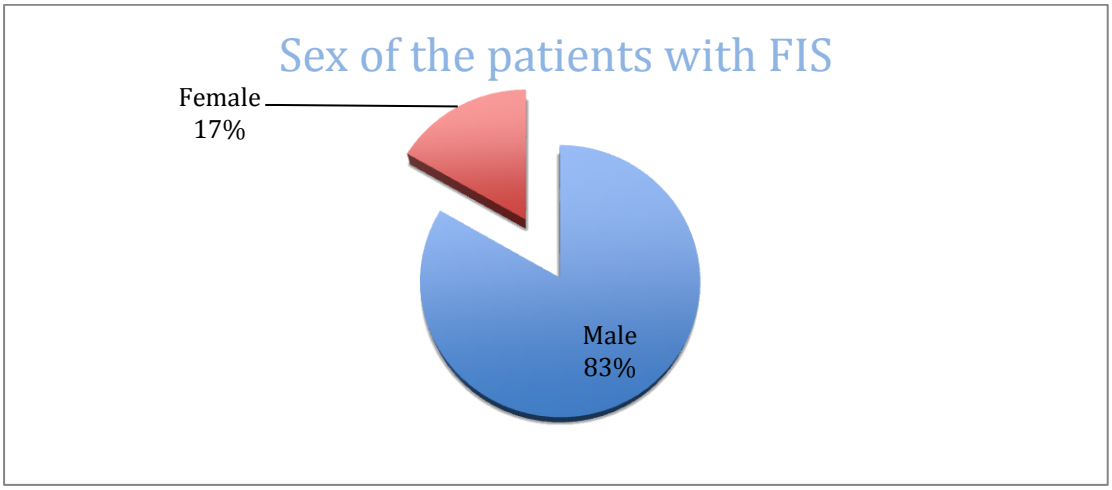


Figure 2 : Exploded Pie chart Illustrating difference in sex of patients presenting with FIS in percentage.

With regard to distribution by age, a peaks was noted between the ages of 26-45 (33% of patients) followed by the 13-25 age group (26.2%). The 61-70 demographic had the lowest number of patients with 2 (4.8%).

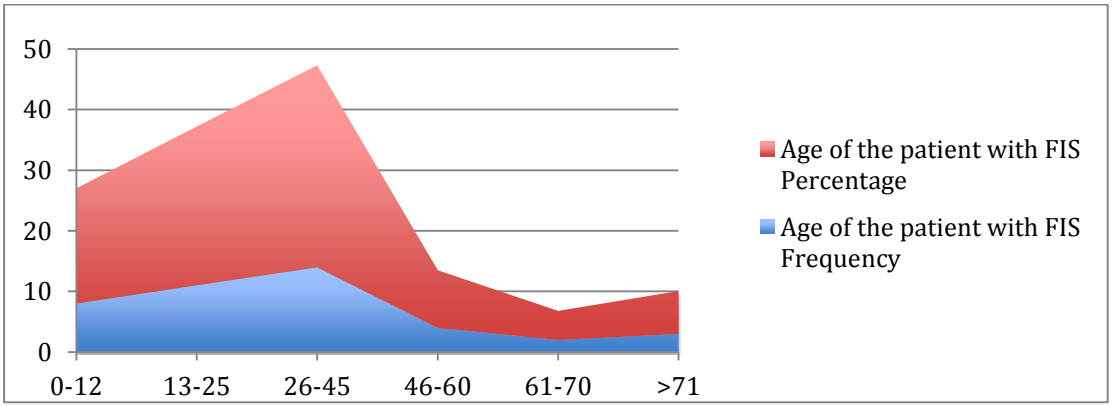


Figure 3: 2D stacked area graph illustrating the Age distribution of patients in frequency and percentage.

Despite being in what is colloquially known as the “marrying “ age in greater African culture more than half of the patients were single 59.5% vs 38.1% married and 2.4% divorced (a single patient).

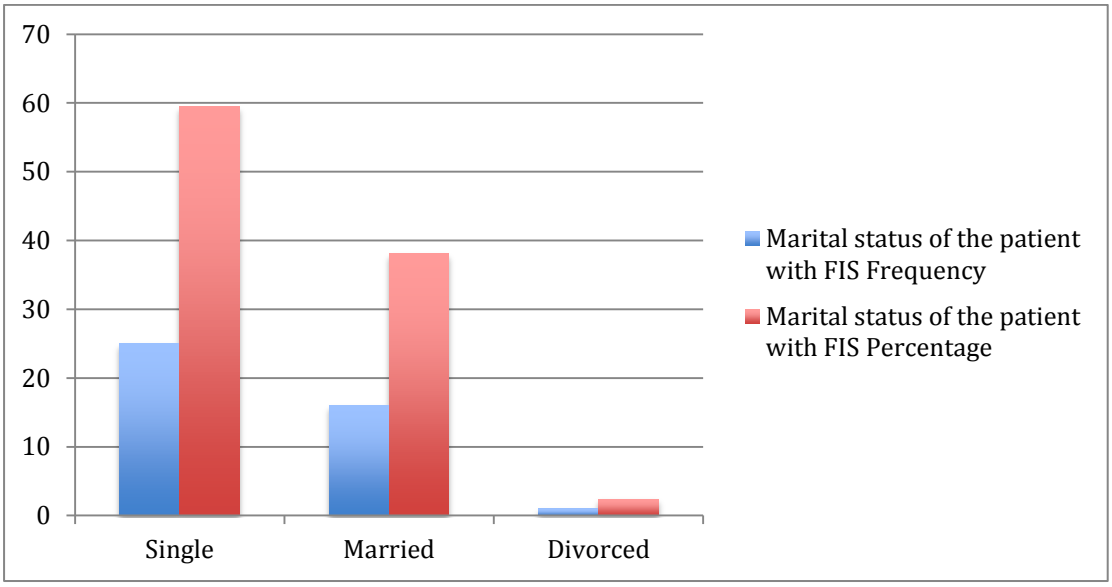


Figure 4: 2D column graph of Frequency of Marital Status of patients with FIS.

Most of the Patients identified as students, with only one patient achieving Tertiary education. A majority achieved either Primary Education (47.6%) or Secondary Education (38.1%). Pointing towards significant vocational and informal education.

LEVEL OF EDUCATION		
	FREQUENCY	PERCENT
NONE	5	11.9
PRIMARY	20	47.6
SECONDARY	16	38.1
TERTIARY	1	2.4
TOTAL	42	100

Table 1: Frequency table of Level of education.

OCCUPATIONAL STATUS		
	FREQUENCY	PERCENT
EMPLOYED	6	14.3
UNEMPLOYED	12	28.6
SELF EMPLOYED	8	19
RETIRED	2	4
STUDENT	14	33.3
TOTAL	42	100

Table 2: Frequency table of Occupational Status.

More than half of the patients were tranfered to Kenyatta National hospital after a period of treatment from peripheral facilities (62%). Of these referred patients exactly half of them (50%) were from Hospitals around Nairobi. Followed by Kiambu(11.9%) and Nyeri county (7.1%) respectively. The patient that presented from the farthest away was noted to be from Mombasa county.

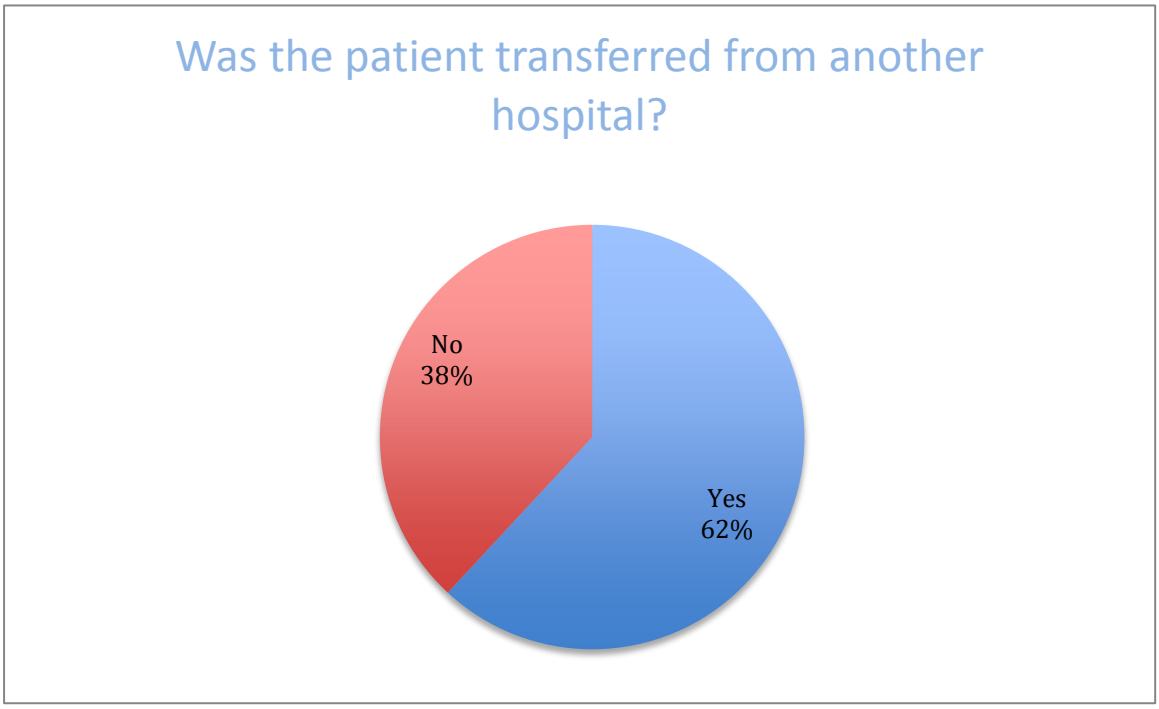


Figure 5: Pie chart of frequency of referral from Peripheral facilities.

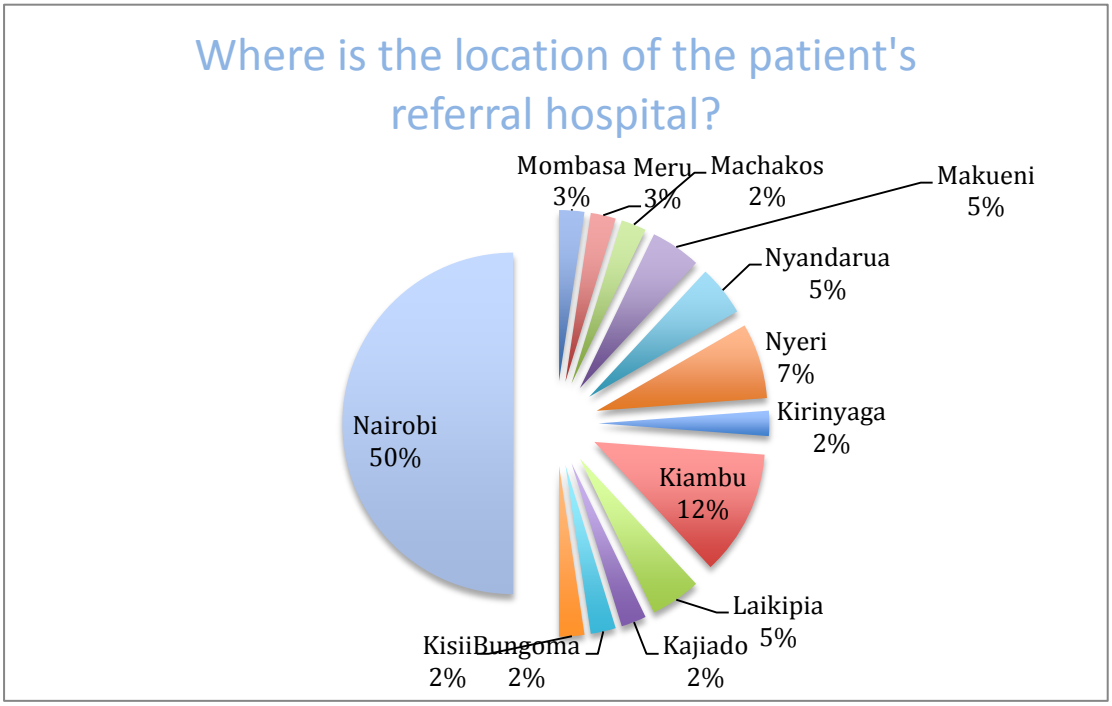


Figure 6: Exploded Pie chart of frequency of location of hospitals referring patients with FIS to KNH.

SYMPTOMATOLOGY

The Duration of symptoms varied from less than 3 days to > 28 days. With two peaks of presentation at 8-14 days and >28 days and a mean duration of symptoms in days of 8-14 days.

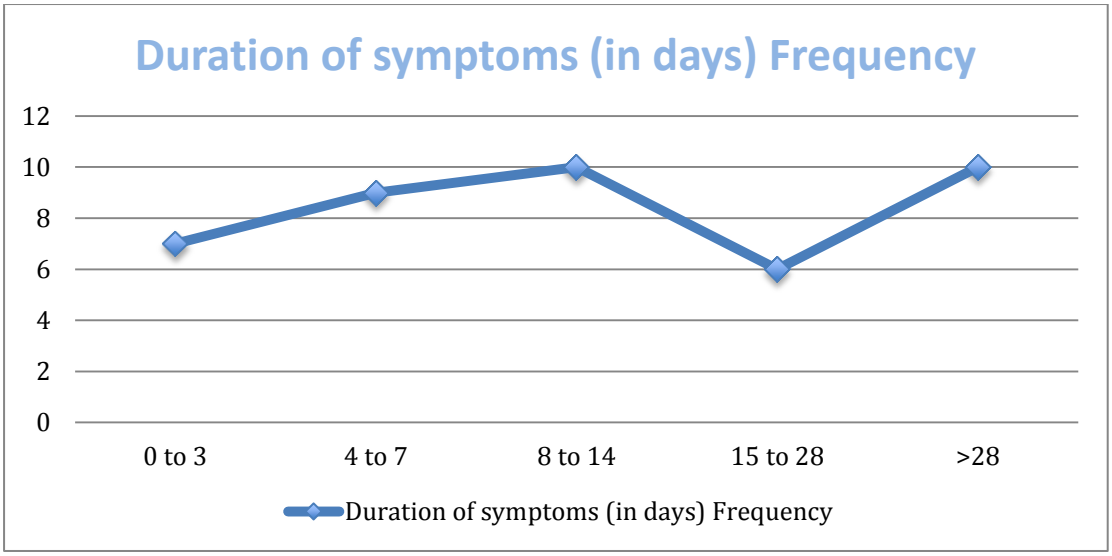


Figure 7: Frequency Histogram of duration of symptoms in days.

With regard to the Glasgow coma scale of patients at presentation. 27 of the patients (64.3%) presented with a relatively good GCS of between 12-15. 9 patients (21.4%) were moderately ill with GCS' of 8-11 and 5 (11.9%) were gravely ill with GCS' of < 5. One infant was included.

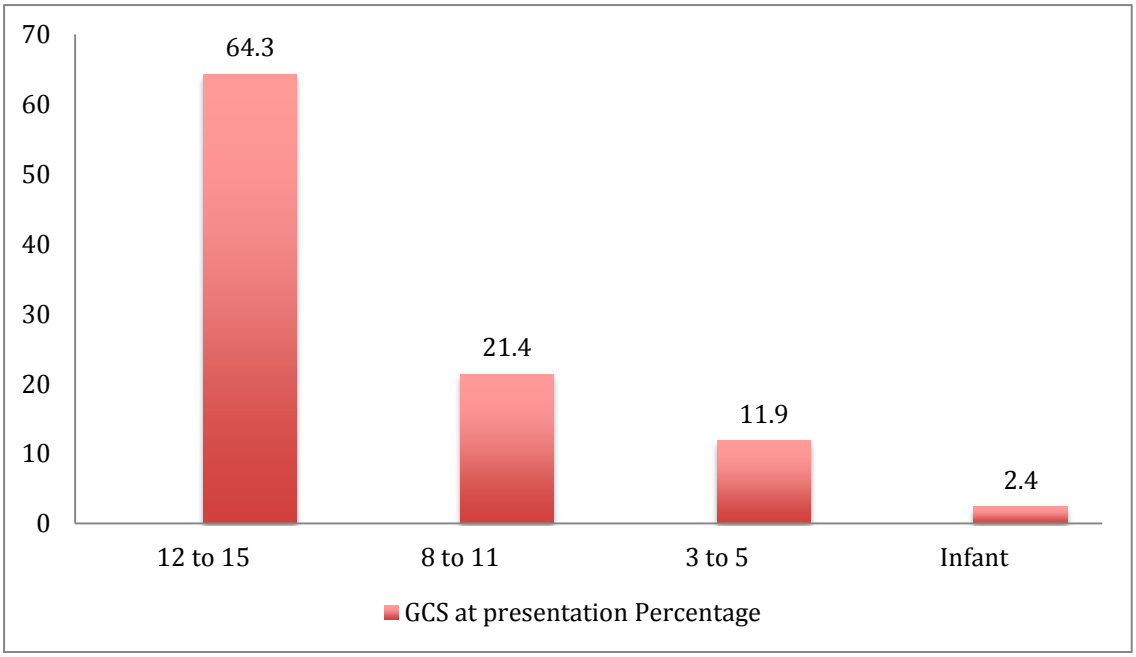


Figure 8: Bar graph showing Percentage frequency of GCS at presentation.

Of the specific symptoms being captured. The commonest by far was headache, of which 71.4% of patients presented with. This was followed closely by seizures which over one third (35.7%), of patients presented with. 28.6% had fevers.

The gravest neurologic deficit noted was hemiparesis with 40.5% of patients presenting, and 4 patients with complete hemiplegia. 7 patients (16.7%) presented with features of meningism and nuchal rigidity. 8 were vomiting. 9 patients were aphasic and only 4 patients had cranial nerve palsies 3 of whom had Facial nerve palsies. 6 Patients presented in a comatose state.

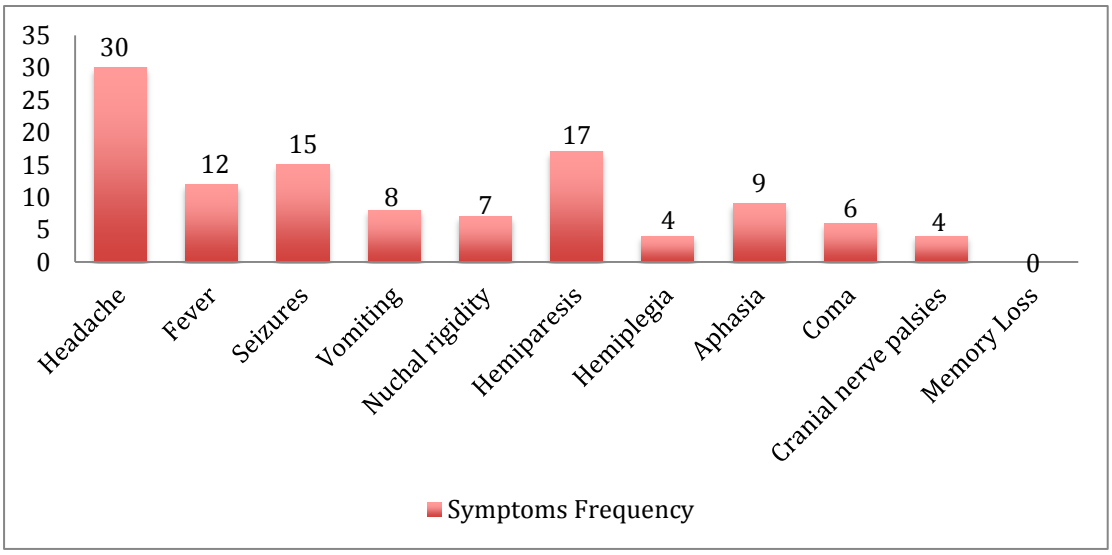


Figure 9: Frequency table of symptoms of patients presenting with FIS.

AETIOLOGY

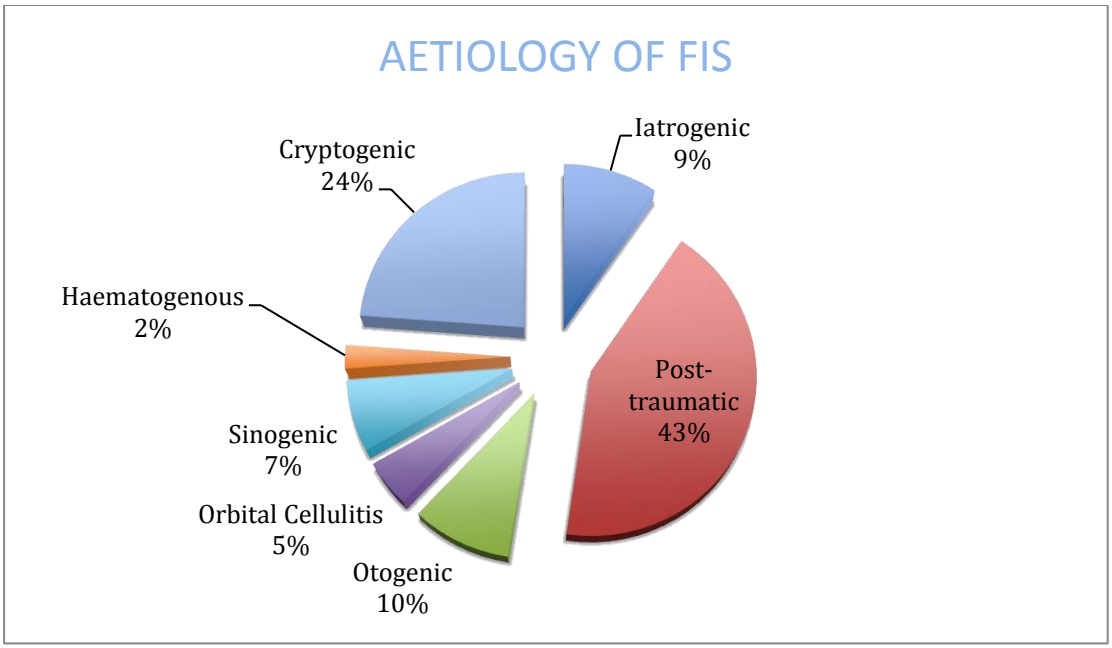


Figure 10: Exploded pie chart showing percentage aetiology of FIS.

As seen in the diagrammatic representation. A majority of the aetiology of FIS was Post traumatic with 18 patients (42.9%) followed by Cryptogenic 10(23.8%) patients. Both Otogenic and Iatrogenic had 9.5% of patients each.

AETIOLOGY		
	FREQUENCY	PERCENTAGE
IATROGENIC	4	9.5
POST-TRAUMATIC	18	42.9
OTOGENIC	4	9.5
ORBITAL CELLULITIS	2	4.8
SINOGENIC	3	7.1
HAEMATOGENOUS	1	2.4
CRYPTOGENIC	10	23.8
TOTAL	42	100

Table 3: Frequency and Percentage of Aetiology of FIS.

IMMUNE STATUS OF THE PATIENT

Only 2 patients were seropositive for HIV and one patient was noted to have a malignancy. No patients were known to be diabetic or on immunomodulant therapy.

ORGANISMS IDENTIFIED

ORGANISMS IDENTIFIED.			
GRAM POSITIVE COCCI		FREQUENCY	PERCENTAGE
	Staphylococcus aureus	7	16.7
	Enterococcus faecalis	1	2.4
	Coagulase negative Stapylococci	1	2.4
GRAM NEGATIVE RODS	Pseudomonas aeuroginosa	1	2.4
	Klebsiella pneumoniae	1	2.4
	Enterobacter cloacea	1	2.4
ALCOHOL AND ACID FAST BACILI	Mycobacterium tuberculosis	1	2.4
STERILE ABSCESS	No growth obtained	29	69
	TOTAL	42	100

Table 4: Organisms identified from Pus samples of patients.

A majority of the patients presented with sterile abscess' (69%). 21.4% of pus samples from patients had gram positive cocci. 7.1% had gram negative rods. Only 4.8% of patients has anaerobic bacteria. One case of a tuberculous abscess secondary to mycobacterium tuberculosis was identified in a seropositive patient. Of note mostly singular organisms/ colonies were identified and only one polymicrobial culture obtained. No fungal abscess' were detected.

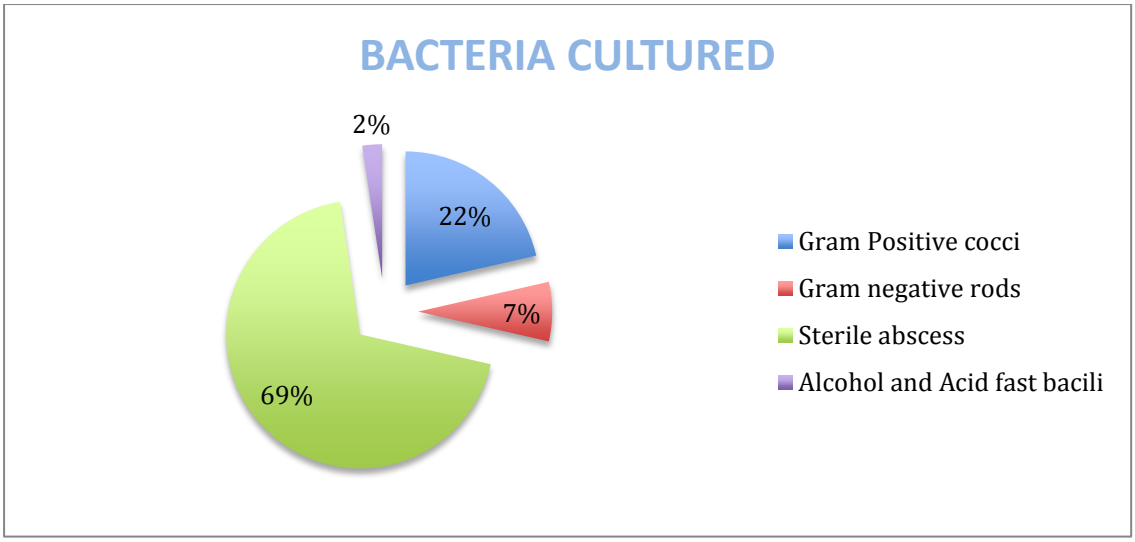


FIGURE 11: Exploded Pie chart showing classification of bacteria identified.

ANTIBIOTIC SENSITIVITY

SENSITIVITY FOR GRAM POSITIVE COCCI

ANTIBIOTIC	SENSITIVE	RESISTANT	NOT DONE
BENZYL PENICILIN	1	6	2
GENTAMYCIN	8	0	1
LEVOFLOXACIN	7	0	2
ERYTHROMYCIN	6	2	0
LINEZOLID	7	0	2
TEICOPLANIN	7	0	2
VANCOMYCIN	9	0	0
TETRACYCLIN	4	3	2
CO-TRIMOXAZOLE	4	3	2

Table 5: Antibiotic sensitivity of Gram positive cocci. excluding coagulase negative staphylococci

SENSITIVITY FOR GRAM NEGATIVE RODS

ANTIBIOTIC	SENSITIVE	RESISTANT	NOT DONE
AMPICILLIN	1	2	0
AMOXICILLIN AND CLAVULINIC ACID		2	1
PIPERACILLIN/ TAZOBACTAM		3	0
CEFUROXIME		2	1
CEFOTAXIME		3	0
CEFTAZIDIME		3	0
CEFTRIAXONE		3	0
CEFEPIME		3	0
MEROPENEM	2	1	0
AMIKACIN	2	1	0
VANCOMYCIN	2		1
GENTAMYCIN	1	2	0
ERYTHROMYCIN		1	2
CIPROFLOXACIN		2	1
NITROFURANTOIN	1	1	1
ORFLOXACIN	1		2
NETILMYCIN	1		2

Table 6 : Antibiotic Sensitivity of Gram negative Rods and Coagulase negative Stapylococci.

NEURORADIOLOGIC FINDINGS

PATTERN OF FIS

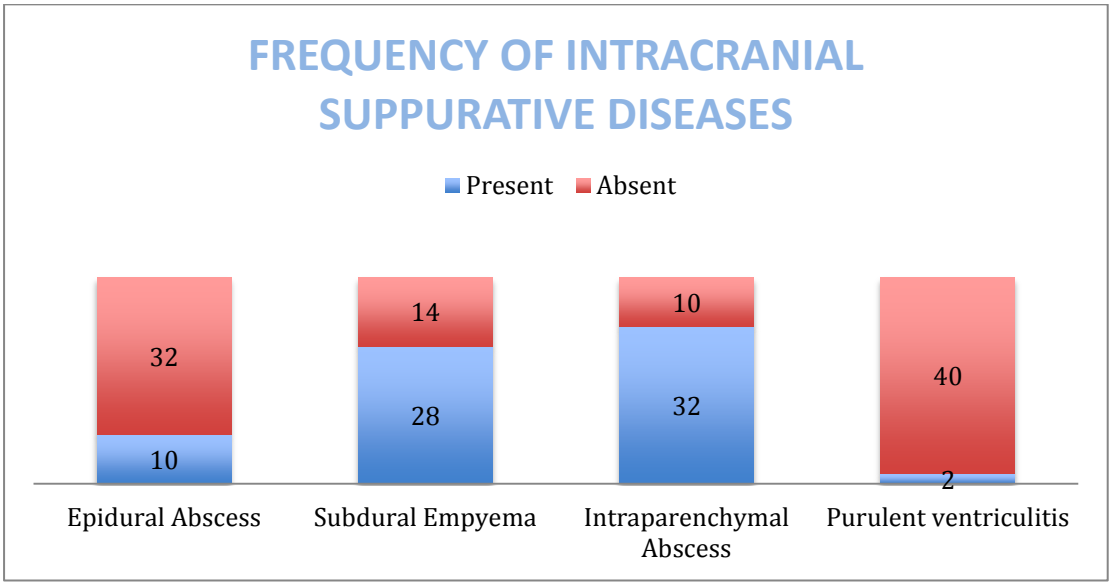


Figure 12: Stacked Column Chart Showing frequency of Intracranial suppurative diseases

As noted 32 patients had intraparenchymal abscess'(76.2%), however only 7 had purely intraparenchymal abscess'(16.6%). Following was subdural empyema with 28 patients (53.9%) however only 2 had pure empyema (4.8%). 10 (23.8%) had epidural abscess' with 6 (14.2%) being purely epidural. Only 2 patients had purulent ventriculitis (4.8%) with only one patient with a pure ventriculitis recorded. A neonate that developed it post meningitis. The association between the intracranial suppurative diseases is illustrated below in a venn diagram.

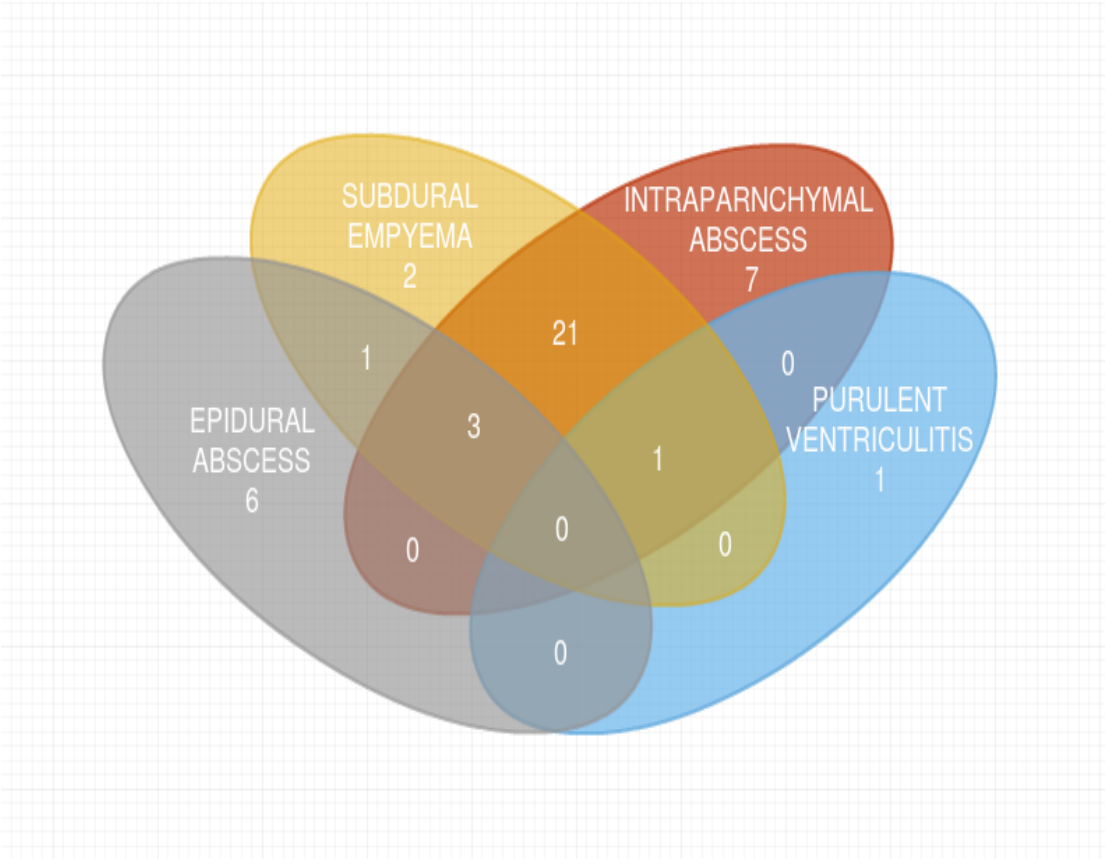


Figure 13: Venn diagram illustrating groupings of FIS.

VOLUME OF PUS

The different volumes of pus are illustrated in the figure below.

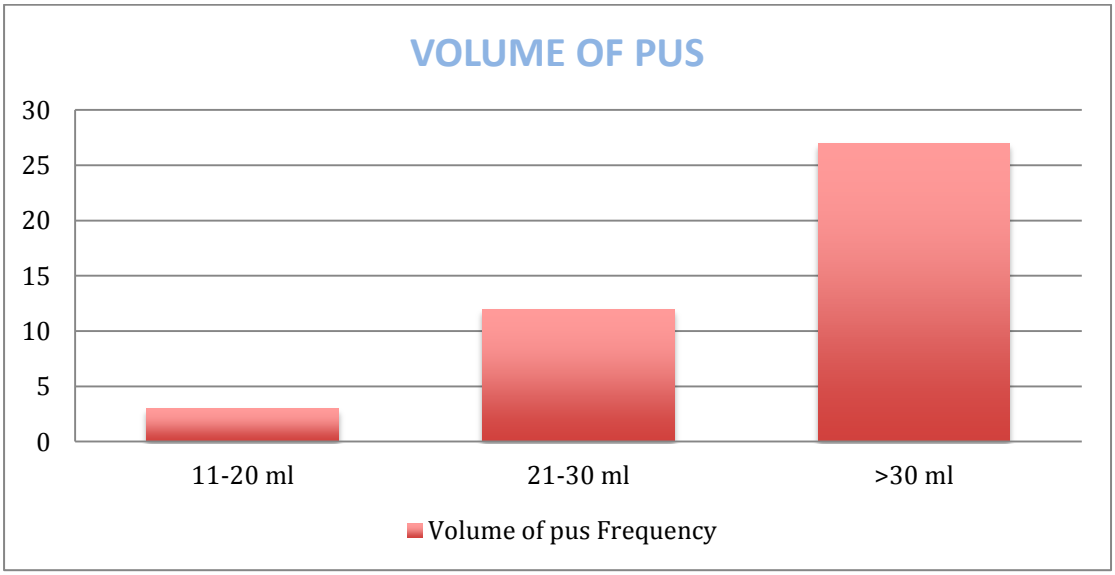


Figure 14: Clustered column graph illustrating the frequency of the different volumes of Pus within the abscess.

27 Abscess (64%) were > 30ml, of these 15 of them were intraparenchymal abscess' with subdural extension. 5 (11% of total) were intraparenchymal abscess with a volume of > 30ml. One was IVRBA with subdural extension.

EXTENTION OF FIS WITH VOLUME > 30ML	NUMBER OF CASES
SUBDURAL + INTRAPARENCHYMAL	15
EPIDURAL,SUBDURAL + INTRAPARENCHYMAL	3
SUBDURAL,INTRAPARENCHYMAL + INTRAVENTRICULAR	1
INTRAPARENCHYMAL	5
EPIDURAL	1
SUBDURAL	2

Table 7 : Frequency Table of abscess' with volume of >30ml

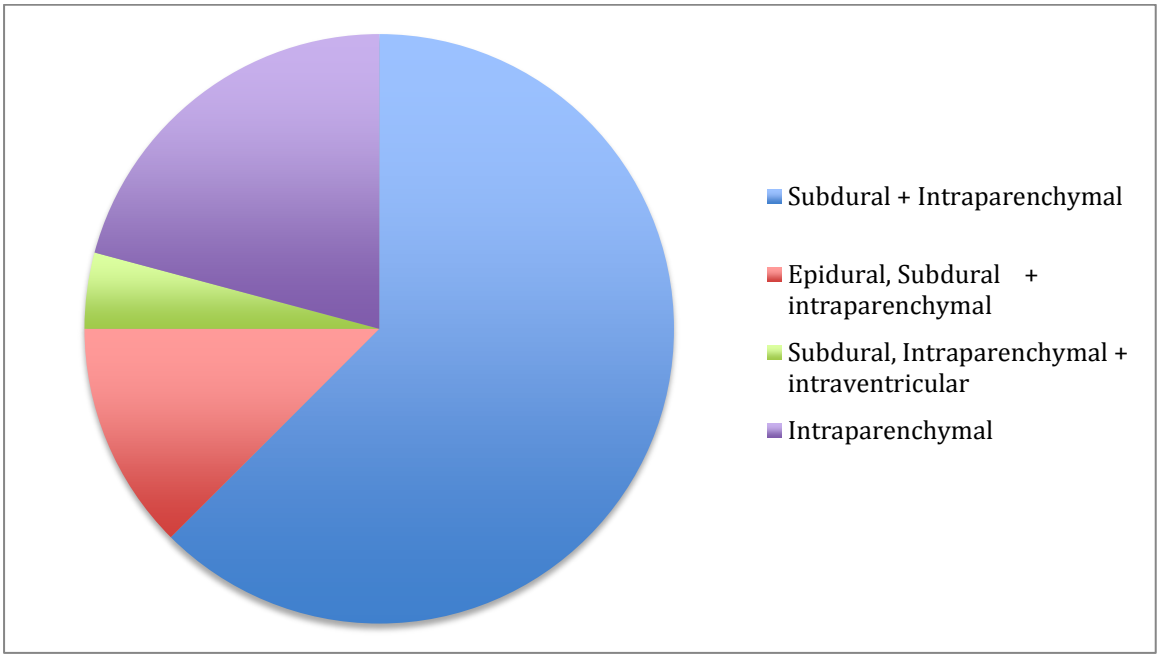


Figure 15: Pie Chart illustrating distribution of FIS with volume of >30ml.

29% (12 cases) of FIS were between 21-30 ml of these : 6 were intraparenchymal, 5 were epidural, 5 were Subdural + Intraparenchymal and one was both epi and subdural.

Only 2 cases were < 20ml, one was an intraparenchymal abscess and the other was an intraparenchymal abscess with subdural extension.

LOCATION OF ABSCESS

	FREQUENCY	PERCENTAGE
FRONTAL	13	31
PARIETAL	9	21.4
TEMPOROPARIETAL	3	7.1
FRONTOPARIETAL	8	19
CEREBELLAR	1	2.4
FRONTOTEMPORAL	3	7.1
FRONTO-TEMPORO-PARIETAL	1	2.4
PARIETO-OCCIPITAL	4	9.5
TOTAL	42	100

Table 8: Frequency and Percentage of anatomic location of FIS.

97% of the FIS was supratentorial with 31% being frontal followed by 21% parietal and 19% frontoparietal. There was only one infratentorial cerebellar abscess (2%).

DISCUSSION

Focal intracranial suppuration is reported to have a relatively rare occurrence with an incidence ranging from 0.4-0.6/100000 (14). The findings in this prospective study are similar to this global pattern as we have reported relative rarity of the condition. The study carried out at Kenyatta National Hospital reported 47 cases (32 of these with an intraparenchymal component) over a relatively short period of one year. This infers an increase in the number of reported cases compared to the findings of other previous investigators in this locality. Mwang'ombe in a previous study at the same hospital reported 65 cases of brain abscess over a five year period from January 1989 to December 1993 corresponding to approximately 13 cases per year (20). Although this study was carried out within one year, clinical case presentations at Kenyatta National Hospital for brain abscess seem to have doubled from about thirteen to thirty two cases per year. This is a significant increase from the findings of Ndirangu in an even earlier study carried out at the same hospital over a ten year period (1970-1979)which reported a much lower occurrence of brain abscesses of 4 cases per year (20,70).

Locally more males were affected by focal intracranial suppuration, which is in keeping with international data. However, most meta-analyses report Male to Female ratios (M/F ratios) of between 2.4:1 – 3:1(38,40,41). Our M: F ratio was 5:1. This could be related to the fact that the aetiology of a majority of the focal intracranial suppuration was post traumatic. This is in keeping with previous studies at the institution that showed M:F ratios of 2.4:1(20).

Focal intracranial suppuration is normally reported in the developed world as being common within the first 4 decades of life in numerous studies. Indeed this is true even locally as 59.2% of our patients were between the ages of 13-45. This however differs from the two previous studies conducted at this facility that showed a majority of cases (25%) being below 5 years of age. This could be due to an increased use and availability of antibiotics resulting in a decrease of focal intracranial suppuration secondary to complications of Meningitis, Otitis and Sinusitis. Which are more common aetiologies in the younger age groups.(2,32,39)

A picture of a clear demographic group is brought out in this study. Singles account for (59.5%) and males (83%), 47.6% of whom have only attained primary school education and 38% secondary school education. This is in-keeping with the Kenya demographic and health Survey 2014 that showed a gross attendance ratio (GAR) of 103.3 for primary school that dropped off to 66.1 for secondary school within the region of Nairobi(71). Despite a majority of the patients being of "working age" only 14% had formal employment. These findings set a unique picture of a still developing nation as these statistics set a stage for an increased burden of neurotrauma and with our disease of focal intracranial suppuration, Penetrating head trauma is a known aetiology.

Kenyatta National Hospital is one of only two national teaching and referral hospitals to date offering specialized neurosurgical care to the country (including Moi Teaching and referral hospital in Eldoret). This is reflected in the wide catchment group with patients reporting from as far away from Mombasa with a diagnosis of focal intracranial suppuration which in itself causes significant morbidity and mortality.

50% of patients were from Nairobi and its environs. Despite this, 62% of patients were referred from a prior medical facility after an initial treatment with antibiotics resulting in a relatively long duration of symptoms in our patients, with most patients having symptoms lasting longer than 8 days.

Developing countries report that in about two thirds of patients, symptoms are present for 2 weeks or less (42,52). The clinical course ranges from indolent to fulminant. With regards to the patients involved in our study, the progression of symptoms appeared to be more indolent. This may be due to a prolonged course of antibiotics at previous facilities. This is common practice as although computerized tomography is now more widely available throughout the country, it still remains an expensive modality, which outside teaching hospitals and private facilities remains a diagnostic modality of last resort post trial of antibiotics for a nonspecific febrile illness. And indeed for 65% of our patients the CT scan image was the primary reason for referral (i.e patients with GCS of between 12-15). For the remaining 33.3% the primary reason for referral was escalation of care and need for a specialized care and i.e I.C.U services (GCS <8). Upon presentation based on symptomatology a CT scan was done and upon the radiological diagnosis of an intracranial space occupying lesion probably focal intracranial suppuration. The neurological Service was involved and once focal intracranial suppuration was confirmed the patient was enrolled into the study.

Most symptoms are a result of the size and location of the space-occupying lesion or lesions. The classic triad of fever, headache (often severe and on the side of the abscess) reported in standard neurosurgical text books, and focal neurologic deficit

occurs in less than half of patients and upto < 20% in some series(58). The most common clinical features our patients presented with were headache, hemiparesis and seizures. This is interesting as although multiple studies report fever as appearing to be the only constant presentation in 50-75% of cases (42, 48). Fever was only present in 29% in our study. Perhaps this may again be due to prolonged empirical treatment with antibiotics.

The pathophysiology of focal intracranial suppuration may be due to direct extension, haematogenous spread or intracranial trauma. Which is discussed earlier in this text. Direct extension is noted to be the most frequent cause of infection in focal intracranial suppuration (50-52). In our series intracranial trauma was the most common pathophysiology at 43%, 52% if you include post surgical intervention. This is not unusual given the primary demographics of young males identified earlier. A secondary factor could also be due to the reported relative decline of otogenic brain abscess'. Newer series also support this increase in abscess' due to intracranial trauma and intervention via neurological surgery. With studies showing incidences as high as 2-37% (42,48). Focal intracranial suppuration may form as an immediate or delayed complication; direct inoculation of pathogens can quickly lead to abscess formation, whereas a retained foreign body such as soil, bone fragments, any penetrative foreign object or focus of necrotic tissue can serve as a nidus of infection months or years after the initial insult. Fortunately for all the patients involved they presented within a period of < 28days.

21.4% of focal intracranial suppuration was due to direct extension Sinogenic, Orbital cellulitis, Otogenic. These are common and well known causes of focal intracranial

suppuration. However, complications of these infections have decreased in incidence with improvements in diagnostic modalities and antibiotic therapy. This is supported by our findings. Overall, abscess caused by direct extension now comprises 12-25% of all brain abscesses(48).

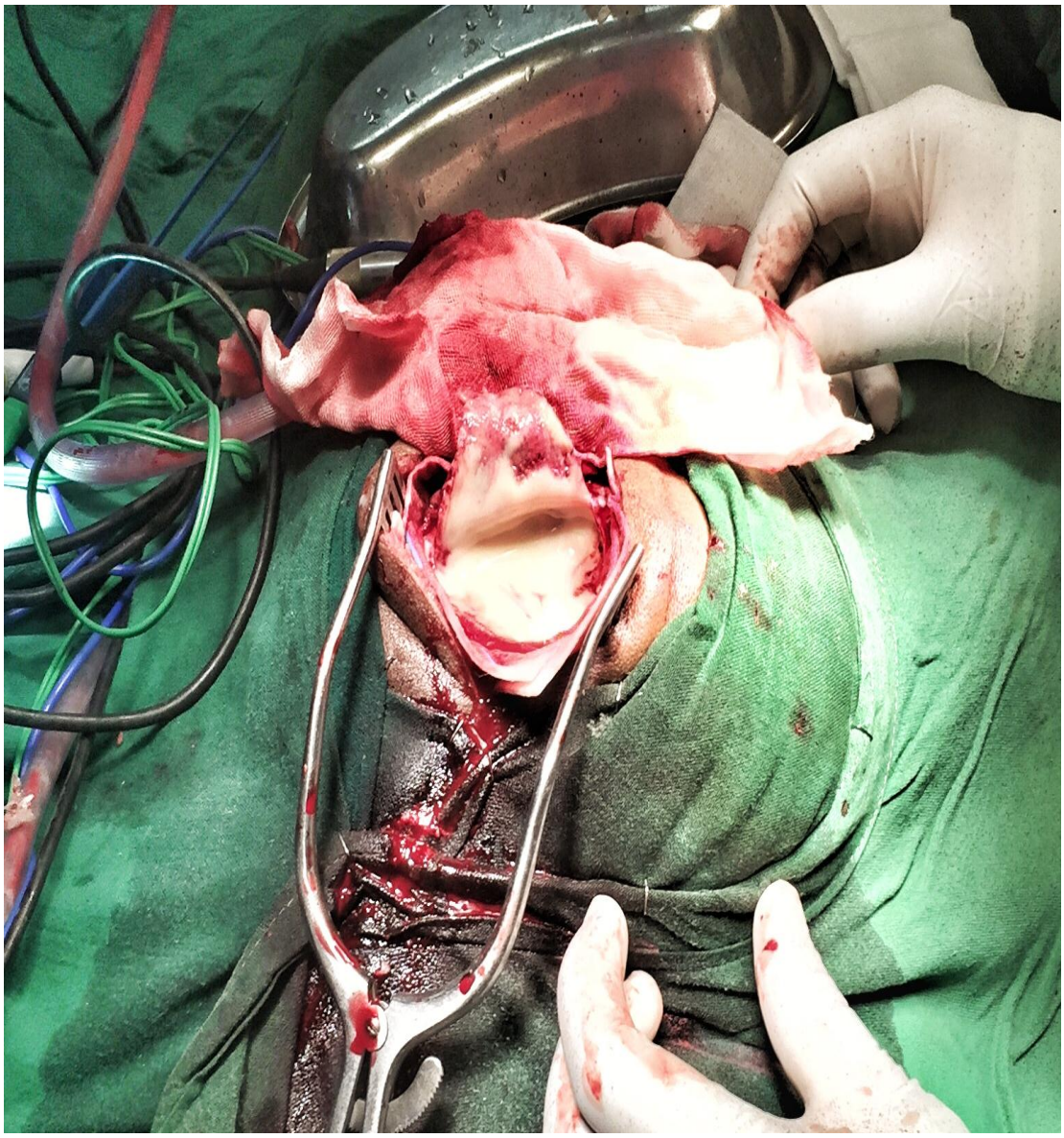
The previous study by Mwang'ombe between 1989-1993 showed a similar picture, with intracranial trauma being most common at 35% followed by direct extension at 20%. This is interesting that more than 24 years later the same picture is noted, albeit with a higher prevalence.(20)

Only one patient had an abscess secondary to haematogenous spread (2.4%). This differs from other series from more developed countries which report it as normally the second most common cause and is usually as high as 25%.(50)

Regarding organisms identified, 69% of the focal intracranial suppuration was due to sterile abscess with no identifiable organism. This is a unique situation perhaps due to the prolonged use of empirical antibiotics prior to definitive diagnosis and referral.

As most of the abscesses were post traumatic, it is corollary that 22% of them were due to gram positive cocci namely Staphylococcus aureus and coagulase negative staphylococci. Meta-analysis implicate staphylococcus at 34% (38). The bacteria were noted to be resistant to benzyl penicillin (67%). 33% were resistant to erythromycin, tetracyclin and co trimoxazole; however these numbers were too low to be statistically significant at only 3 organisms each.

The study illustrates regardless of the initial inoculation focal intracranial suppuration is a continuum with the most common pattern of extension being intraparenchymal to subdural at 45.7%. One patient had IVRBA with a large supratentorial abscess abutting the ventricle that also violated the arachnoid extending into the subdural space. Eghwrudjakpor et al also reported case of brain abscess extending into the subdural space in Nigeria (1). No other local studies have reported on the phenomenon.



Picture 1: Osteoplastic craniotomy for intraparenchymal abscess extending into the subdural space done at the Kenyatta National Hospital during the study period.

CONCLUSION

1. FIS is not as uncommon as previously thought and is increasing in prevalence .
2. Young men of working age and the commonest affected with a M:F ratio of 5:1 and 59% between the ages of 13-45.
3. The commonest aetiology is intracranial trauma with more than half of the cases at 52%.(including post craniotomy).
4. Headache seizures and hemiparesis were their primary presentation.
5. 62% of patients presented after 8 days of antibiotic therapy at primary facilities.
6. An overwhelming majority of the abscess presenting are sterile at 69% of cases.
7. Unimicrobial abscess' caused by Stapylococcus aureus are the commonest microbe identified at 22%.
8. Large frontal abscess of > 30 ml are the commonest at 31%
9. The commonest pattern of FIS is an Intracranial abscess with subdural extension at 50%.

RECOMMENDATIONS

1. Increase the study period and sample size to increase the power of the study. Thereby also giving a clearer picture of the epidemiology of FIS.

2. To carry out a follow up study on the outcomes of FIS to get a picture of the current mortality and Glasgow outcome scores.

3. To disseminate information to primary facilities on the increasing prevalence of FIS particularly secondary to intracranial trauma increasing the index of suspicion in order to decrease the delay in transfer time.

4. A follow up study on purely FIS secondary to intracranial trauma in order to identify and quantify the local risk factors.

5. Prompt detection and treatment of FIS.

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APPENDIX I

CONSENT FORM

PART 1: CONSENT TO PARTICIPATE IN THE STUDY

Study number.....

Title of the study

Study

CLINICAL PATTERNS OF FOCAL INTRACRANIAL SUPPURATION, AND COMMON CAUSATIVE ORGANISMS, AS SEEN AT THE KENYATTA NATIONAL A PROSPECTIVE STUDY.

Introduction

This study will be carried out by Dr. Michael Augustus Magoha, a post graduate student in the department of neurosurgery, University Of Nairobi. Focal intracranial suppuration is a severe life-threatening condition. The limited resources in developing countries and lack of widespread availability of imaging modalities namely computerized tomography and magnetic resonance imaging tend to delay diagnosis and prompt referral to facilities with neurosurgical personnel.

Objectives of the study

This study aims to determine the clinical pattern of focal intracranial suppuration, risk factors associated with and identification of the bacterial causative agents and antimicrobial susceptibility patterns.

Benefits of the study

The participant may directly benefit from this research if and when any suppuration is detected and associated organisms' isolated and antimicrobial sensitivity done. The knowledge of incidence, risk factors and micro- organisms, will allow health professionals to implement protocols to reduce the infection rates and improve the quality of life of patients.

Risks of the study

The participant shall at no time be exposed to any health risk.

Costs

All the costs of this study will be undertaken by the principal investigator.

Voluntarism

I understand my participation is voluntary and that I am free to withdraw at any time, without giving reason. This will not affect my future care or treatment.

Confidentiality

All the obtained information will be held in the strictest confidence and will not be disclosed without the consent of the clinical unit concerned. I will do everything I can to protect your privacy and your identity will not be revealed in any publication arising from this study.

Type of specimens and amount to be obtained

Patients will be observed for presence Focal intracranial suppuration and samples will be collected during operative procedures. Pus swabs from the surgical site will be

collected aseptically using a sterile cotton swab and taken to the laboratory within one hour. The collected samples will be cultured to identify the causative bacteria and then inoculation done to determine the sensitivity patterns to commonly used antibiotics.

Follow up schedules /expected time in the study

The study will be conducted in ward 4C and ICU in KNH between July 2016 and June 2017. The participants will be followed up for 2 weeks post operatively.

PROBLEMS OR QUESTIONS:

Information on researchers and telephone numbers, Any queries, concerns or problems arising from this study should be directed to the following people:

Principle investigator: Dr. Michael Magoha 0710388279

Supervisors:

Professor Nimrod Mwangombe 0736222191, Dr C.K Musau 0722512740, Dr Ann Maina 0727490540.

The KNH/UON ethics and research committee. 020-2726300 ext 4435

IDHINI YA KUJIHUSISHA NA UTAFITI.

Namba ya utafiti.....

Jina la utafiti

Ruwaza Kliniki ya usaha inayeshughulikia kichwani , na vimelea kawaida kuonekana kwa kenyatta hospitali ya taifa. Utafiti wanaotazamiwa.

Kuanzishwa

Utafiti huu utafanywa na Dk Michael Augustus Magoha , mwanafunzi baada ya kuhitimu katika idara ya upasuaji wa kichwa , Chuo Kikuu cha Nairobi.

usaha inayeshughulikia kichwani ni kali kutishia maisha hali. mdogo wa rasilimali katika nchi zinazoendelea na ukosefu wa upatikanaji ulioenea wa upigaji yanayofanywa yaani kompyuta tomography na mwangwi wa sumaku huwa na kucheleweshe utambuzi na rufaa haraka kwa vifaa pamoja na wafanyakazi upasuaji wa kichwa.

Malengo ya utafiti

Utafiti huu unalenga kuamua muundo kliniki ya usaha inayeshughulikia kichwani, hatari zinazohusiana na na utambuzi wa mawakala vimelea kawaida na chati ya kuhisi kiuavijasumu.

Faida za utafiti

mshiriki inaweza moja kwa moja faida kutokana na utafiti huu ikiwa na wakati usaha yoyote ni wanaona na viumbe kuhusishwa ' wametengwa na l unyeti kiuavijasumu kufanyika. maarifa ya matukio , hatari na viumbe micro- , itaruhusu wataalamu wa afya ili kutekeleza itifaki kupunguza viwango vya maambukizi na kuboresha ubora wa maisha ya wagonjwa.

Hatari ya utafiti

Afya ya mshiriki haitakuwa kwa hatari wakati wowote.

Gharama

Gharama zote za utafiti huu zita simamiwa na mpelelezi mkuu.

Kujitolea

Naelewa ushiriki wangu ni kwa hiari yangu na kwamba niko na uhuru wa kuondoka wakati wowote, bila ya kutoa sababu. Hii haitaathiri huduma yangu ya baadaye ama ya matibabu.

Siri

Habari zote zilizopatikana zitafanyika katika imani kali na hazitafunuliwa bila ridhaa ya kitengo cha kliniki husika. Mimi nitafanya kila kitu naweza kulinda faragha yako na utambulisho wako hautafafunuliwa kwa uchapishaji kutokana na utafiti huu.

Ina ya vielelezo na kiasi kwa kupatikana

Wagonjwa itakuwa aliona kwa uwepo usaha inayeshughulikia kichwani na sampuli itakuwa zilizokusanywa wakati taratibu wa upasuaji. Usaha kutoka tovuti upasuaji zitakusanywa kutumia kuzaa usufi pamba na kupelekwa maabara ndani ya saa moja . sampuli zilizokusanywa itakuwa cultured kutambua vimelea na kisha chanjo kufanyika kwa kuamua chati kwa unyeti wa kawaida kutumika kiuavijasumu.

Kufuatilia ratiba / inatarajiwa wakati katika utafiti

utafiti utafanywa katika kata 4C na ICU katika KNH kati ya Julai 2016 na Juni 2017.Washiriki itakuwa na kufuatiwa up kwa wiki 2 baada ya upasuaji.

<u>MATATIZO AU MASWALI</u> :

Taarifa juu ya watafiti na maswali nambari ya simu.wasiwasi au matatizo yanayotokana na utafiti huu lazima kwa madhumuni ya watu yafuatayo:

Kanuni mpelelezi : Dr. Michael Magoha 0710388279

wasimamizi : Profesa Nimrod Mwangombe 0736222191 Dr C.K Musau 0722512740 Dr Ann Maina 0727490540.

KNH / UON maadili na utafiti wa kamati. 020-2726300 ext 4435

PART 2: CONSENT CERTIFICATE / CHETI RIDHAA

I..... Of …….....

Parent/guardian of .....….study no..... do hereby consent to be included in this study on surveillance of surgical site infections, after being having been satisfactorily explained to about the research in verbal and / or written form by the researcher. The nature of the study has been fully explained to me by Dr..... I have not been promised any material gain toparticipate.

Signed..... (Parent/guardian)

Date.....

PROBLEMS OR QUESTIONS:

Information on researchers and telephone numbers, Any queries, concerns or problems arising from this study should be directed to the following people: Principle investigator: Dr. Michael Magoha 0710388279

Supervisors: Professor Nimrod Mwangombe 0736222191, Dr C.K Musau 0722512740, Dr Ann Maina 0727490540.

The KNH/UON ethics and research committee. 020-2726300 ext 4435

Mimi.....wa.....……M

zazi / mlezi wa.....numbari ya usajili.....nimepatiania ruhusa ya kuhusishwa katika utafiti huu juu ya ufuatiliaji wa maambukizi ya upasuaji.baada ya kuelezwa na kuridhika na maelezo yenye nimeelezewakuwa na iliyoandikwa na mtafiti. Mshiriki kwa utafiti huu

hatakuwa na hatari yoyote ya afya. Mshiriki anaweza moja kwa moja kufaidika kutokana na utafiti huu ikiwa na wakati maambukizi yanapopatikana na kuhusishwa viumbe pekee na antimikrobiell unyeti kufanyika. Naelewa ushiriki wangu ni wa hiari na kwamba mimi niko na ruhusa ya kujiondoa wakati wowote, bila ya kutoa sababu. Hii si kuathiri huduma yangu ya baadaye au matibabu.

Asili ya utafiti nimeelezewa kikamilifu na Dk ..... Mimi sija ahidi ali faida yoyote kwa mushirika Saini ..... (Mzazi / mlezi) Tarehe .....

MATATIZO AU MASWALI :

Taarifa juu ya watafiti na maswali nambari ya simu.wasiwasi au matatizo yanayotokana na utafiti huu lazima kwa madhumuni ya watu yafuatayo:

Kanuni mpelelezi : Dr. Michael Magoha 0710388279

wasimamizi : Profesa Nimrod Mwangombe 0736222191 Dr C.K Musau 0722512740 Dr Ann Maina 0727490540.

KNH / UON maadili na utafiti wa kamati. 020-2726300 ext 4435

APPENDIX II

SCREENING PROFORMA

Study NO DATE: ……/……/……

Age (Yrs) :_____ Date of birth (dd/mm/yyyy):_____/_____/_____

Date of Diagnosis (dd/mm/yyyy):_____.

DEMOGRAPHICS

Gender: M____ F____

Marital Status:
Single___ Married___ Divorced___ Widowed___ Separated___

Occupation:
Employed___Unemployed___Self employed____Retired____Student___

Level of education:
None_____ Primary_____Secondary_____ Tertiary _____

Transfer from other Hospital:
Yes _____ No_____If yes, Location of hospital (Province)_____

SYMPYOMATOLOGY

Duration of symptoms prior to diagnosis (In days)_____

Glassgow Coma Scale on Presentation_____

SYMPTOM	YES	NO	N/A
HEADACHE			
FEVER			
SEIZURE			
COMA			
VOMITTING			
NUCHAL RIGIDITY			
HEMIPLEGIA			
HEMIPARESIS			
APHASIA			
MEMORY LOSS			
CRANIAL NERVE PALSY			

If cranial nerve Palsy present state nerves Involved_____

PATHOGENESIS

	YES	NO	N/A
IATROGENIC			
POST TRAUMATIC			
OTOGENIC			
DENTAL			
ORBITAL CELLULITIS			
SINOGENIC			
HAEMATOGENOUS			
CRYPTOGENIC			

IMMUNE STATUS

	YES	NO	N/A
HIV INFECTION			
DIABETES MELLITUS			
IMMUNOMODULANT THERAPY			
MALIGNANCY			
OTHER			

If Malignancy or Other please state_____

CULTURES

	YES	NO	ORGANISM
PUS			

NEURORADIOLOGIC FINDINGS

TYPE (TICK AS MANY AS APPLY)

EXTRADURAL	SUBDURAL	BRAIN ABSCESS	PURULENT VENTRICULITIS

VOLUME

<10ML	11-20ML	21-30ML	>30ML

LOCATION

FRONTAL	
PARIETAL	
TEMPORAL	
TEMPOROPARIETAL	
OCCIPITAL	
FRONTOPARIETAL	
CEREBELLAR	
THALAMIC	

APPENDIX III

ETHICAL APPROVAL LETTER

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

KENYATTA NATIONAL HOSPITAL APPROVED 27 SEP 2016 KNH/UoN-ERC P.O. Box 20723-00202

Ref: KNH-ERC/A/379

27th September, 2016

Dr. M.A. Magoha
Reg. No.H58/66701/11
Dept.of Neurosurgery
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Magoha

REVISED RESEARCH PROPOSAL: CLINICAL PATTERNS OF FOCAL INTRACRANIAL SUPPURATION, AND COMMON CAUSATIVE ORGANISMS, AS SEEN AT THE KENYATTA NATIONAL HOSPITAL; A PROSPECTIVE STUDY (P88/02/2016)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above revised proposal. The approval period is from 27th September 2016 – 26th September 2017.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH-UoN ERC before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Protect to discover