A STUDY ON BACTERIOLOGICAL PROFILE OF VENTRICULOPERITONEAL SHUNT INFECTIONS

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CERTIFICATE

This is to certify that this dissertation titled **"A STUDY ON BACTERIOLOGICAL PROFILE OF VENTRICULO PERITONEAL SHUNT INFECTIONS"** is a bonafide record of work done by **DR.SHEEBA.V,** during the period of her Post graduate study from June 2010 to April 2013 under guidance and supervision in the Institute of Microbiology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-600003, in partial fulfilment of the requirement for **M.D. MICROBIOLOGY** degree Examination of The Tamilnadu Dr. M.G.R. Medical University to be held in April 2013.

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DECLARATION

I declare that the dissertation entitled **"A STUDY ON BACTERIOLOGICAL PROFILE OF VENTRICULO-PERITONEAL SHUNT INFECTIONS"** *submitted by me for the degree of M.D. is the record work carried out by me during the period of* **November 2011 to October 2012** *under the guidance of Prof.* **Dr.T.SHEILA DORIS M.D.** *Professor of Microbiology, Institute of Microbiology, Madras Medical College, Chennai. This dissertation is submitted to the Tamilnadu Dr.M.G.R. Medical University, Chennai, in partial fulfillment of the University regulations for the award of degree of M.D., Microbiology (Branch IV) examination be held in April 2013.*

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CONTENTS

INTRODUCTION

Hydrocephalus is the most frequent neurosurgical problem encountered in the paediatric age group with an incidence of 1 in 2000 births. It may also occur as a complication of any insult to the nervous system like infections, intra-ventricular haemorrhage, brain tumours, and head injury.[28]

Cerebrospinal fluid (CSF) shunting is a process by which CSF is diverted from the lateral ventricles to another part of the body for absorption Cerebrospinal fluid diversion devices are essential in the management of this pathology [25]. Ventriculoperitoneal shunt, a device inserted for the treatment of hydrocephalus results in significant improvement in neurological function and survival of patients.

Infection is one of the most serious complications after CSF shunt or external ventricular drain placement. It increases both morbidity and mortality and causes an increased incidence of seizures and neurological disturbances[15].

A typical CSF shunt comprises of three parts, a proximal portion – ventricular catheter, which is inserted into the CSF space, a valve and reservoir and a distal portion – terminating in the peritoneal (ventriculoperitoneal shunt), pleural (ventriculopleural shunt) or vascular space (ventriculoatrial shunt) .

CSF shunts may become infected by retrograde infection from the distal end, through the skin, by haematogenous seeding or by colonization at the time of surgery [2].

The clinical features of shunt infection depend upon the pathogenesis of infection, virulence of organism and the site of infection (proximal or distal portion). Fever is typically present in the majority of patients. Other symptoms seen are headache, nausea, vomiting, lethargy, changes in mental status, seizures, pain at the distal end and features of peritonitis.

Children are more likely to acquire shunt infections than adults because of immature immune system, long hospital stay and higher concentration of bacteria in the skin[2]. Some of the factors commonly associated with increased risk of CSF shunt infection are premature birth, aetiology of hydrocephalus, previous shunt infection, length of procedure and shunt revision. About 90% of infections are diagnosed in the first 6 months, majority in the first 3 months[23].

The organisms frequently isolated from CSF shunt infections are *Staphylococcus epidermidis* (47-64%), followed by *S.aureus* (12-29%) and gram negative bacilli like *Escherichia coli*, *Klebsiella*, *Proteus* and *Pseudomonas* species (19- 22%).

Diagnosis is established by direct culture of the CSF or of fluid within or around the shunt or ventricular reservoir. CSF obtained from the ventricular reservoir is ideal for culture. Neuroimaging studies are not useful in identifying shunt infection but show evidence of shunt malfunction.

Treatment of shunt infection includes shunt removal, insertion of external ventricular drain (EVD) and administration of intravenous antibiotics for 7-10 days. Intraventricular antibiotics, via the reservoir or EVD may be required for those not responding to systemic antibiotics. Reshunting is usually done after 7-10 days of antibiotic therapy or when culture becomes negative. Removal of shunt hardware with shunt replacement and intravenous antimicrobial therapy cures approximately 65-75% of patients with shunt infections.

AIM OF THE STUDY

- To isolate the causative organisms.
- To assess the risk factors associated with shunt infection.
- To find the incidence of infection associated with shunt related procedures.
- To determine the antimicrobial susceptibility pattern of the isolates to aid in management.
- To evaluate the outcome of management.

REVIEW OF LITERATURE

Approximately 25,000 shunts are estimated to be placed each year in North America and about twice as many are revised (total of 75,000 shunt operations). Shunt operations are the most frequently performed procedures by paediatric neurosurgeons [29].

The word shunt is derived from the English word *shun*, which denotes being pushed away, suggesting diversion. This seems to be appropriate as the fundamental role of shunts is diverting CSF from within the ventricles to an alternative location outside the subarachnoid space [29].

The most common distal site for diversion is the peritoneum and these are described ventriculoperitoneal shunts.

History of shunting

It was Hippocrates who made the first attempt to drain ventricular CSF in a case of hydrocephalus[17].The first attempt to drain CSF into the peritoneal cavity was recorded in 1898, when a silver wire was introduced into the peritoneal cavity through the vertebral body of L5 in the hope of creating a fistula to drain CSF [5].

In 1907, CSF diversion into the superior sagital sinus was attempted, but the mortality rate was 100% [5].

In 1939, Torkildsen performed a shunt from the lateral ventricle to the cisterna magna and the mortality rate was 50% [5].

In 1952, Nulsen and Spitz made a significant contribution to the treatment of hydrocephalus by introducing the first valve regulated shunt system to prevent the reflux of venous blood [45].

In 1960, Ransohoff et al recorded a success rate of 65% with ventriculopleural shunts[51].

It was reported by Scarff that 55% of 230 patients had arrested hydrocephalus after placement of a VP shunt in 1963[55].

In the 1970s, Ames' work suggested that the peritoneal cavity was the best site for diversion of CSF[5].

The first VP shunt placement is attributed to Cushing in 1908. But, VP shunts did not gain popularity until 1963,when Scarff published his work [55] .

Venticuloperitoneal shunts became first-line therapy for the treatment of hydrocephalus in the 1970s.

HYDROCEPHALUS

Definition

Hydrocephalus is an excessive accumulation of CSF within the head caused by a disturbance of formation, flow or absorption.

Cerebrospinal fluid (CSF)

The intracranial compartment volume consists of 100-150 ml CSF, 100 ml blood and 1000-1200 mg brain. The cerebral perfusion pressure ranges from 50-150mm H_20[5].

The normal CSF production rate in an adult is 0.37 ml/min (20 ml /hour or 500 ml/24 hours) [16].

The CSF is normally clear with a glucose concentration of about 45 to 100 mg/dl, which depends on blood sugar levels and protein concentration of about 14 and 45 mg/dl. It is sterile with a cell count of less than 5 lymphocytes per ml.

The capacity of normal lateral and third ventricles is approximately 20 ml, whereas the total CSF volume is 120 – 150 ml. In normal circumstances CSF is recycled over 3 times each day.

Pathophysiology of Hydrocephalus

Physiologically, hydrocephalus is a hydrodynamic disorder in which the volume of CSF in the subarachnoid and / or ventricular spaces is abnormally elevated due to overproduction, underabsorption, both or increased venous pressure[5].

The accumulation of fluid in various intracranial compartments was recognised by Hippocrates (BC 460-377) and Claudius Galen (130-200 AD). The first morphological description of hydrocephalus is attributed to Andreus Vesalius (1514-64) who recognised the ventricular enlargement and brain destruction. Thomas Willis (1621-75) was the first to propose that choroid plexus is the site of CSF production. [6]

It is presumed that 50-80% of the CSF is produced in the choroid plexus lining the walls of the lateral ventricles, roof of third and fourth ventricles[48]. Once formed in lateral ventricles, CSF circulates through the foramen of Monro, the third ventricle, the aqueduct of Sylvius and the fourth ventricle and exits through the foramen of Luschka and Magendie, where it flows into the basilar cisterns and subarachnoid granulations in the inner table of the sagittal sinus and skull.

Flow of CSF depends on four factors:

- Production,
- absorption,
- resistance and
- sagittal sinus pressure[5].

An obstruction at any point along the CSF pathway may result in hydrocephalus[6].

AETIOLOGY OF HYDROCEPHALUS

Hydrocephalus can be classified into 2 types.

1. Non communicating hydrocephalus (Obstructive hydrocephalus)

When the aetiology lies within the ventricular system or at the fourth ventricular outflow.

2. Communicating hydrocephalus

When the aetiology impairs circulation through the subarachnoid space or absorption into the venous system[6].

Hydrocephalus can be further divided into congenital and acquired forms.

Types of hydrocephalus

OBSTRUCTIVE	COMMUNICATING
Congenital	**Congenital**
1. Aqueductal stenoses	1. Arnold Chiari malformation
2. Dandy Walker malformation	2. Encephaloceles
3. Benign intracranial cysts (Arachnoid cysts)	3. Skull base deformity
4. Vascular malformation (Eg. Vein of Galen aneurysms)	
Acquired	**Acquired**
1. Tumours (Eg. third ventricle, pineal and posterior fossa tumours)	1. Infection (Intra ventricular eg.CMV, Toxoplasma, Post bacterial)
2. Other mass lesions (Eg.Giant aneurysm, abscess)	2. Haemorrhage (Intraventricular haemorrhage of infancy, Subarachnoid haemorrhage)
3. Ventricular scarring	3. Venous hypertension (Venous Sinus thrombosis, Arterio –venous shunts)
	4. Meningeal carcinomatosis
	5. Choroid plexus papillomas

Ventriculo-peritoneal shunting-Goals of surgery

The goals of surgery for hydrocephalus are:

1. To reduce intracranial pressure
2. To maximally improve the patients neurological outcome and
3. To maximize the size of the cortical mantle and minimizing complications

These goals can be achieved by diverting CSF through a shunting apparatus that includes a ventricular catheter, valve (with or without a reservoir) and distal absorption site[5].

About 25% of patients with hydrocephalus (10% with aqueductal stenosis , 10 % with tumours and 5% with cysts) can be cured without a shunt [54].

Hydrocephalus should be treated to prevent destruction of brain mass by ventriculomegaly. Edema of white matter leads to fibrosis, degeneration of neurons and neuronal loss.[64] Distortion of cerebral blood vessels and collapse of capillaries occur with resultant impaired cerebral blood flow. Severe hydrocephalus may cause infarction of posterior cerebral artery. The final consequences are herniation, death or cortical blindness [5].

Thus the ultimate goal in the treatment of hydrocephalus is to prevent this cascade of events.

Clinical features of hydrocephalus

Infants with progressive ventriculomegaly have rapidly enlarging heads (increase in circumference > 2 cm/week) and symptoms of increasing intracranial pressure (tense fontanelles, vomiting, poor feeding, bradycardia and progressive apnoea)

Adults present with symptoms such as headache, vomiting, failing vision, drowsiness, unsteadiness and slowing of mental capacity.

Signs - Papilloedema, enlarged blind spots, reduced visual acuity, large head, dyspraxic gait, general clumsiness.

Indications for CSF shunt surgery

CSF shunting procedures must be performed in patients in whom hydrocephalus cannot be treated conservatively. Some of the indications include idiopathic hydrocephalus, communicating or obstructive hydrocephalus, failed third ventriculostomy, CSF leakage or pseudomeningocele and signs and symptoms of brain stem compression.

Communicating hydrocephalus is usually caused by intraventricular or subarachnoid haemorrhage, trauma or infection [5].

Ultimately, shunting is decided for each individual based on a risk benefit ratio .

Pre-operative investigations

Radiographic imaging and diagnosis of hydrocephalus must be done before surgery.

MRI is the best diagnostic tool in establishing the anatomy and likely pathology of obstructive lesions.

Computed tomography (CT) is required for follow – up of patients with already existing shunt system and also for urgent evaluation of undiagnosed patients .

Ultrasound performed through open fontanelles is the only possible approach in critically ill premature infants with intraventricular haemorrhage or with meningomyclocele[1].

Ventricular shunting procedures

The proximal portion of a CSF shunt is commonly placed in one of the cerebral ventricles, but may also be placed in an intracranial cyst or the lumbar subarachnoid space [25] . The distal placement sites that have been proved to be reliable over time include the peritoneum (ventriculoperitoneal shunt), the atrium (ventriculoatrial shunt) and the pleura (ventriculopleural shunt). CSF is sometimes drained from the lumbar spinal theca to the peritoneal cavity (lumboperitoneal).

Components of a Shunt System

Every shunt system consists of 3 central components – a ventricular catheter, a valve and a distal catheter. Simple shunts have only these 3 components.

Additional components such as tapping reservoirs, on-off devices, pressure transducers, and antisiphon devices may also be present in complex shunts as required for multiloculated hydrocephalus as in Dandy walker malformation.

Ventricular Catheter

This is the component that extends from the lateral ventricle to the valve. The tip of the rostral end is rounded and there are multiple holes along the proximal shaft of the catheter.

Shunt valves

Valve designing has gained the maximum attention in the development of effective shunt systems, following the development of Spitz–Holter and Pudenz valve using silicone.

Valves can be classified into three types

1. **Fixed pressure valve**

   Eg. Hakim valve, PS medical valve and Chabbra valve which is manufactured in India and widely used throughout the world.

2. **Flow regulated valve**

   Eg. Delta valve and OBV II

3. **Programmable pressure valve**

   Eg. Strata, Sophy and Polaris. They play a valuable role in treating adults with hydrocephalus.

Distal catheter

Despite being the longest and the largest component of a shunt, the distal catheter often functions the best with the fewest problems. Barium impregnation allows the radiographic visualization of the location of the catheter.

VENTRICULOPERITONEAL SHUNT

Procedure

- A small semilunar skin incision is made and an occipital burr hole placed on the flat part of occiput, 3-4 cm from the midline along the course of lambdoid suture. If a frontal burr hole is required, it is placed along coronal suture 2-3 cm from midline.

- Abdominal incision is made in para-umbilical and upper midline sites.
- A subcutaneous pocket is designed to house the shunt apparatus
- Shunt tube passer is passed from abdominal incision to cranial incision by gentle subcutaneous tunnelling.
- Peritoneal catheter is passed through the tunnelling device from cranial to abdominal end.
- Insertion into peritoneal cavity is by mini-laparotomy or using trocar.
- Ventricular catheter is introduced into the lateral ventricle and positioned at right angle to the burr hole, the tip anterior to the foramen of Monro. CSF is taken for culture.
- Flushing device is connected to both distal and proximal catheters. Shunt system is then secured to pericranium to prevent migration. After checking for flow of CSF, skin is closed in two layers.
- Prophylactic antibiotics are administered intravenously pre-operatively and a few doses postoperatively.[28]

Complications of Shunts

Mechanical failure and infection together account for the vast majority of shunt complications[6]. Some of the commonly encountered shunts are:

- Infection
- Shunt blockages (proximal, valve or distal)
- Fracture or disconnection

- Migration
- Overdrainage
- Isolation(trapping) of ventricles
- Malposition
- Intracranial haemorrhage
- Viscus perforation

Blockage –

Shunt obstruction is the commonest indication for shunt revision. In the majority, it is due to blockage of ventricular catheter by choroid plexus, brain tissue and cellular debris.

The Slit Ventricle Syndrome

This condition presents clinically with episodic headache which is positional, vomiting and reservoir may be slow to refill. CT shows slit-like ventricles. It is due to loss of compliance of ventricular wall, with the small volume ventricle intermittently collapsing around the catheter and causing temporary blockage.

Abdominal complications

Viscus perforation can occur either as a complication of the initial insertion or as result of chronic erosion of the catheter tip through the viscus wall. Perforation of stomach, large and small bowel, gall bladder and vagina

are described. There may be signs of peritoneal sepsis or occasional extrusion of the catheter tip at the anus, umbilicus or vagina. Catheter disconnected and lost in peritoneal cavity can lead to symptoms and make it difficult to eradicate infection.

Intraabdominal fluid collection

Formation of localised CSF collection within peritoneal cavity is common. Abdominal pain and distension are the common symptoms. They can be readily diagnosed by ultrasound. Presence of pseudocyst generally indicates underlying infection in two-thirds or more of cases.[21]In such cases management is aimed at eradication of the infection by removal or externalization of the infected shunt.[6]

CSF Shunt Infection

Because of their frequency and associated morbidity and cost, infection of CNS shunts remains a significant problem in neurosurgery. Certainly, early detection and aggressive treatment to promptly clear these infections reduces morbidity.

Epidemiology

The incidence of shunt infection can be described as ‘case infection rate’ – the occurrence of infection per given patient, or as an ‘operative

infection rate' – the occurrence of infection per procedure. The case incidence of shunt infection ranges from 8-40% and the operative incidence ranges from 2.8-14% as reported from various studies since 1971.[56]

It has been observed that the distribution of shunt infections is bimodal since last shunt surgery.[33]

70-85% of infections have presented by 6 months post operatively and the second peak after 12 months. [23]

Patient skin preparation and exposure of large areas of patient's skin during the procedures have been considered as sources of infection. [50]

Externalized device infection rate has been found to be in the range of 5-7%.[30]

Prolonged externalization is the most common risk factor associated with infection.[47]

Aetiology

More than two–thirds of all CSF infections are caused by Staphylococcal species; *S.epidermidis* (47-64%) followed by *S.aureus* (12-29%) [34,20].

Gram negative bacilli account for 6-20% of infections, *E.coli* and *Klebsiella spp* being more frequent .*Proteus* and *Pseudomonas* species are not infrequently isolated.

Streptococcal species account for 8-10% infections.

The traditional meningitis pathogens-*H.influenzae*, *S.pneumoniae* and *N.meningitidis*, are seen in approximately 5% of infections.[57 ,41,37]

Multiple organisms are implicated in 10-15% of patients, with one isolated organism usually being *Staphylococcal* species or *E.coli*. [56, 23, 46]

Shunt system with peritoneal end have been considered at greater risk of infection with gram negative organisms more common to the gut. [66, 22]

This is more often due to perforation of a hollow viscus by the catheter causing a mixed infection of gram negative bacilli.[22]

Fungal infections of shunt are rare, but they may occur because of the increased number of susceptible patients. The factors contributing to fungal infections are prior use of broad spectrum antibiotics, hyperalimentation, leukaemia, diabetes mellitus, corticosteroid use and immunocompromised states (AIDS, post chemotherapy, post transplantation) [62]

Pathogenesis

There are four mechanisms by which CSF shunts may become infected [31]

1. Retrograde infection from the distal end
2. Through the skin
3. Haematogenous seeding
4. Colonization during surgery

Retrograde infection from the distal end of the shunt is rare and may occur as a result of bowel perforation. It is the most likely mechanism of infection of external ventricular devices (EVDs). Microorganisms may enter the device from the exit site or during injection through the tubing.

The second mechanism is through the skin, such as inserting a needle into the reservoir or the shunt to culture the CSF or assess patency or for injecting drugs and by breakdown of the skin overlying the shunt.

The infection may be due to failure of the incision to heal, or due to scratching of the wound or the other spontaneous infections of the skin.

Haematogenous seeding causing shunt infection is unusual in VP shunts, but very common in ventriculoatrial shunts.

Colonization of the catheter during surgery is the main mechanism of shunt related infections. [31] This is suggested by the timing of the shunt infections and by the microorganisms isolated. In one study, 62% of infections

occurred within the first month after shunt surgery and 72% were acquired intraoperatively. [2]

Direct exposure and handling of the shunt during the surgery allows bacterial contamination. Other interrelated factors may also be associated with the colonization of the devices. In vitro studies have shown that shunt catheters reduce neutrophil chemotaxis and the ability to phagocytose bacteria effectively.[25]

Bacterial adherence to the shunt is the initial step for the colonization and infection of the device.[25] Catheter biomaterial is altered with passage of time, enabling adherence of microorganism and formation of a mucoid film called biofilm or slime.

This is a polysachharide film that incorporates bacterial micro colonies and interferes with phagocytosis, immune response and antibiotic penetration. Also, an increased genetic transference among bacteria forming the slime causes a higher resistance to antibiotics.

RISK FACTORS

Factors associated with an increased risk of cerebrospinal fluid shunt infection are:

- Premature birth
- Younger age
- Previous shunt infection
- Cause of hydrocephalus
- Experience of the neurosurgeon
- Number of people traversing the operating theatre
- Exposure to perforated surgical gloves
- Intraoperative use of the neuroendocope
- Length of the shunt procedure
- Patient skin preparation
- Shaving of skin
- Exposure of large areas of patient's skin during the procedure.
- Shunt revision

The factor most commonly associated with increase in shunt infection is the patient's age.[23,63,5] The risk is higher in neonates, especially premature infants and the elderly.[23]

Another important factor is prematurity [34, 40, 50, 52] This is explained by changes in the density and microbial flora of skin according to the age and higher susceptibility to infection due to a deficiency in immune system. The

IgG levels in infants less than 6 months of age is just half of those present in adults .[50,52]

Among the other risk factors, previous shunt infection [40,52], post operative CSF leak [18,34] ,neurosurgeons experience [8,23] and spinal dysraphism are the most accepted ones.

Clinical features

The clinical features of shunt infection are variable, depending on the pathogenesis of infection, virulence of organism and type of shunt.[31,63,22.]

The most common symptoms are headache, nausea, lethargy and changes is mental status (seen in about 65% of infected patients) which occur in shunt malfunction secondary to the infection.

Fever is reported in as few as 14% to as many as 92% of cases. Although present in majority of patients, absence of fever does not exclude infection.

Symptoms and signs are referable to the proximal or distal portion of the shunt .Infections arising in the proximal portion of the shunt causes meningitis or ventriculitis in about 30% of cases with resultant shunt obstruction or decreased function.

Symptoms referable to the distal portion may be due to peritonitis such as fever, anorexia, abdominal distension and other signs of acute abdomen. With low virulence organisms few signs such as abdominal tenderness or guarding only may be present. There may be fluid collections due to encystment of the shunt catheter. The deposited CSF is not absorbed causing loculation of pockets of fluid within the abdomen resulting in partial or complete shunt obstruction.

Some shunt infections are insidious and cause few or no symptoms such as intermittent low grade fever or general malaise.

Diagnosis

The diagnosis of CSF shunt infections is made by culture of the shunt CSF or of the fluid within or around the shunt.[57,22] Fluid can be obtained from the reservoir by tapping percutaneously under strict aseptic precautions. Lumbar CSF cultures are usually negative in shunt infections. Lumbar CSF cell count, glucose and protein concentrations also may not indicate infection.

Blood leukocyte counts have a limited value as they are normal in about 25% of infections.[36,57,39]

Blood culture is also of limited value. But it is positive in up to 90% of vascular shunts.

The CSF sample, once tapped is subjected to cell count including differential count, biochemical analysis (CSF glucose and protein), gram stain and culture.

High white blood cell counts reflect infection, but infection may be present even with normal cell counts. Normally the CSF has less than 5 lymphocytes per ml.

CSF eosinophil count may be elevated and has been found to be associated with indolent infection.

Cell counts may be altered by recent surgery due to inflammatory response (chemical meningitis) or due to the spilled blood.

The CSF glucose level may be reduced and protein levels elevated. Glucose levels may be in the normal range in most cases and is not very useful.

Gram staining may be of some value in denoting the type of causative microorganism. Again a negative result does not exclude infection. [46]

Routine analysis of the above said parameters may not have an accurate predictive value as a marker of infection.[36,57,38]

CSF culture from the shunt or reservoir is the most valuable test in establishing the diagnosis of infection. Cultures are usually positive even in the absence of CSF pleocytosis or abnormal biochemical parameters.

Administration of antibiotics in patients with suspected shunt infection before CSF culture reduces the likelihood of obtaining a positive culture. Cultures may require several days of incubation before being discarded as negative.

Occasionally, a positive culture may be reported in shunts tapped for evaluation of function in the absence of infections. The likely reason being contamination, shunt should be retapped for culture. A repeat positive culture indicates true infection.

In patients with external ventricular drain, CSF pleocytosis and a positive culture (obtained from the ventricular catheter) indicates definite infection.

On the other hand, absence of a positive gram stain of CSF culture but a progressive decrease in CSF glucose and increase in CSF protein with advancing pleocytosis indicates a suspected infection.

A contaminating microorganism is defined as an isolated positive CSF culture and / or positive gram stain with normal biochemical parameters and cell counts.

When infection is limited to the distal portion of the VP shunt, culture of the reservoir fluid may be negative in the absence of retrograde infection. However, patients with distal occlusion of VP shunt presenting as acute abdomen should undergo early revision and get investigated for possible infection. A CT or ultrasound scan of the abdomen may identify CSF loculations at the terminus. Peritoneal symptoms usually clear within 12 hours after removal of an infected distal catheter.

IMAGING STUDIES

1. Plain radiographs are used to determine whether a shunt system is in continuity

2. In many cases, shunt infection causes a degree of shunt obstruction causing increased ventricular size. This is easily seen on an ultrasound scan if fontanelles are open or with CT scan or MRI.

3. Peritoneal infection results in the formation of loculated fluid collections detected by sonography or CT.

Abdominal pseudocyst is caused by a progressive accumulation of fluid due to localized reaction of the omentum. Antibiotic treatment usually results in rapid improvement.

Treatment

Most shunt infections caused by *Staphylococcus spp.* do not cause significant tissue damage or a severe inflammatory response. Intravenous antibiotic treatment usually results in rapid bacteriologic clearance with resolution of the CSF pleocytosis.

Aims of the treatment of CSF shunt infections are:

1. Reduction in mortality and morbidity due to the complication of operative treatment
2. Maintenance of a functioning device and
3. Cure for infection .[25]

Factors to be considered in the therapy of an infected CSF shunt include:

1. Selection of antimicrobial therapy
2. Timing of hardware removal
3. Timing of shunt replacement and
4. Duration of antimicrobial therapy.[2]

Antimicrobial therapy

The antimicrobial agent selected must penetrate the central nervous system and have bactericidal activity against the infecting pathogen. Empirical therapy is initiated when the culture results are awaited. The most

likely organisms associated with shunt infections are *CONS, S.aureus* and gram negative bacilli. Hence empirical therapy with vancomycin plus either cefepime, ceftazidime or meropenam would be appropriate. Once cultures have returned, antibiotics can be selected based on the identified organism and drug sensitivities. For example in the absence of methicillin resistant *S.aureus* or pencillin allergic patients both *S.epidermidis* and *S.aureus* can be treated with oxacillin or nafcillin with good results.[43]

For *Candida* shunt infection, intravenous amphotericin-B often combined with 5 flucytosine or fluconazole is recommennded.[2]

Direct instillation of antimicrobial agents into the ventricles may be required when the shunt infections are difficult to eradicate or when the patient is unable to undergo surgery.

The doses of antimicrobial agents for intraventricular use have been determined empirically based on the ability of the agent to achieve adequate CSF concentration.[53, 27]

Antimicrobial agents administered by the intraventricular route

Antimicrobial agent	Daily intraventricular dose
Vancomycin	5-20 mg.
Gentamicin	1-8 mg.
Tobramycin	5-20 mg.
Amikacin	5-50 mg.
Polymixin B	5 mg.
Colistin	10 mg.
Teicoplanin	5-40 mg.
Amphotericin B	0.1-0.5 mg

SHUNT REMOVAL AND REPLACEMENT

Shunt removal with immediate placement

Removal of shunt hardware with immediate shunt replacement and intravenous antimicrobial therapy cures approximately 65 % to 75 % of patients with shunt infections.

Shunt removal with delayed replacement

Shunt removal, antimicrobial therapy in the absence of any foreign devices and delayed replacement is another option, but the reason for which the shunt was placed initially is left untreated.[63]

Shunt removal with placement of an exrernal CSF drain

Antimicrobial use, removal of all components of the infected shunt and the use of some component of external drainage appears to be the most effective treatment for CSF shunt infection.[65]

A new shunt is usually not placed until CSF culture is negative for bacterial growth. The recommnended interval between shunt revision and reinsertion is approximately 10-14 days with atleast 48 hours between the final negative CSF culture and reinsertion.[43]

In this interval, a variety of methods are used to support shunt deprived patients that include shunt exteriorization, placement of external ventricular drain or lumbar drainage catheters.

In premature infants with very low birth weight, intermittent lumbar puncture or ventricular tapping can be preformed.

Ventriculitis of shunt infections clear more quickly with external drainage, the treatment success usually greater than 85 % .[31, 66,] The greatest risk of the EVD is that of secondary infection.[31, 38] Maintaining a sterile closed system and avoiding injections into the system usually reduces this risk.

Duration of Antimicrobial therapy and Shunt reinsertion

In patients with shunt infection caused by *CONS* with normal CSF findings, negative cultures for 48 hours after externalization confirms a cure and patient can be reshunted on the third day after removal.

If *CONS* was isolated with abnormal CSF biochemistry and pleocytosis, 7 days of antimicrobial therapy is recommended once repeat culture is negative before reshunting.

For shunt infections caused by *S.aureus* or gram negative bacilli, 10 days of antimicrobial therapy with negative culture is recommended before reshunting.[31, 12]

Regardless of the manner of treatment, CSF shunt infection can recur. In one study, the recurrence rate was 26%, with two thirds of cases caused by the same microrganisms.[32]

Prevention

Good surgical techniques and adherence to infection control measures are important in preventing infection. Double gloving may decrease CSF shunt infection rates.[59]

Several meta-analyses have concluded that periprocedural prophylactic antibiotics can reduce rates of infection by about 50%.[26]

Antibiotic impregnated catheters for EVD and CSF shunts have been shown to reduce colonization and infection of the catheter with gram- positive organisms.[67, 24]

A prospective trial of 306 patients with placement of EVDs impregnated with minocycline and rifampin showed reduction in the infection rate from 9.4 % to 1.3 %.[67]

Another trial of 110 patients with placement of shunts impregnated with clindamycin and rifampin showed a decrease in infection rate from 16.6 % to 6 %.

Future developments

Future advances in technology, such as nanocoatings for shunt components should increase the biocompatibility of shunt system prolonging the life span. Measures such as avoiding barium impregnated catheters and removing distal slit valves can also prolong shunt survival.

MATERIALS AND METHODS

This is a cross sectional study involving 397 patients, among whom 275 patients had undergone primary ventriculoperitoneal shunt insertion and 122 patients had undergone shunt related procedures like shunt removal, revision, reinsertion, exteriorization and external ventricular drain placement. In this study population, 122 cases had developed symptoms of shunt infection and malfunction.

Place of study

Institute of Microbiology and Institute of Neurosurgery, Rajiv Gandhi Government General Hospital & Madras Medical College, Chennai.

Period of Study

November 2011- October 2012

Ethical consideration

Approval was obtained from the Institutional Ethics Committee before the study was commenced. Informed consent was obtained from the study population. All patients satisfying the inclusion criteria were included in the study and they were interviewed by a structured questionnaire.

Study Group

122 patients who showed signs and symptoms of shunt infection and malfunction were included in the study. Patients of both sexes and belonging to all age groups were evaluated. Patients with hydrocephalus who had previously undergone ventriculoperitoneal shunt insertion and presenting with symptoms and signs suggestive of shunt infection or malfunction during the study period and who had undergone shunt related procedures were evaluated.

Relevant data were collected from the patients as mentioned in the enclosed proforma. They include patients' age and sex, aetiology of the hydrocephalus requiring ventriculoperitoneal shunt, date of shunt placement, number of prior revisions, history of prior shunt infections, results of culture of CSF, shunt tube or pus and follow-up.

COLLECTION AND TRANSPORT OF SPECIMENS

The samples that were collected for culture include

1. Cerebrospinal fluid
2. Ventriculoperitoneal shunt tube
3. Wound swab from sites of wound infection-proximal or distal and
4. Intraabdominal fluid collections
5. Blood.

All the samples were collected from the patients under strict aseptic precautions and processed immediately.

Cerebrospinal Fluid

In suspected cases of CSF shunt infections, CSF was obtained under strict aseptic conditions by lumbar puncture or percutaneous puncture of ventricular reservoir which is in an easily accessible subcutaneous location or from the external ventricular drain.

Lumbar puncture technique

1. The patient is made to lie on the side with knees flexed and back arched.

2. The area over the lumbar spine is disinfected.

3. The space between the vertebrae L3 and L4 is palpated.

4. With aseptic precautions, the spinal needle is inserted into the spinal canal through the intraspinous ligaments and CSF is tapped.

In patients undergoing surgery for revision, removal or replacement of the shunt device, CSF is collected directly from the lateral ventricles through the ventricular or peritoneal catheter.

CSF was collected from each patient in 3 separate sterile test tubes. The tubes were screw capped or plugged with sterile cotton.

One tube was used for biochemical analysis - for CSF glucose and protein.

Second tube was used for Gram stain and culture.

Third tube was used for cell count and differential staining. CSF samples were processed immediately in the laboratory.

Ventriculoperitoneal shunt tube

The CSF shunt tubes used for culture included a part of the tube or the entire tube depending on the procedures the patients underwent.

In patients who had undergone revision of the cranial or the peritoneal end of the shunt tube, the ventricular catheter (with or without the reservoir) or the peritoneal catheter respectively was processed. In patients who had undergone removal of the entire CSF shunt tube, the tips of both the ends- ventricular and peritoneal were subjected to Gram stain and culture.

Wound Swab

Wound swabs were taken from patients with CSF shunts who developed wound infection of the incisional surgical site.

The infected site was decontaminated with 70% ethanol, washed with normal saline and dried before taking a swab. Two specimens were collected using sterile cotton swabs from the depths of the lesion, one for Gram stain and the other swab for culture which was processed immediately.

Intraabdominal fluid collection

CSF or pus collection within the peritoneal cavity aspirated at the time of revision surgery was collected in sterile test tubes and processed immediately.

Blood

Blood was collected from patients after careful preparation of the venipuncture site with povidone iodine and 70% alcohol. About 10-15 ml of blood was collected from adults and 5-10 ml from children using disposable needle and syringe and inoculated into brain – heart infusion broths directly and incubated at 37^{o}C.

PROCESSING OF SAMPLES

Processing of CSF

CSF was tested for cell count and biochemical analysis and reports documented.

Measurement of CSF glucose and protein

The CSF glucose level was measured using a calorimeter. The normal CSF glucose levels are between 45 and 100 mg/dl.

The CSF protein concentration was also measured by calorimetric method. Normally, the CSF protein concentration is in the range of 14 to 45 mg/dl.

Macroscopic appearance

The CSF sample was examined macroscopically for turbidity and deposits, and whether purulent or blood obtained.

Gram Stain

The CSF specimen was centrifuged to concentrate the bacteria and from the sediment, a smear of about 1 cm diameter was made on a clean glass slide and marked. The smear was allowed to air dry and Gram staining was done. The stained smear was examined for presence of pus cells and organisms.

Culture

Culture is the standard diagnostic method to detect bacterial infections. The sediment of the centrifuged CSF specimen was inoculated on MacConkey agar, blood agar and chocolate agar plates. The first two plates

were inoculated at 37^{o}C for 24-48 hours. The chocolate agar plate was incubated at 37^{o}C in candle jar with 5% CO_2 for 24-72 hours.

The plates were examined after 24 hours and if any growth was observed, the colony morphology was noted and a smear made from the colonies for Gram stain, The plates showing no growth were incubated further for another 24-48 hours.

The morphology and the staining characteristics of the isolates helps in preliminary identification.

Motility of the bacteria was demonstrated by hanging drop method after incubating a peptone water culture for 2 hours at 37^{o} C.

Identification of the isolates was done by processing the colonies further by biochemical tests for assessing the metabolic characteristics. They include catalase test, oxidase test, carbohydrate utilization test, indole production, Methyl red test, Voges Proskauer test, Citrate Utilization, Urease production, Decarboxylation of lysine,ornithine and arginine, Phenylalanine deaminase production,Nitrate reduction, Hugh & Leifson’s O/F test

PROCESSING OF SHUNT TIPS

Macroscopic examination

Shunt tips were examined macroscopically for biofilms or slime.

Gram stain

Smear was made from any fluid within the ventricular reservoir and Gram staining was done. The stained smear was examined for pus cells and organisms.

Culture

If any fluid was noted in the ventricular reservoir, the tube was gently squeezed and the expressed fluid plated on to culture plates. The ventricular catheter and the peritoneal catheter tips irrespective of the presence or absence of fluid within the tube placed in separate tubes of brain heart infusion broth and incubated at 37^{o}C for 18-24 hours.

After overnight incubation, the broths were observed for turbidity and subcultured onto MacConkey agar, blood agar and chocolate agar plates and incubated for 24-48 hours at 37^{o}C as done for CSF specimen. Further processing done as for CSF,

WOUND SWABS & INTRAABDOMINAL FLUID COLLECTION

Direct gram stain:

Smear examined for any pus cells or bacteria

Culture:

Specimens plated on to culture plates as done for CSF and processed.

Blood

After 48 hours of incubation, the BHI broth inoculated with blood was observed for turbidity and haemolysis and subcultured on MacConkey agar, blood agar and chocolate agar plates and incubated at 37^0C .Further processing carried out as done for the previous specimens.

Interpretation of bacterial cultures

Bacterial isolates were identified by means of colony morphology, Gram staining, motility and biochemical reactions by standard microbiological techniques as recommended by Clinical and Laboratory Standards Institute. (CLSI).[14]

Antimicrobial Susceptibility Testing:

Antimicrobial susceptibility testing was done on Mueller-Hinton agar (MHA) [Hi-media laboratories, Mumbai, India]. Four to five colonies of pure growth from an overnight culture of organism was transferred to a tube containing 4-5 ml of peptone water and incubated at 37ºC for 2 hrs and adjusted to match 0.5McFarland turbidity. A lawn culture of the isolate was made on MHA with a sterile cotton swab and antibiotic discs (Hi-Media Laboratories, Mumbai, India) were placed at appropriate distances and incubated at 35 $\pm$ 2ºC in ambient air for 16-18 hours.[4] Standard strains of *Staphylococcus aureus*-(ATCC 25923), *E.coli* (ATCC 25922) and *P.aeruginosa* (ATCC 27853) were used as controls and tested in a similar way. The zone of inhibition was measured carefully and interpreted according to CLSI 2011 guidelines.[14] The antibiotics tested are listed in the tables below.

Modified Hodge Test (MHT):

A 0.5 McFarland of ATCC *E.coli* 25922 was prepared by direct colony suspension method. It was diluted 1:10 in normal saline, and a lawn culture was made on MHA plate. Plate was allowed to dry for 5 to 10 minutes, and imipenem disc was placed in the centre of the plate. 3-5 colonies of test and QC organism (ATCC *Pseudomonas aeruginosa* 27853) grown overnight on a blood agar plate were taken with a 4 mm loop and inoculated in a straight line of 20-25 mm out from the edge of the disc. The plate was incubated for 16- 20

hours at 35 ± 2 ºC in ambient air. Enhanced growth at the intersection of streak and zone of inhibition was interpreted as positive for possible MBL production. As carbapenemase produced by the test organism inactivates the imipenem which diffused into the medium, growth of ATCC *E.coli* 25922 was enhanced around the MBL producing test organism.[5,6,7]

Combination Disc Test(CDT):

Discs of imipenem (IPM-10µg) and imipenem-EDTA (IE-10+750µg) were placed on a MHA plate inoculated with 0.5 McFarland turbidity of the test isolate and incubated at 35 + 2 ºC for18- 24 hours. Any isolate showing an increase in zone size of at least 7 mm around the imipenem-EDTA disc compared to imipenem disc alone was recorded as a MBL producing strain.[8,9]*E.coli* (ATCC 25922) and *P. aeruginosa* (ATCC 27853) were used as control strains.[10]

DETERMINATION OF MINIMUM INHIBITORY CONCENTRATION (MIC) OF IMIPENEM

All isolates of *Pseudomonas* aeruginosa were tested by Macrobroth dilution method for their MIC against imipenem. Standard strain of *P.aeruginosa* (ATCC 27853) was used as control. Results were interpreted as per CLSI 2011 guidelines.[14] MIC values of ≤4µg/ml, 8µg/ml and ≥16µg/ml were interpreted as sensitive, intermediate and resistant respectively .

The panel of antibiotics included in the antimicrobial sensitivity testing for Gram negative bacilli (Himedia, Mumbai)

Antibiotic	**Zones Of inhibition**		
	Resistant	**Intermediate**	**Sensitive**
Amikacin 30µg	14	15-16	17
Ampicillin 10µg	13	14-16	17
Ceftazidime 30µg	14	15-17	18
Cefotaxime 30µg	14	15-22	23
Ciprofloxacin 5µg	15	16-20	21
Gentamicin 10µg	12	13-14	15
Imipenam 10 µg	13	14-15	16
Ofloxacin 5µg	12	13-15	16
Cefaperazone-Sulbactum 75/30 µg	15	16-20	21

The panel of antibiotics included in the antimicrobial sensitivity testing for Gram positive cocci

Antibiotic	**Zones of inhibition**		
	Resistant	**Intermediate**	**Sensitive**
Amikacin 30µg	14	15-16	17
Ampicillin 10µg	28	-	29
Cotrimoxazole 1.25/23.75 µg	10	11-15	16
Cefotaxime 30µg	14	15-22	23
Ciprofloxacin 5µg	15	16-20	21
Chloramphenicol 30 µg	12	13-17	18
Amoxycillin-Clavulanic acid 20/10µg	19	-	20
Vancomycin 30µg	12	13-15	16

EXTENDED SPECTRUM B LACTAMASE (ESBL) DETECTION METHODS:

1) Screening method:

Isolates of gram negative bacilli showing the following resistance pattern were considered to be possible ESBL producing strains.

Antibiotic zone diameter for possible ESBL producing strain:

- Ceftazidime (30μg) ≤ 22mm
- Cefotaxime(30 μg) ≤ 27mm
- Ceftriaxone(30 μg) ≤ 25mm
- Aztreonam (30 μg) ≤ 27 mm**.**

2) CLSI phenotypic confirmation method:

With a sterile bacterial loop, 3-5 identical colonies were picked from a fresh overnight grown culture and inoculated into 5 ml of nutrient broth. The broth was incubated at 35°C for 2-4 hrs and turbidity matched with 0.5 McFarland standard. Lawn culture of the test organism was made on to MHA plate (Himedia, Mumbai). Antibiotic discs Ceftazidime (CAZ 30μg) and Ceftazidime/ Clavulanic acid (CAZ/ CA 30μg/ 10μg) were placed on the plate and incubated at 35°C overnight. An increase in zone diameter of 5mm or more for Ceftazidime/ Clavulanic acid compared to Ceftazidime alone confirmed an ESBL producing organism .

3. Double disc diffusion synergy test

In this test, discs of third generation cephalosporins and augmentin (20μg/10μg) (Himedia, Mumbai) were kept 30mm apart, from centre to centre on inoculated Muller-Hinton Agar(MHA). A clear extension of the edge of the inhibition zone of cephalosporin towards augmentin disc was interpreted as positive for ESBL production.

4. ESBL detection strip method

The ESBL detection strip is coated with ceftazidime, cefotaxime and cefepime on the upper half and clavulanic acid and tazobactum along with the above mixure on the lower half in a concentration gradient. 3-5 colonies of overnight culture of the test organism is transferred to a BHI broth and turbidity matched to 0.5 McFarland standard. The suspension is streaked on a MHA plate with a sterile swab and a Ezy MIC strip is placed on it with an applicator and incubated. The value of MIC where the ellipse of growth intersects the scale on the strip is read.

DETECTION OF METHICILLIN RESISTANCE IN STAPHYLOCOCCUS AUREUS BY DISC DIFFUSION METHOD:

3-5 identical colonies of *S.aureus* isolated from overnight agar culture plate were suspended into BHI broth and turbidity matched with 0.5Mcfarlands standard. A lawn culture of the growth was made on a MHA

plate and Oxacillin 1µg disc was applied. Incubation was done at 35° C for 24 Hrs. According to CLSI criteria with 1µg Oxacillin disc, Zone of inhibition of diameters of ≤10, 11-12, ≥ 13 mm were categorized as resistant, intermediate or susceptible respectively [14].

Minimum inhibitory concentration (MIC) of Vancomycin for gram positive cocci

Cation adjusted Mueller Hinton broth (pH 7.2-7.4)was used.

Stock Antibiotic solution was prepared using the formula:

Stock antibiotic solution was prepared using the formula: W = × C

$$W = \frac{1000}{P} \times V \times C$$

Where P= potency of the antibiotic corresponding to the base.

P= 950/1000 mg for vancomycin (Himedia)

V = volume of the stock solution in ml

C =final concentration of the antibiotic solution (1024µg/ml)

W = weight of the antibiotic to be dissolved

2 rows of sterile test tubes arranged in a rack (one for test and another for ATCC control).In a universal container 8ml of broth containing the working stock solution (128 µg/ml concentration) is prepared and 1ml transferred to the first tube in each row. With a fresh pipette 4ml of broth

added to 4ml of the working stock solution and 1ml transferred to the second tube of each row. Further dilutions are prepared as per requirement.

1 ml of the antibiotic free broth is kept in the last tube for growth control. Sterility controls for the antibiotic solution is kept.

Test organism inoculated to one row and ATCC control strain to the second row.

Test inoculum is prepared by transferring 3-5 identical colonies from overnight growth of the test organism to 4.5 ml of MH broth, incubated at 35^{o} C for 2 – 6 hours and turbidity matched with 0.5 McFarland standard which contains approximately

1-2 x 10^{8} CFU/ml. The suspension is diluted 1 in 100 times to attain a final concentration of 5 x10^{5} CFU/ml. 1ml of this dilution is added to the tubes containing antibiotic solutions. The racks incubated at 35^{o} C for 24 hours.

The lowest concentration of the antibiotic in which there is no visible growth is inferred as the MIC break point of vancomycin for the test organism.

RESULTS

A total of 426 shunt related procedures were performed in 397 patients over a period of one year from November 2011 to October 2012 which included 275 primary VP Shunt insertions and 151 shunt revision surgeries like removal ,reinsertion, exteriorization and EVD placements performed in 122 patients. 21 patients had undergone more than one revision surgery.

122 patients who developed signs and symptoms of shunt malfunction/infection were included in the study group.

Table 1 : Patients category

Nature of Surgery	**Children(<12 yrs)**	**Adult(>12 yrs)**	**Total**
Primary VP Shunt Insertions	108 (27.20%)	167 (42.07%)	275 (69.27%)
Shunt Revisions	98 (24.69%)	24 (6.04%)	122 (30.73%)
Total	**206 (51.89%)**	**191 (48.11%)**	**397**

Paediatric population was categorized under 12 years of age and adult population was categorized above 13 years of age.

External ventricular drains were placed in 7 patients with shunt infections. 3 patients underwent radiotherapy for intracranial mass. 4 patients were on antituberculous treatment. 1 patient underwent tracheostomy for ventilator support and also developed pressure sores over the sacrum.

Table 2 : Sex distribution

Male			**Female**		
Children	**Adult**	**Total**	**Children**	**Adult**	**Total**
110 (27.71%)	129 (32.49%)	239 (60.20%)	96 (24.18%)	62 (15.62%)	158 (39.80%)

Among the 397patients who underwent shunt related procedures the male population was considerably higher (60.2%) than the female population (39.8%).

Table 3 : Age distribution of patients who underwent primary VP shunt insertion

Age distribution	M	F	Total	Percentage
Children				
0-3Months	14	21	35	12.73%
4-6Months	7	8	15	5.45%
7-12Months	5	2	7	2.55%
1-2Years	7	1	8	2.91%
3-5Years	5	8	13	4.73%
6-10Years	6	10	16	5.82%
11-12Years	9	5	14	5.1%
Total	**53**	**55**	**108**	**39.27%**
Aduilts				
13-20Years	10	8	18	6.55%
21-30Yrs	21	9	30	10.91%
31-40Yrs	25	9	34	12.36%
41-50Yrs	22	11	33	12.00%
51-60Yrs	19	12	31	11.27%
>60Yrs	16	5	21	7.64%
Total	**113**	**54**	**167**	**60.73%**

Among the 275 patients who underwent primary VP shunt insertions, 108 patients were children (39.27%) and 167 patients were adults (60.73%).

Table 4 : Age distribution of patients who underwent shunt revisions

Age	M	F	Total	Percentage
Children				
0-3Months	3	5	8	6.56%
4-6Months	5	3	8	6.56%
7-12Months	18	8	26	21.31%
1-2Years	6	11	17	13.93%
3-5 Years	15	8	23	18.85%
6-10 Years	8	6	14	11.48%
11-12 Years	2	0	2	1.64%
Total	**57**	**41**	**98**	**80.33%**
Adult				
13-20 Years	2	4	6	4.92%
21-30 Years	4	1	5	4.10%
31-40 Years	5	0	5	4.10%
41-50 Years	2	2	4	3.28%
51-60 Years	1	0	1	0.82%
>60 Years	2	1	3	2.46%
Total	**16**	**8**	**24**	**19.67%**

Among the 122 patients, who underwent shunt revision surgeries, 98 patients were children (80.33%) and 24 patients were adults.(19.67%)

Table 5 :Etiological profile of hydrocephalus of the study population

Etiology	Children (<12yrs)	Adult (>12 yrs)	Total	Percentage
Congenital Malformations				
Dandy Walker malformation	6 (4.92%)	-	6 (4.92%)	4.92
Aqueductal Stenosis	6 (4.92%)	1 (0.82%)	7	5.74
Meningomyelocele	9 (7.38%)	-	9	7.38
Arachnoid cyst	4 (3.28%)	-	4	3.28
Others	24 (19.67%)	-	24	19.67
Infective				
Post meningitic	16(13.11%)	4 (3.28%)	20	16.39
PostTBM (Tuberculous meningitis)	12 (9.84%)	2 (1.64%)	14	11.48
Tuberculoma	3 (2.46%)	2 (1.64%)	5	4.10
Intracranial abscess	1 (0.82%)	-	1	0.82
Intracranial tumours	8 (6.56%)	3 (2.46%)	11	9.02
Haemorrhage				
Spontaneous	1 (0.82%)	5 (4.1%)	6	4.92
Post traumatic	-	3 (2.46%)	3	2.46
Others	8 (6.56%)	4 (3.28%)	12	9.84
Total	**98**	**24**	**122**	**100**

Congenital malformations were the most common underlying cause for the development of hydrocephalus in children (45.24 %).Intracranial hemorrhage was the most common cause for hydrocephalus in adults (6.56%).

Table 6 : Category of patients in the study group

Patients	**Underwent one revision (%)**	**Underwent multiple revisions (%)**	**Total (%)**
Number	101 (82.79)	21 (17.21)	122
Culture positive	26 (21.31)	16 (13.11)	42 (34.42)
Culture negative	75 (61.48)	5 (4.10)	80 (65.58)

Among the 122 patients treated for malfunction 42 patients were culture positive, with an infection rate of 10.58%, 21 patients underwent a total of 50 revision surgeries. Of them 15 underwent two revisions (30), 5 patients underwent 3 revisions (15) and 1 patient underwent 5 revisions.

Table 7-Interval between VP shunts insertion and malfunction

Duration	**No of cases infected (Culture positive)**	**No of cases uninfected (Culture negative)**	**Total**	**Percentage**
<1Month	9 (7.38%)	25 (20.49%)	34	27.87
2-3Months	8 (6.56%)	29 (23.77%)	37	30.33
4-6Months	6 (4.92%)	14 (11.48%)	20	16.39
7-12Months	7 (5.74%)	6 (4.92%)	13	10.66
1-2Months	8 (6.56%)	6 (4.92%)	14	11.48
>2years	4 (3.28%)	0	4	3.28
Total	**42 (34.42%)**	**80 (65.58%)**	**122**	**100**

Majority of the shunt infections were noted to occur within 1 month of primary insertion 27.87%. About 74.59% of infections occurred within 6 months of postoperative period.

Table 8- Clinical presentation of patients

Symptoms	No of cases(n=122)	Percentage
Fever	38	31.15
Vomiting	42	34.43
Head ache	21	17.21
Altered sensorium	16	13.11
Visual disturbances	6	4.92
Seizures	14	11.56
Progressive increase in head size	18	14.75
CSF leak	9	7.38
Abdominal distension	4	3.28
Extrusion through anus/abdominal wound	3	2.46
Wound discharge	21	17.21
Shunt tract inflammation	12	9.84

Fever (31.75%) , vomiting (34.43%) wound discharge (17.21%) and altered sensorium (13.11%) were the most common symptoms of presentation in the pediatric and adult patients. Seizures and progressive increase in head size were more common in children. Headache and visual disturbances were more common in adults.

Table 9- Correlation of age as a risk factor for shunt infection

Age	No of cases	No. infected (n=42)	Percentage for 42
0-3M	43	4	9.52
4-6M	23	5	11.90
7-12M	33	15	35.71
1-2Yr	25	6	14.29
3-5Yr	36	4	9.52
6-10Yr	30	2	4.76
11-12Yrs	0	0	0
13-20Yrs	40	2	4.76
21-30Yrs	35	1	2.38
31-40Yrs	39	2	4.76
41-50Yrs	37	-	0
51-60Yrs	32	1	2.38
>60Yrs	24	-	0
Total	**397**	**42**	**100%**

The maximum incidence of infection was found in infants between 7 to 12 months of age (35.71%). A high incidence of infection following shunt insertions was observed in children below 2 years of age (71.43 %).

Table 10 : Correlation of Etiology of hydrocephalus as a risk factor for infection

Etiology	No. of patients with malfunction	No. of patients infected			Percentage (%)
		Children(%)	Adults(%)	Total	
Congenital Malformation	50(40.98%)	18(42.86)	1(2.38)	19	45.24
Meningitis	40(32.79%)	9(21.43)	2(4.76)	11	26.19
Intracranial mass	11(9.02%)	5(11.9%)	0	5	11.90
Intracranial hemorrhage	9(7.38%)	1(2.38%)	3(7.14)	4	9.52
Others (Idiopathic)	12(9.84)	3(7.14)	0	3	7.14
Total	122	36	6	42	100

Shunt infections were more common in infants operated for hydrocephalus due to congenital malformations (42.86%) and meningitis (21.43%).In adults, shunt infections occurred with increasing frequency in patients with intracranial hemorrhage (7.14%) and following meningitis.(4.76%)

Table 11- Correlation of CSF gram stain with infection

Gram Staining (n=81)(%)	Culture Positive n=31(%)	Culture Negative n=50(%)
Positive 30(37.04)	26(32.1)	4(4.94)
Negative 51(62.96)	5(6.17)	46(56.79)

Gram staining was done for all the 81 CSF specimens received .Among the 30 CSF specimens which showed pus cells and organisms, 26 were culture positive(32.1%) and 4 were culture negative.(4.94%)

Table 12-Correlation of CSF biochemical parameters with infection

Variable	Infected n=42	Uninfected(%)
CSF PROTEIN >45mg/dl	28(66.67%)	4(9.52)
CSF GLUCOSE<45mg/dl	27(64.29)	2(4.76)
Raised Cell Count	3(7.14)	-

Among the 42 patients who were culture positive, a significant proportion of patients showed elevated protein (66.67%) and reduced glucose (64.29%). Only 3 patients had raised cell count (7.14%).

Table 13- Correlation of Blood counts with Shunt infection

Variable	No. of Infected cases	Percentage
Increased total count	30	71.43
Differential count (Neutrophilia)	28	66.67
Reduced Haemoglobin	14	33.33

A significant proportion of patients who were culture positive showed raised white blood cell count and neutrophilic leucocytosis (66.67%). 14 patients had anemia(33.33%)

Table 14- Details of samples processed from cases of malfunction

Sample	No.	Culture positive			Culture Negative
		First sample	Repeat sample	Total	
CSF	81	25(30.86)	6(7.41)	31(38.27)	50(61.73)
Shunt tube	67	29(43.28)	10(14.93)	39(58.21)	28(41.79)
Pus	9	6(66.67)	-	3(66.67)	3(33.33)
Peritubal collection	3	2(66.67	-	2(66.67)	1(33.33)

Table15- Pathogens isolated from cases of shunt infection

Type of organism	Percentage
Gram positive cocci	47.73%
Gram negative bacilli	52.27%
Total	**100%**

The study highlighted a slightly higher rate of CSF shunt infection with gram negative bacilli (52.27%) as compared to that of gram positive cocci (47.73%)

Table 16- Microbiological Profile of Infected Ventriculoperitoneal Shunts

Organisms	Number (n =44)	Percentage
Staphylococcus epidermidis	10	22.73
Staphylococcus aureus	9	20.45
Pseudomonas aeruginosa	7	15.91
Escherichia coli	3	6.82
Klebsiella oxytoca	3	6.82
Proteus vulgaris	3	6.82
Acinetobacter baumanii	3	6.82
Klebsiella pneumoniae	2	4.55
Proteus mirabilis	2	4.55
Enterococcus faecalis	1	2.27
S.lugdunensis	1	2.27

S. epidermidis was the predominant pathogen isolated (22.73%) from cases of shunt infection. Organisms like *S.aureus* (20.45%) and *Pseudomonas aeruginosa*(15.91%) also showed a high incidence of infection.

The other pathogens commonly isolated were *E.coli, K.oxytoca, K.pneumoniae, Proteus mirabilis* and *Acinetobacter baumanii*.

Enterococcus faecalis(2.27%) *and S.lugdunensis* (2.27%) were isolated from one patient each.

Table 17- Pathogens isolated in Polymicrobial Infection

Organisms	**Number of isolates**
S.epidermidis + Proteus mirabilis	2
S.aureus + Acinetobacter baumanii	2

Mixed infection was seen in two patients, with one organism isolated being a gram positive cocci and the other, a gram negative bacilli. Both occurred in patients who underwent external drainage procedures of the distal end of ventriculoperitoneal shunt.

Table 18- Pathogens isolated from blood culture of Shunt Malfunctions

Patient No	Blood Culture	Shunt tip/CSF
1	*S.epidermidis*	*S.epidermidis*
2	*Klebsiella oxytoca*	No growth
3	*Enterococcus faecalis*	No growth

Although bacteraemia was seen in 3 patients with VP shunt malfunction, only one patient had a similar pathogen -*S.epidermidis* isolated from both the blood culture and shunt tip.

Other 2 patients who had blood stream infection with *K.oxytoca* and *Enterococcus faecalis* respectively had a negative culture from shunt tip and CSF.

Table 19- Antibiotic sensitivity pattern of gram positive cocci

Organism	Ampicillin	Amikacin	Ciprofloxacin	Cefotaxime	Amoxycillin-Clavulanic Acid	Cotrimoxazole	Vanco	Chloramphenicol	High level Genta
S.epidermidis (10)	4(40)	6(60)	5(50)	4(40)	8(80)	4(40)	10(100)	6(60)	-
S.lugdunensis (1)	1(100)	0	1(100)	1(100)	1(100)	-	1(100)	1(100)	-
S.aureus (9)	4(44.44)	7(77.78)	4(44.44)	3(33.33)	7(77.78)	5(55.56)	9(100)	5(55-56)	-
Enterococcus faecalis (1)	-	1(100)	0	0	1(100)	0	1(100)		1(100)

The gram positive cocci showed a high sensitivity spectrum to amoxycillin- clavulanic acid, amikacin and chloramphenicol. All the strains isolated were sensitive to Vancomycin (100%)

Table 20 - Antibiotic sensitivity pattern of Gram negative bacilli

Organisms	Amik	Cip	Cef	Oflox	Gara	Cefta zidime	CS	Imipenam	Ampicillin
P.aeruginosa n=7	6 (85.71)	3 (42.86)	-	4 (57.14)	3 (42.86)	4 (57.14)	6 (85.71)	6 (85.71)	4 (57.14)
E.coli n=3	3 (100)	1 (33.33)	0	1 (33.33)	1 (33.33)	-	3 (100)	-	1 (33.33)
Kleb. Oxytoca n=3	2 (66.67)	1 (33.33)	1	2 (66.67)	1 (33.33)	-	3 (100)	-	1 (33.33)
Kleb. pneumoniae n=2	1 (50)	2 (100)	0	2 (100)	1 (50)	-	2 (100)	-	1 (50)
Pr.vulgaris n=3	3 (100)	2 (66.67)	1 (33.33)	2 (66.67)	1 (33.33)	-	3 (100)	-	1 (33.33)
Pr.mirabilis n=2	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	-	2 (100)	-	0
Acinetobacter baumanii n=3	2 (66.67)	1 (33.33)	1 (33.33)	1 (33.33)	1 (33.33)	-	2 (66.67)	3 (100)	0

Most of the isolates were highly sensitive to cefaperazone sulbactum and amikacin and moderately sensitive to ofloxacin,ciprofloraxin and garamycin. *A.baumanii* showed 100% sensitivity to Imipenam and *P.aeruginosa* 85.71% sensitivity.

Table 21- Gram Negative bacilli with ESBL production

Organism	No. of cases	ESBL production (%)
E.coli	3	2(66.67)
S.pneumoniae	2	1(50)
K.oxytoca	3	2(66.67)
Proteus mirabilis	2	2(100)

ESBL production was checked by disc diffusion method and confirmed by double disc synergy test and ESBL strip method.

Table 22- Gram negative bacilli with metallo β latamanse production

Organism	No of isolates	MBL
Ps.aeruginosa	7	1(14.29)

MBL production was detected using Imipenem disc for screening and confirmed by MHT and CDT with Imipenem and Imipenem with EDTA.

Table 23- Detection of MRSA among isolates of *S.aureus*

Organism	Isolates	Disc diffusion method strains
S.aureus	9	7(77.78)

Methicillin resistance was screened using oxacillin disc (1µ g) by disc diffusion method.

Table 24-MIC of Vancomycin for Gram positive cocci

Organism	0.25µg/dl	0.5µg/dl	1µg/dl	2µg/dl	4µg/dl	8µg/dl
S.epidermidis (10)	-	3	5	1	1	-
S.aureus (9)	1	4	4	-	-	-
S.lugdunensis (1)	-	-	-	1	-	-
E.faecalis (1)	-	-	1	-	-	-

All the strains of *Staphylococcus aureus* (≤ 2µg/dl). and *CONS* (≤ 4µg/dl) were sensitive to vancomycin The MIC breakpoints of the isolates were between (0.25µg/dl - 4µg/dl)

Table 25 MIC of Imipenam for isolates of *Pseudomonas aeruginosa*

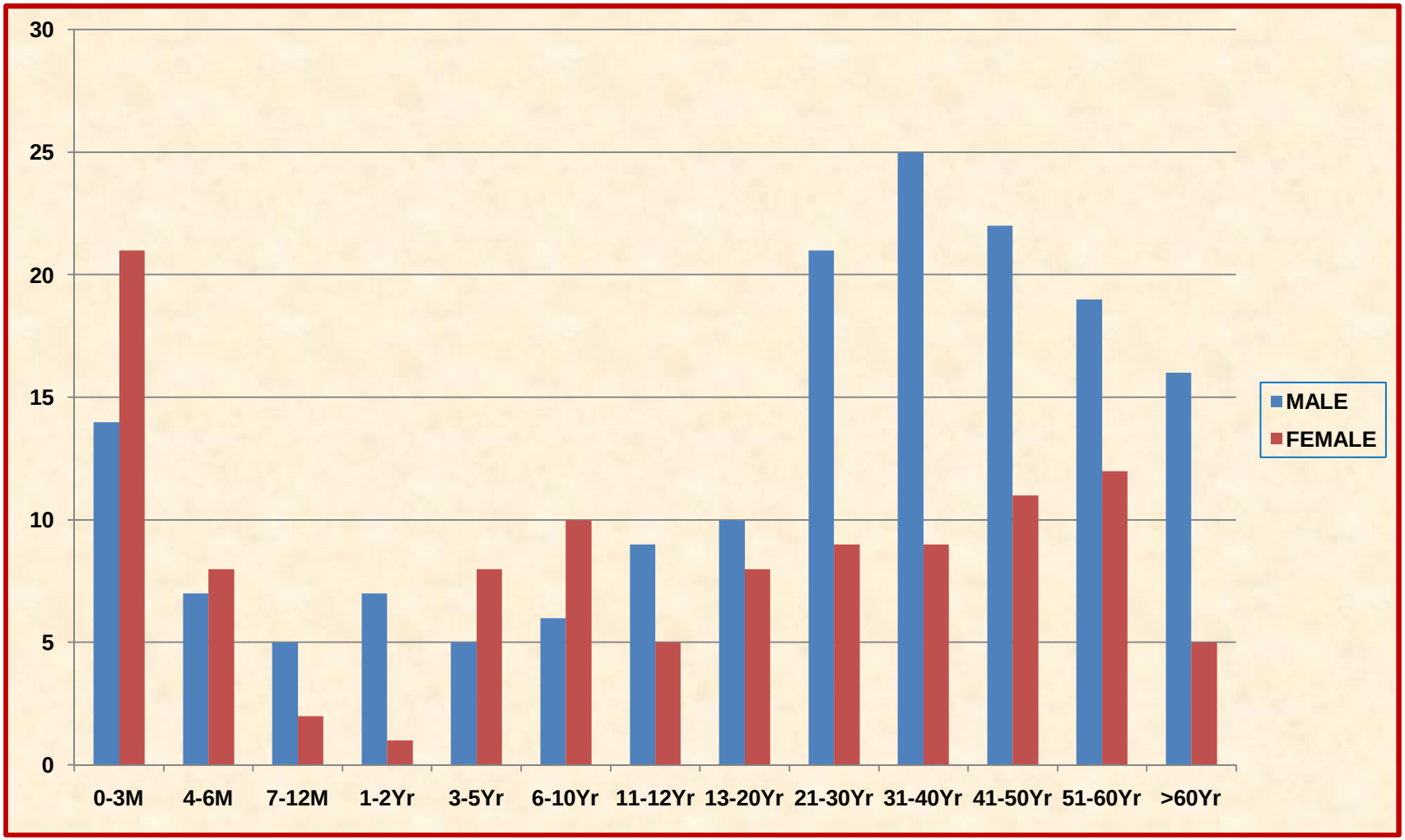
Organmism	**No isolates**	**1**	**2**	**4**	**8**	**16**	**32**
P.aeruginosa	7	2	3	1	-	-	1

Table 26 - Outcome of Patients With shunt infection

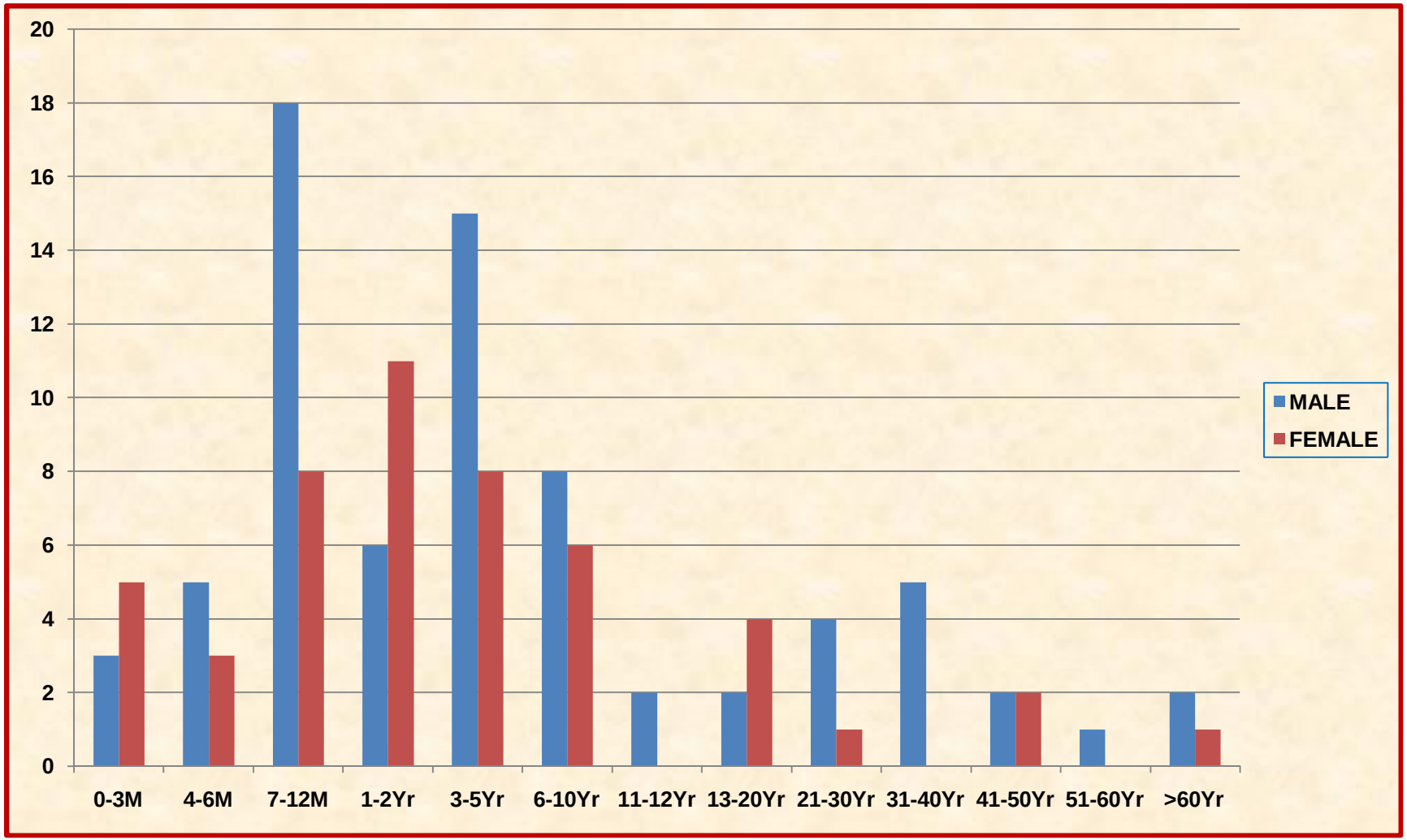
Outcome	**Children n= 36**	**Adult n=6**	**Total N= 42**
Survived	35(83.33)	5(11.91)	40(95.24)
Died	1(2.38)	1(2.38)	2(4.76)

The mortality rate was 4.76% (1.64% among cases of shunt malfunction).

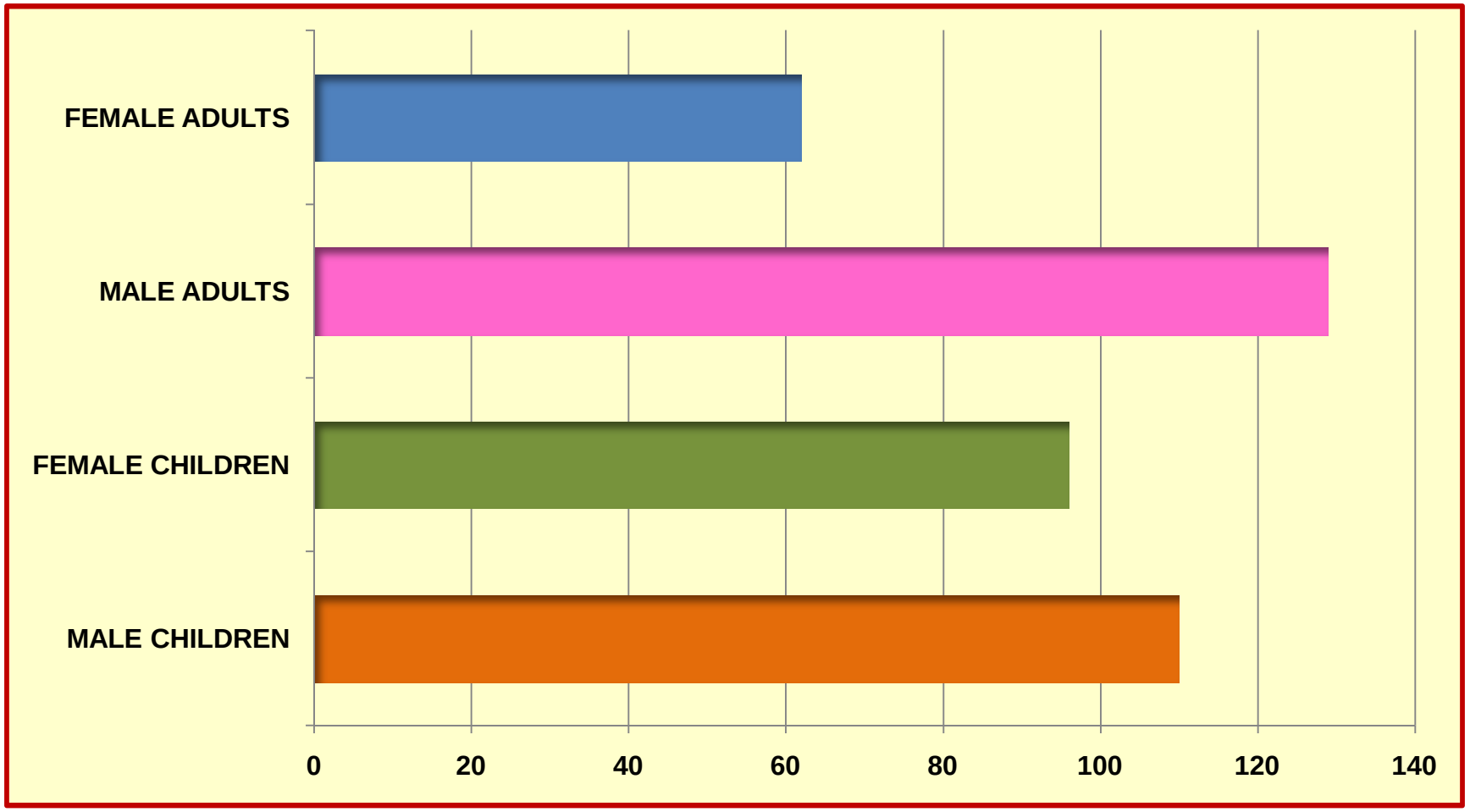
GRAPH 1 : AGE DISTRIBUTION OF PATIENTS WHO UNDERWENT PRIMARY VP SHUNT INSERTION



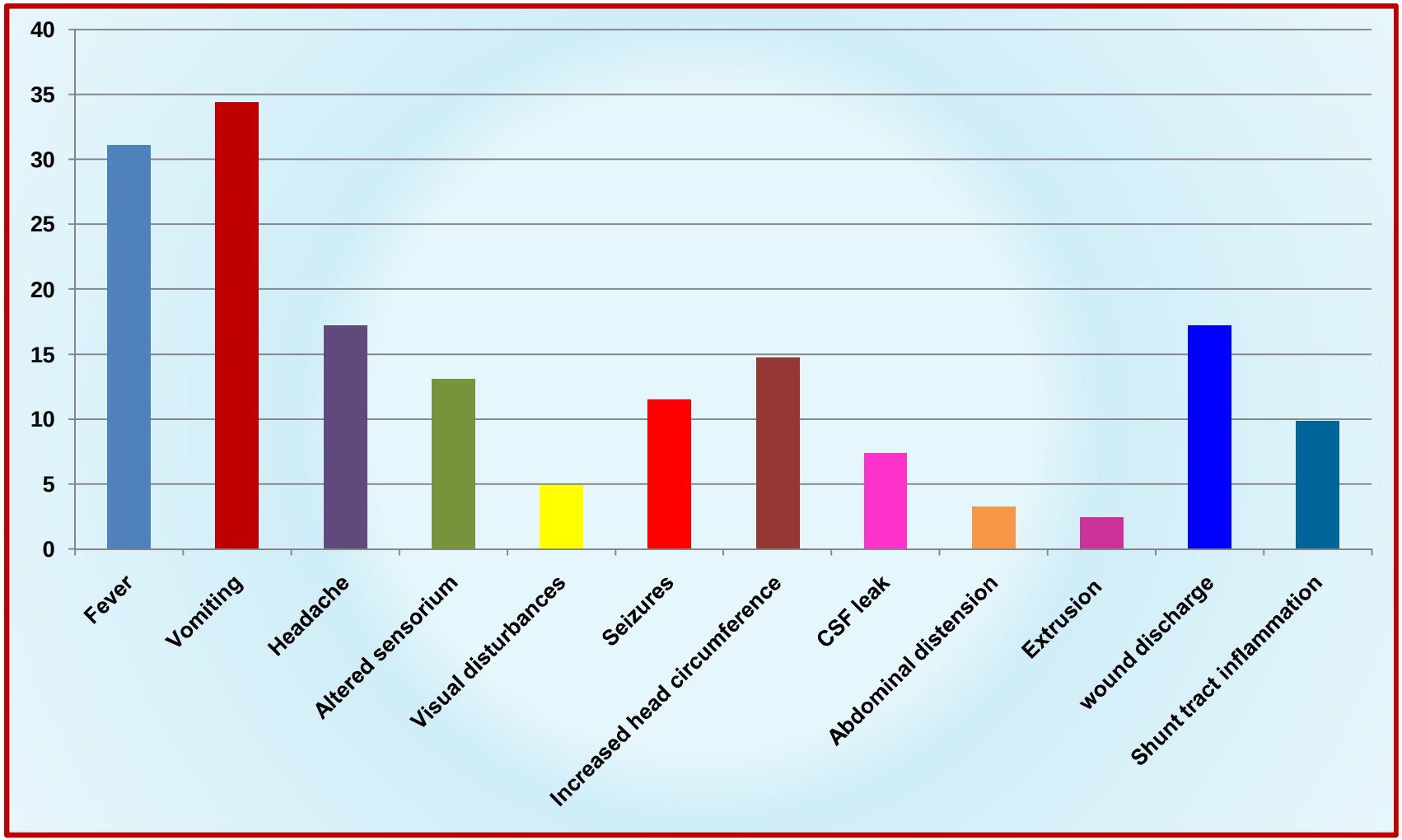
GRAPH 2 : AGE DISTRIBUTION OF PATIENTS WHO UNDERWENT PRIMARY VP SHUNT REVISIONS



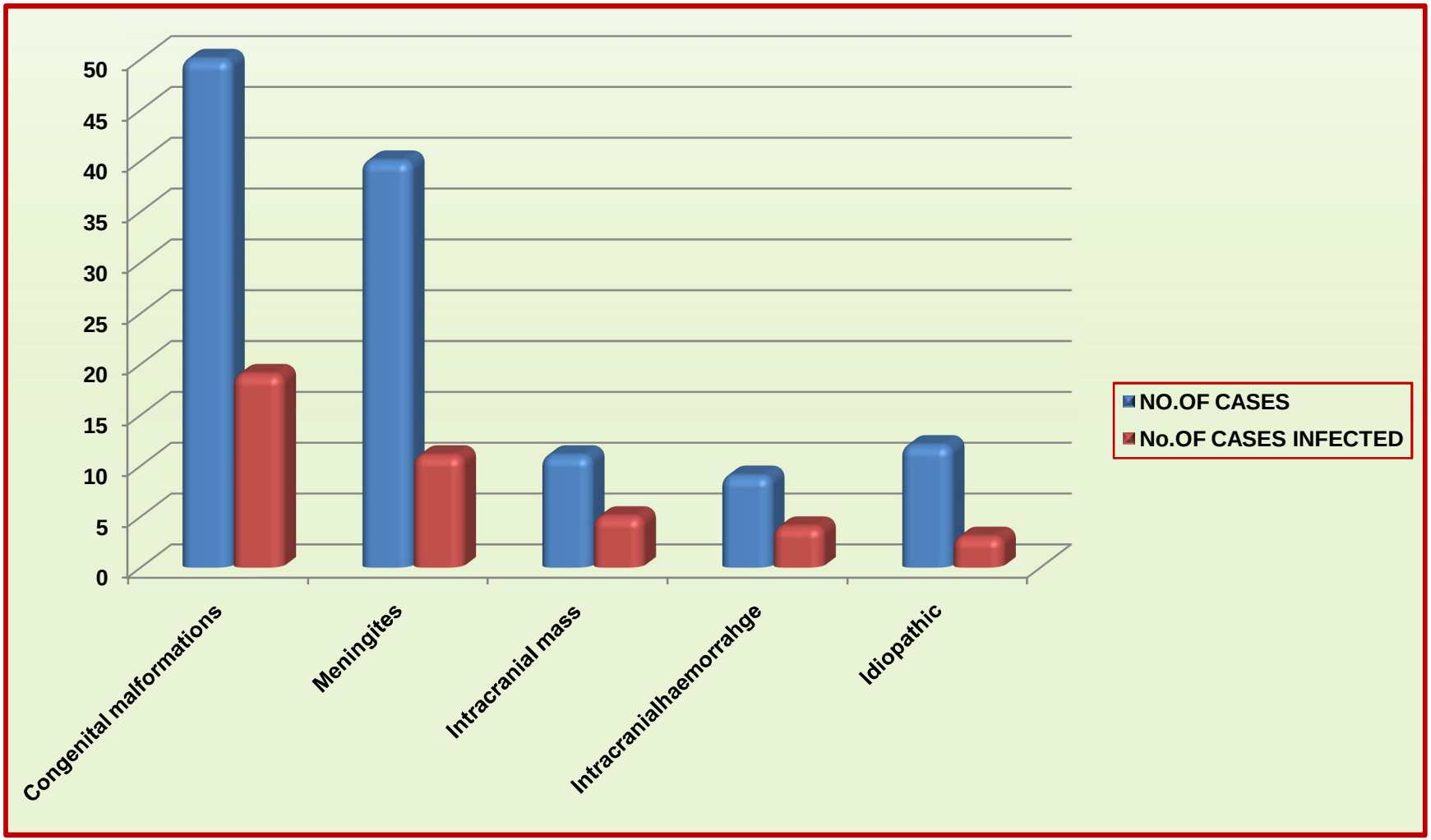
GRAPH 3 : SEX DISTRIBUTION



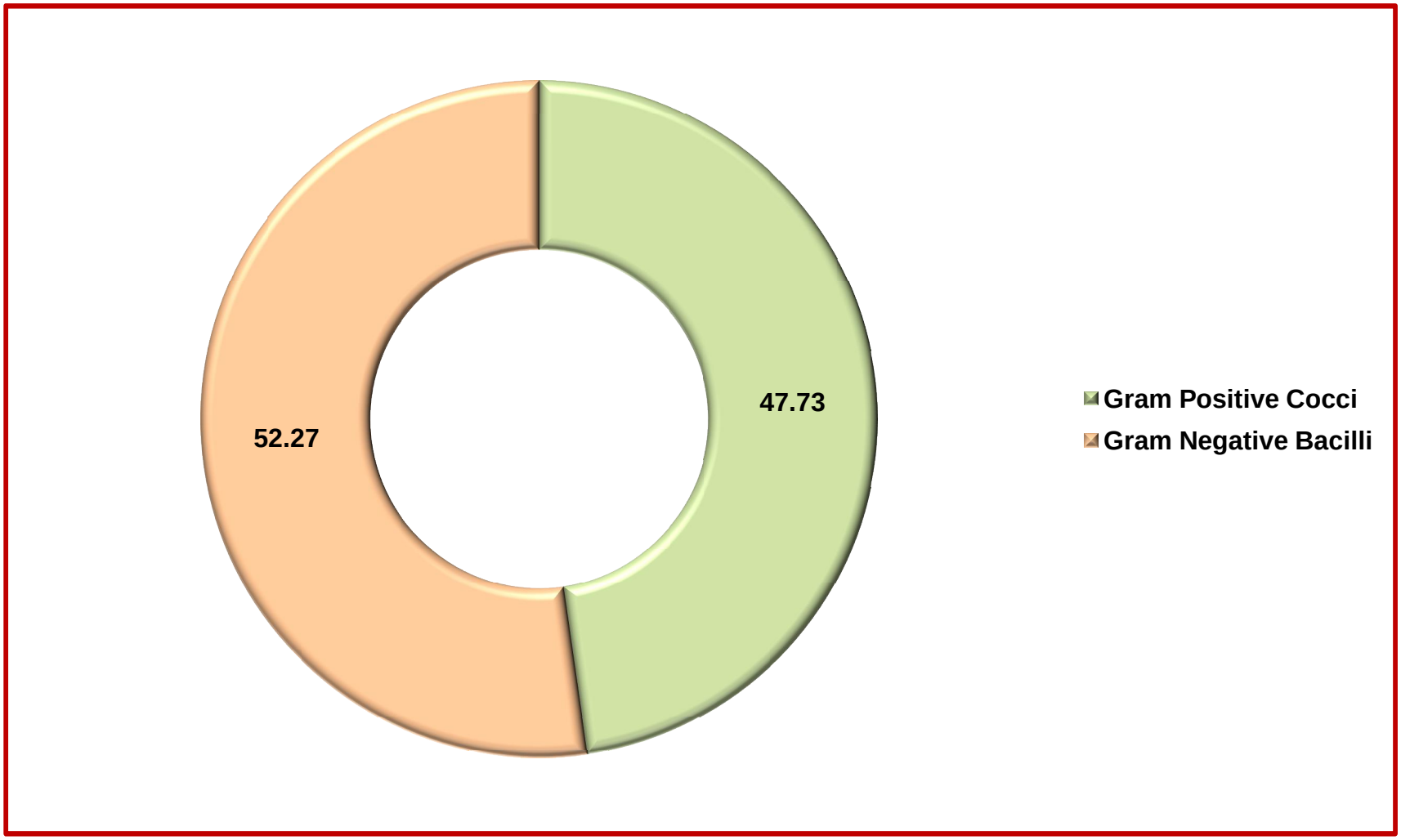
GRAPH 4 : CLINICAL PRESENTAION OF PATIENTS WITH VP SHUNT INFECTION



GRAPH 5 : CORRELATION OF ETIOLOGY OF HYDROCEPHALUS AS A RISK FACTOR FOR INFECTION



GRAPH 6 : PATHOGENS ISOLATED FROM CASES OF SHUNT INFECTION



GRAPH 7 : MICROBIOLOGICAL PROFILE OF INFECTED VENTRICULOPERITONEAL SHUNTS

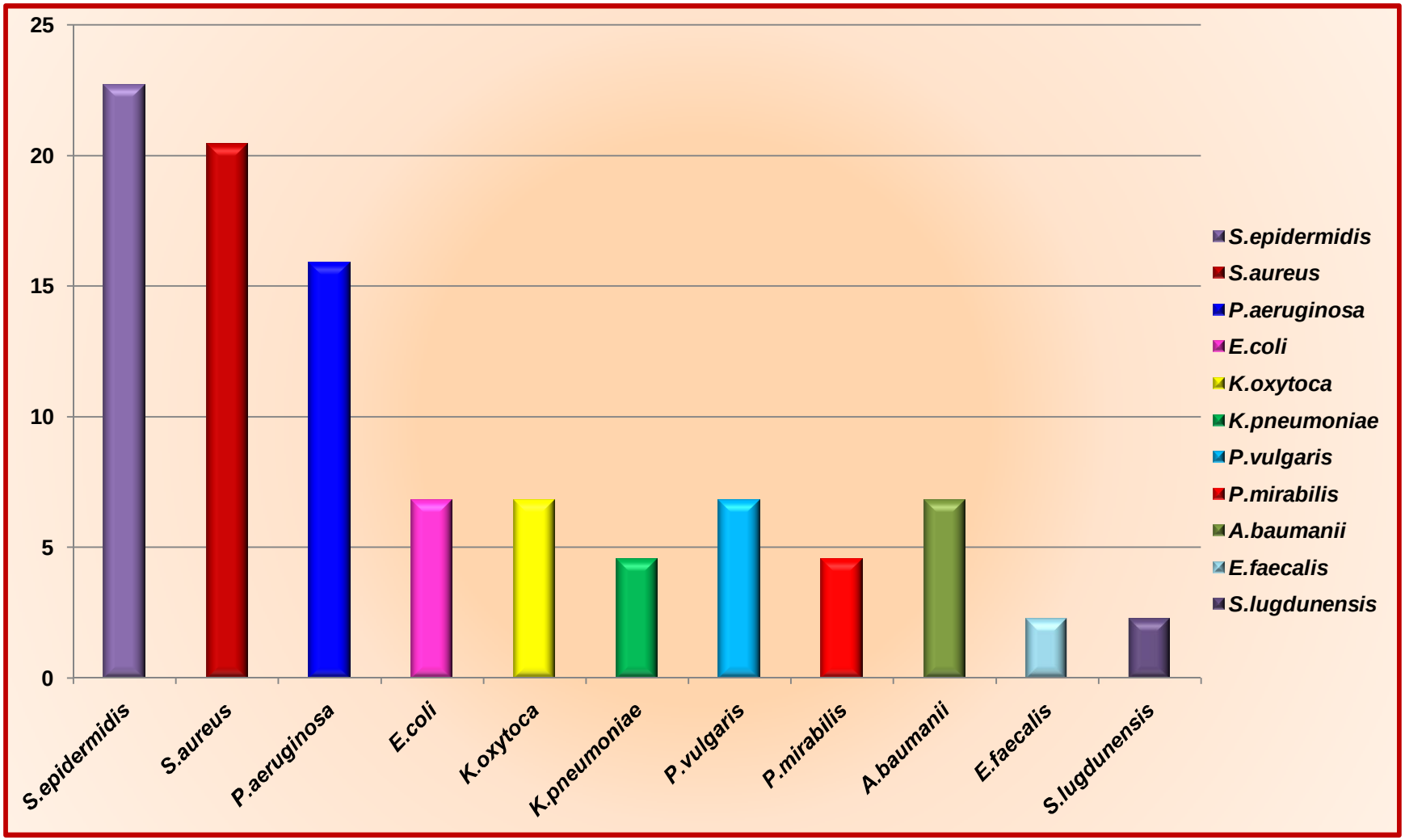


Fig. 1: Ventriculoperitoneal shunt tube

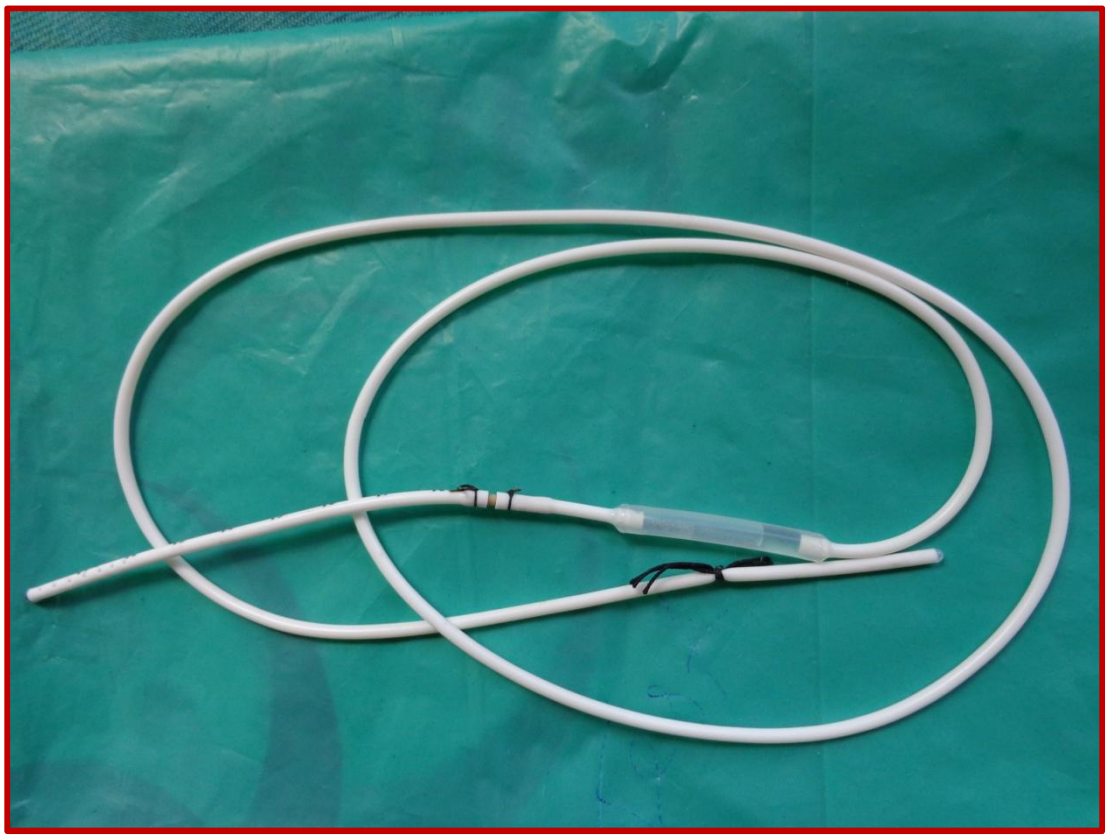


Fig. 2: Infected ventricular and peritoneal catheter tips in BHI broth

Fig. 3: A case of congenital hydrocephalus with replaced VP shunt tube

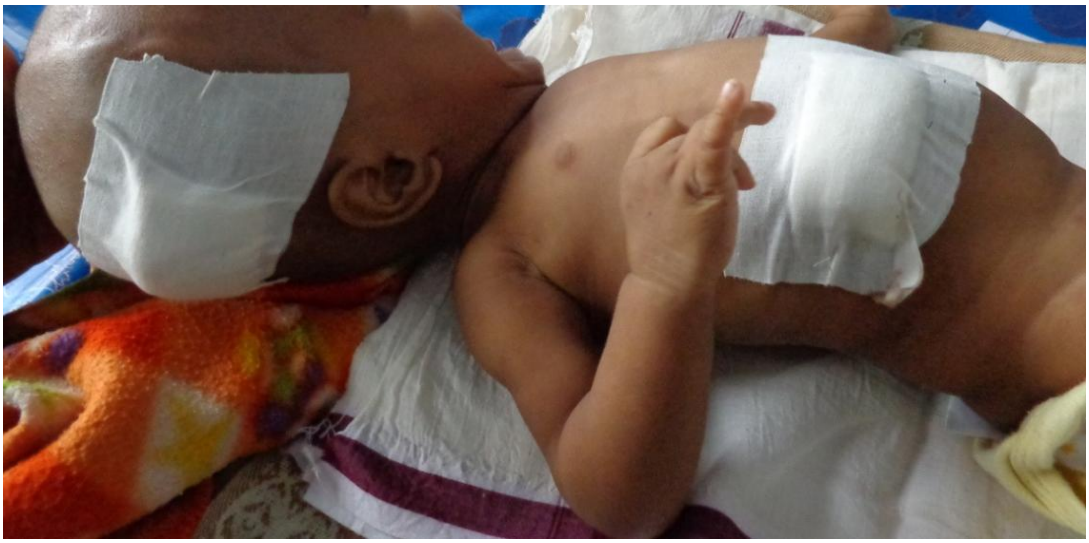


Fig. 4: A case of post menningitic hydrocephalus with shunt tract infection

Fig.5 : CT scan image of a case of hydrocephalus with bilateral VP shunt tubes

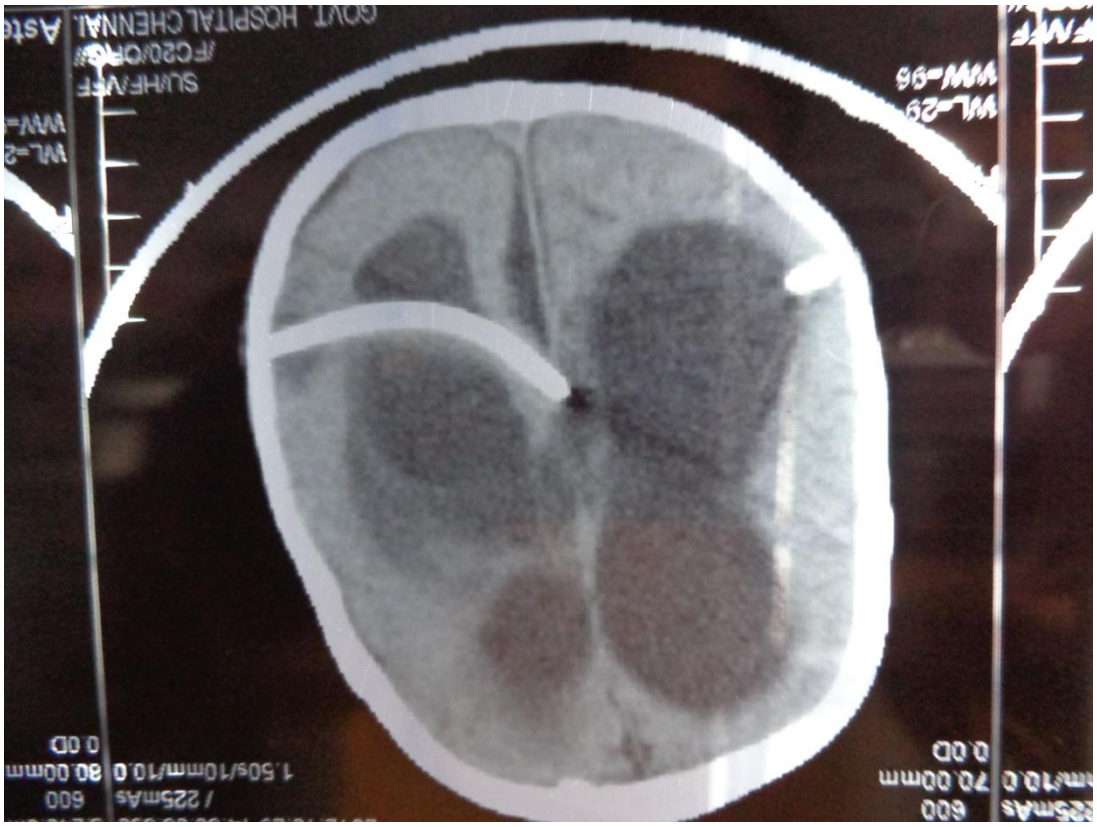


Fig.6 : X-ray chest of a case of hydrocephalus showing shunt tube inside the peritoneal cavity

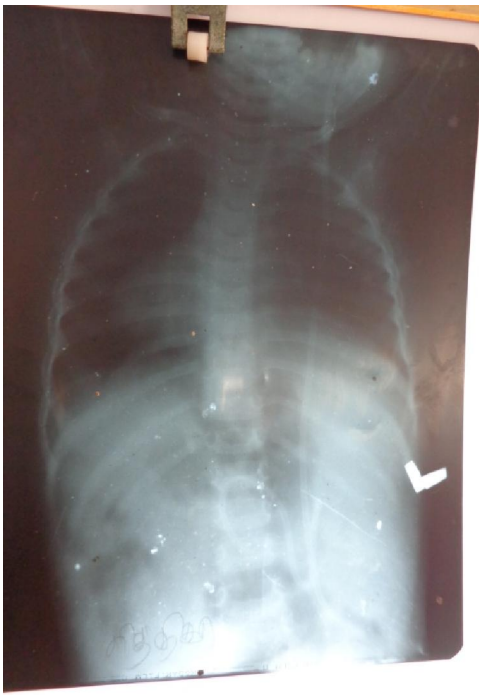


Fig. 7: Procedure showing insertion of proximal catheter into the lateral ventricle

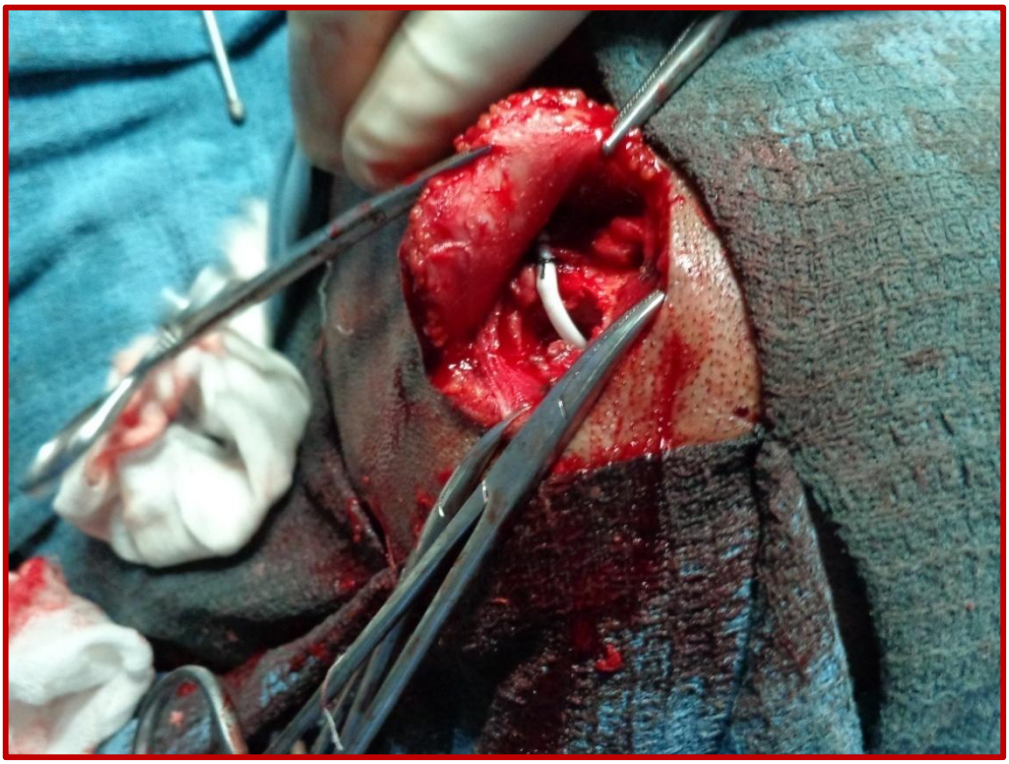


Fig. 8: Insertion of distal catheter into the peritoneal cavity

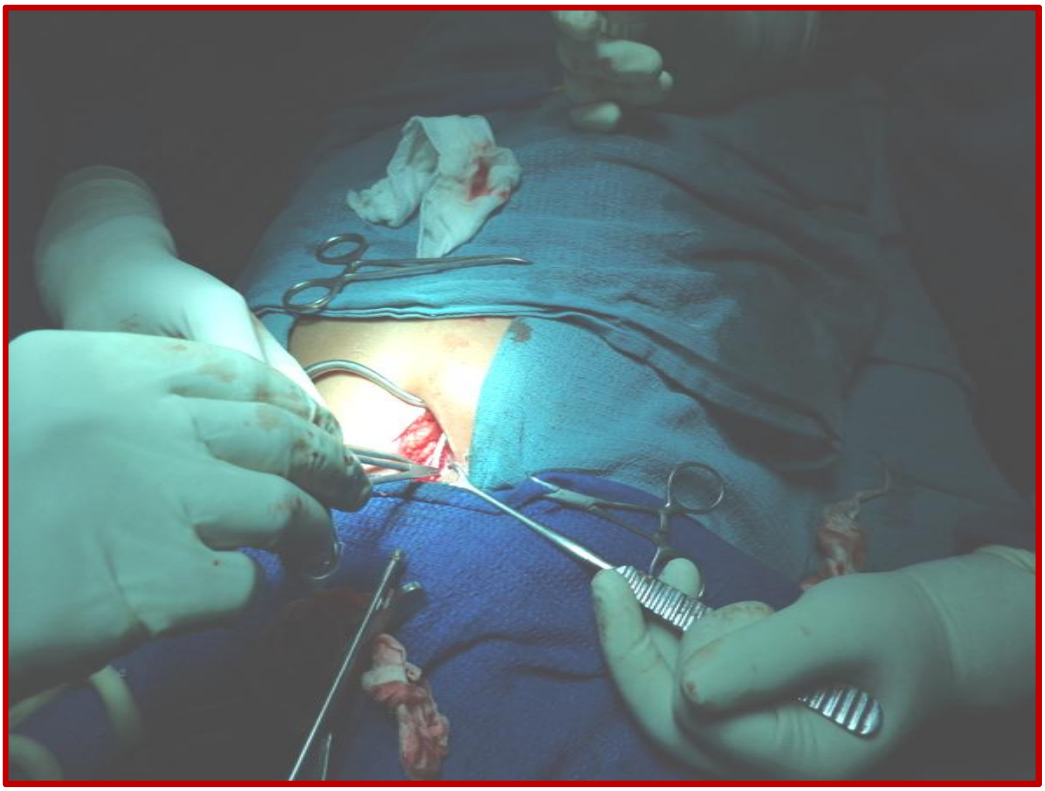


Fig.9 : Direct Gram stain of CSF showing pus cells and GPC

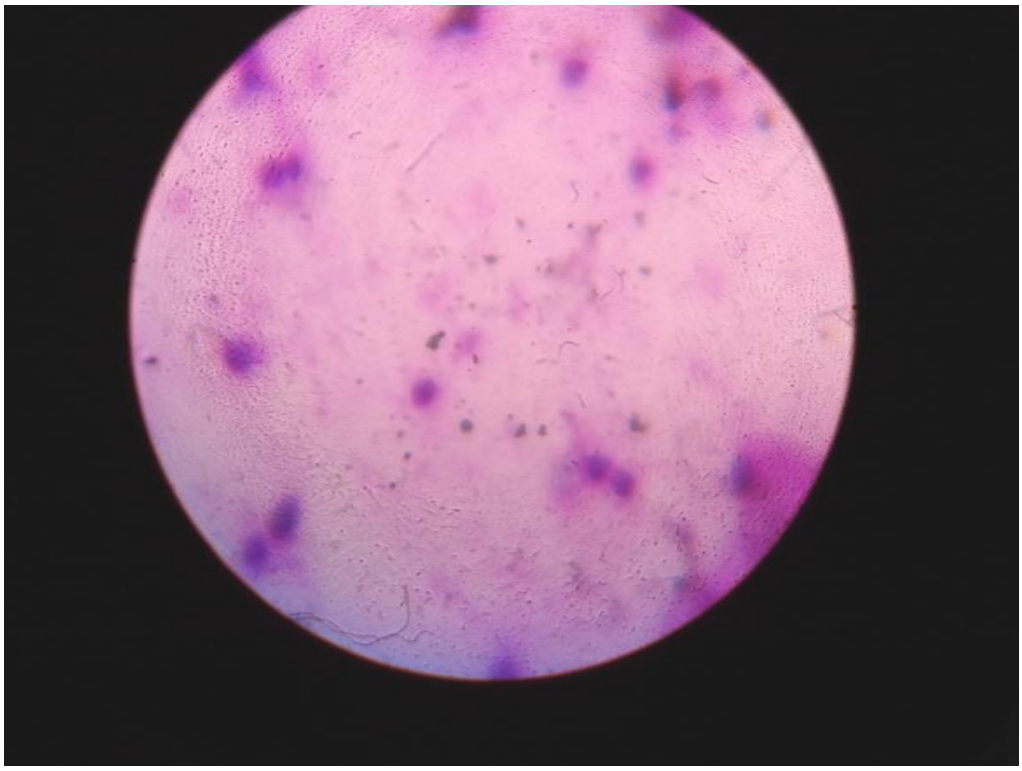


Fig. 10: Direct Gram stain of CSF showing pus cells and GNB

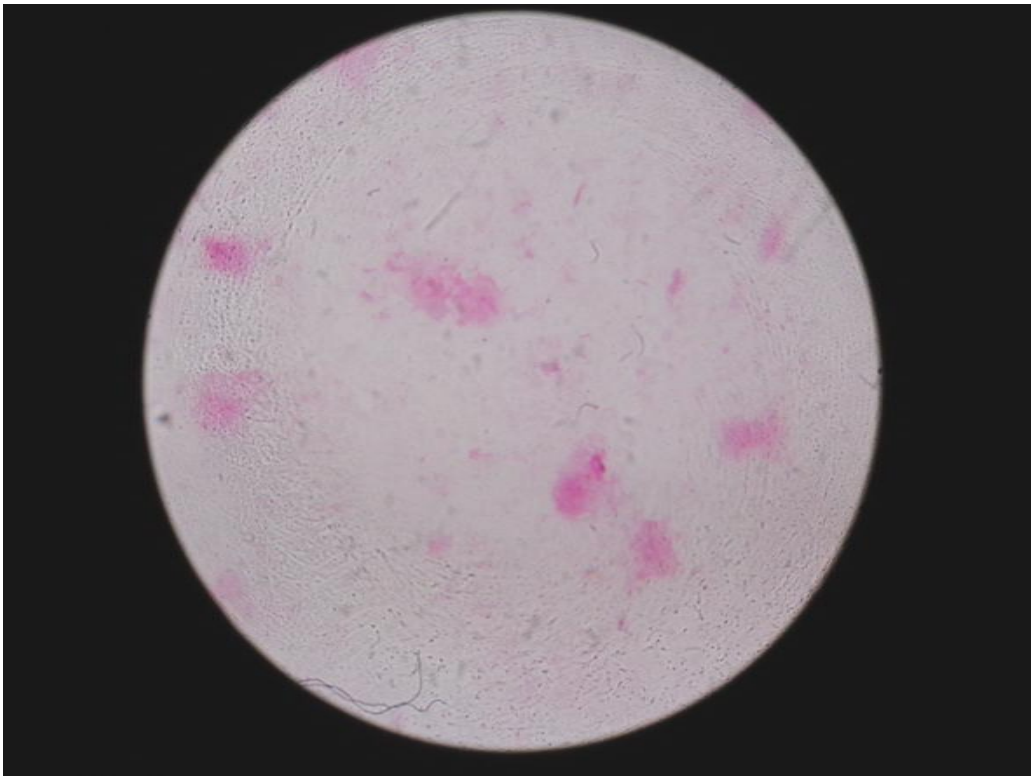


Fig. 11: *Escherichia coli* on McConkey agar plate

Fig.12 : Biochemical reactions of *Escherichia coli*

Fig. 13: Tube coagulase test of *Staphylococcus aureus*

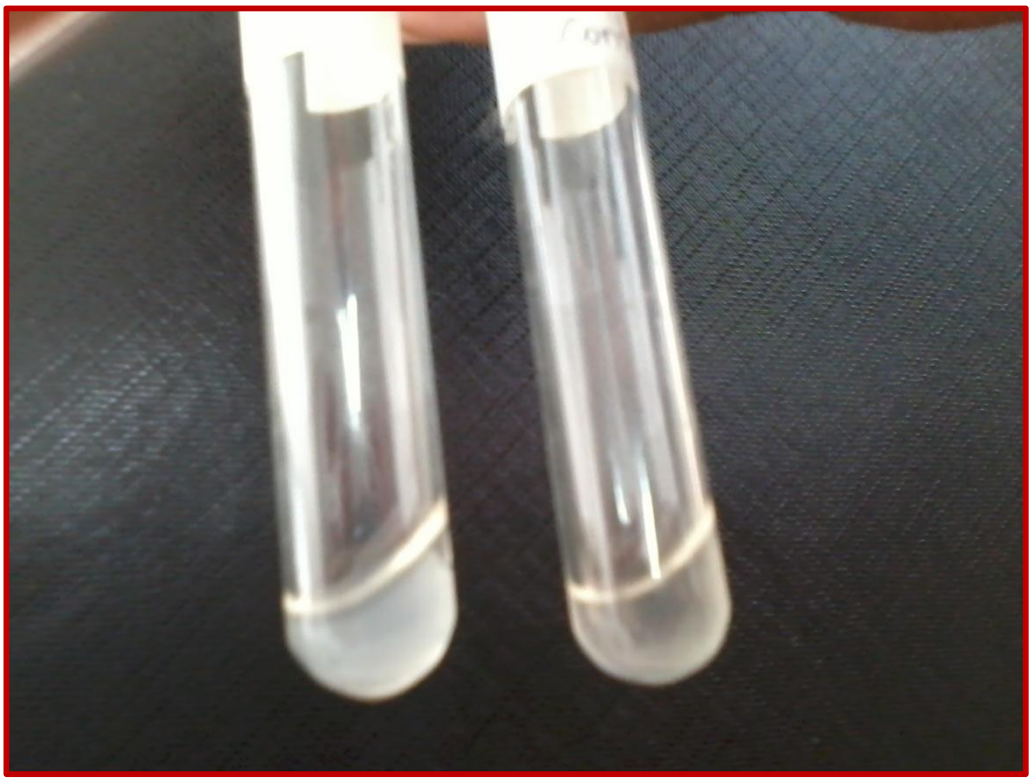


Fig.14 : Antibiotic sensitivity of *S.epidermidis* on MHA

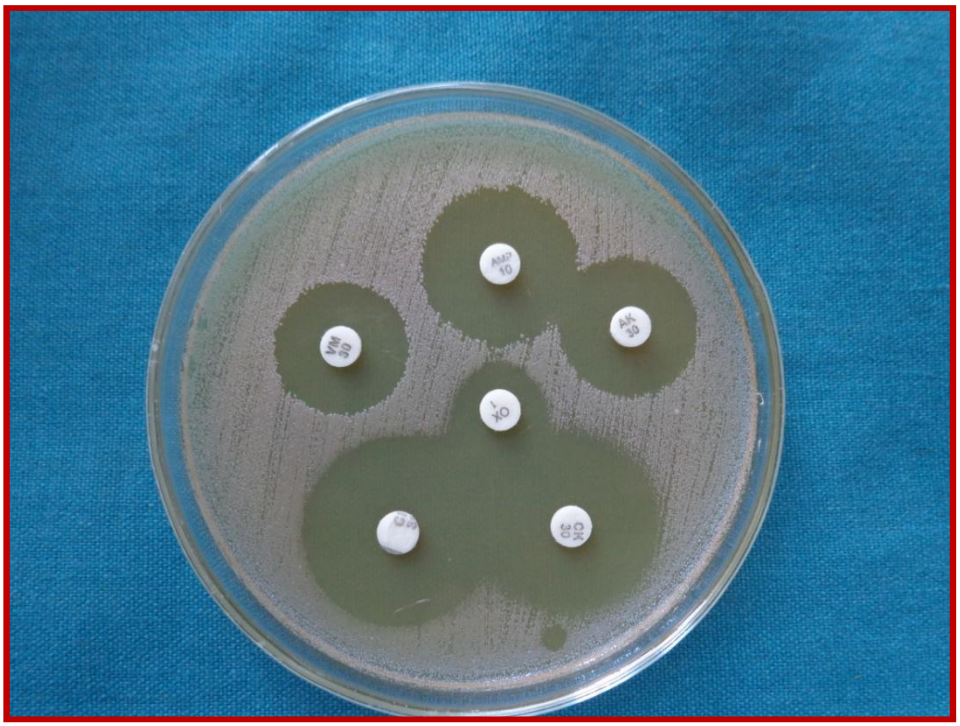


Fig. 15: Biochemical reactions of *S.epidermidis*

Fig. 16: Biochemical reactions of *S.lugdunensis*

Fig. 17: Biochemical reactions of *Acinetobacter baumanii*

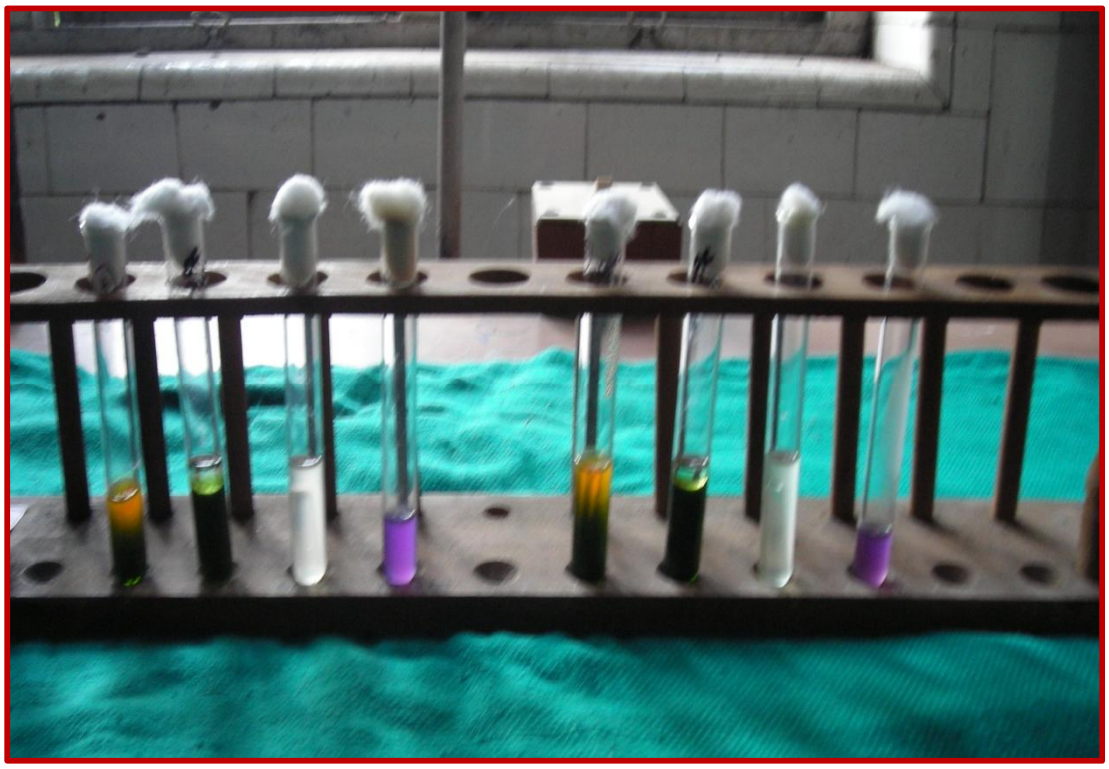


Fig.18: Biochemical reactions of *Proteus vulgaris*

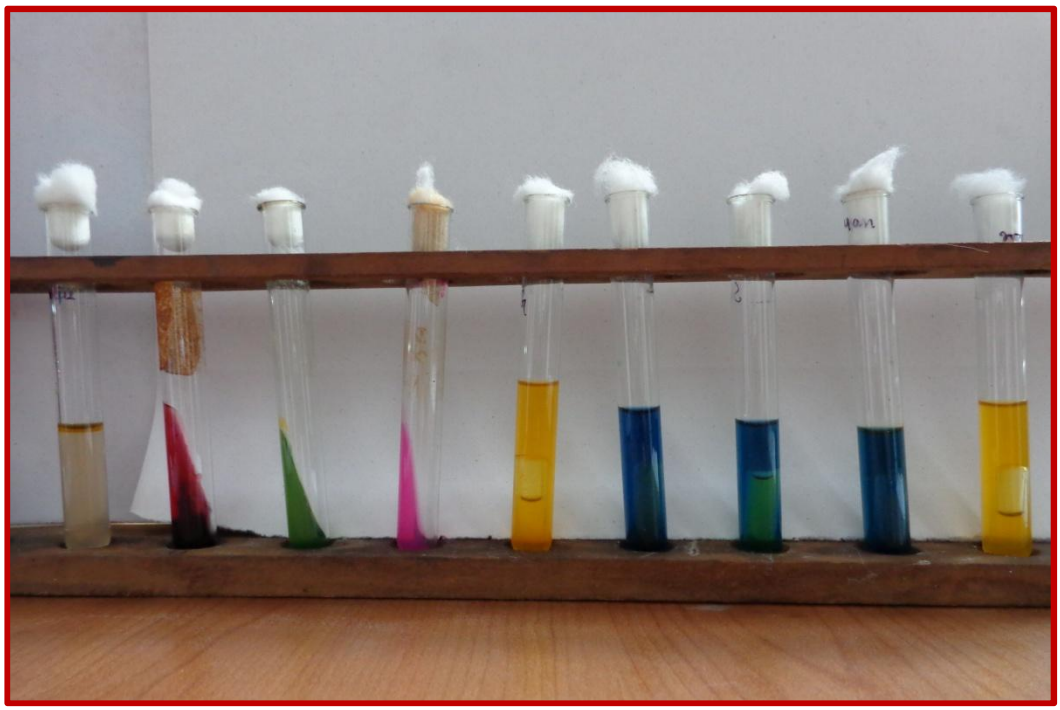


Fig. 19: Antibiotic sensitivity of *Pseudomonas aeruginosa*

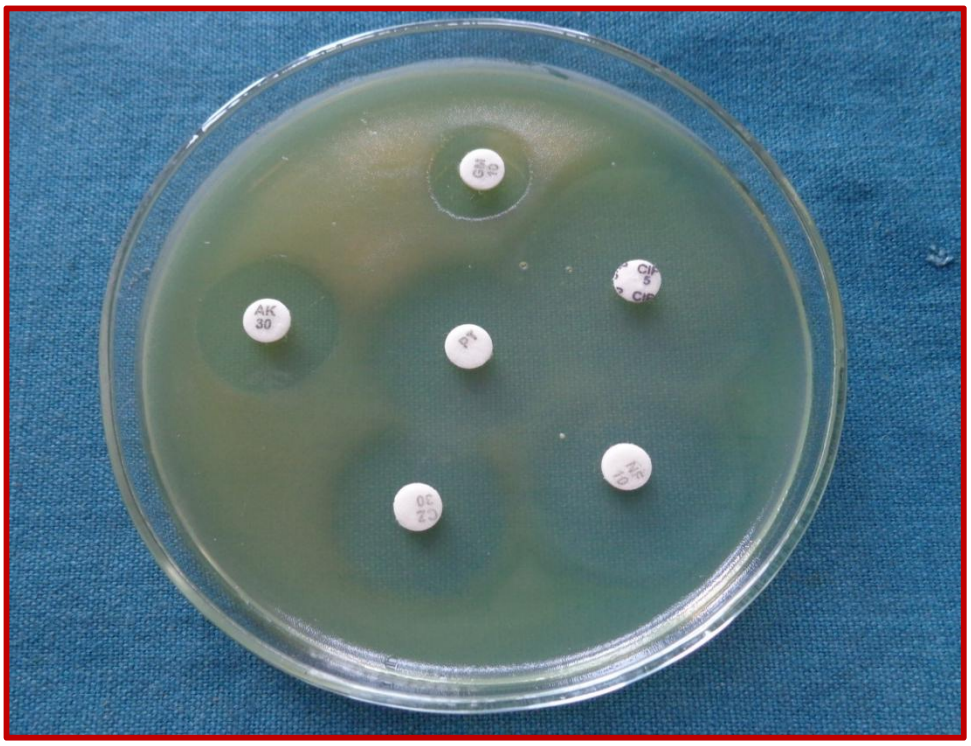


Fig. 20: MIC of Imipenam for *Pseudomonas aeruginosa* (MIC-32 µg/ml)

Fig. 21: DDST for ESBL detection using cefotaxime, ceftazidime and amoxicillin-clavulanic acid

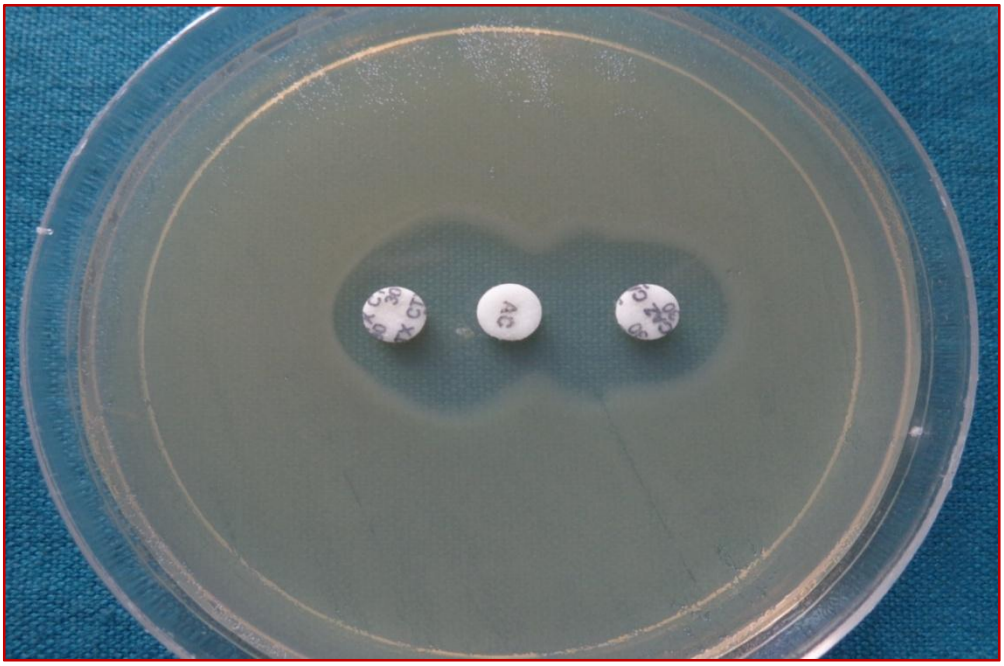


Fig. 22:Combined disc test for ESBL detection using ceftazidime and ceftazidime + clavulanic acid

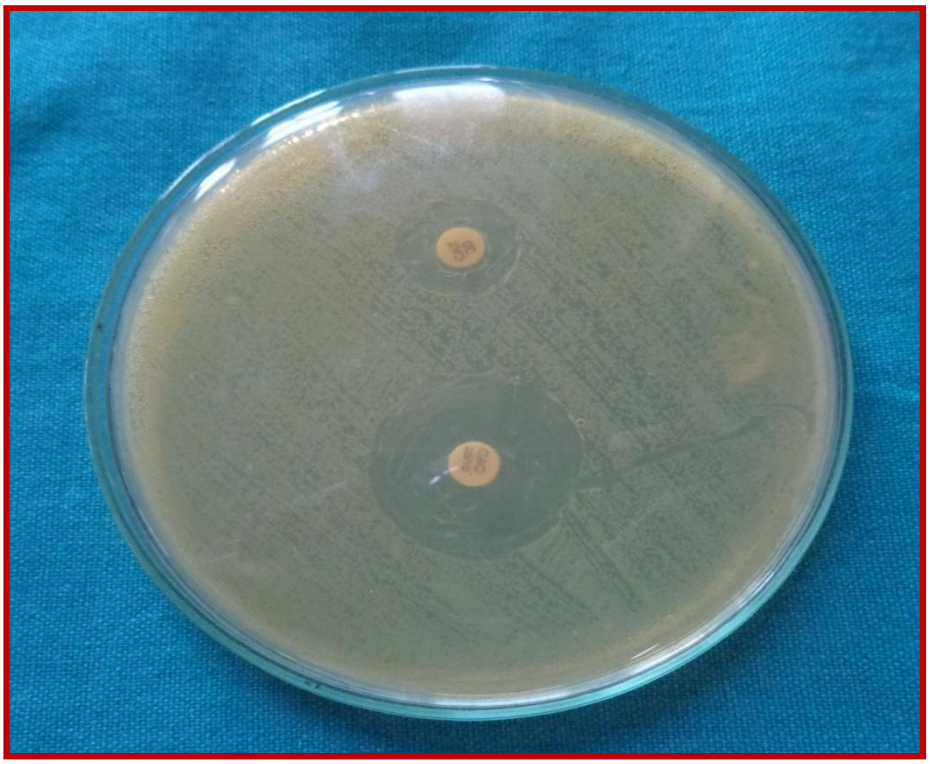


Fig. 23: Modified Hodge Test for MBL detection

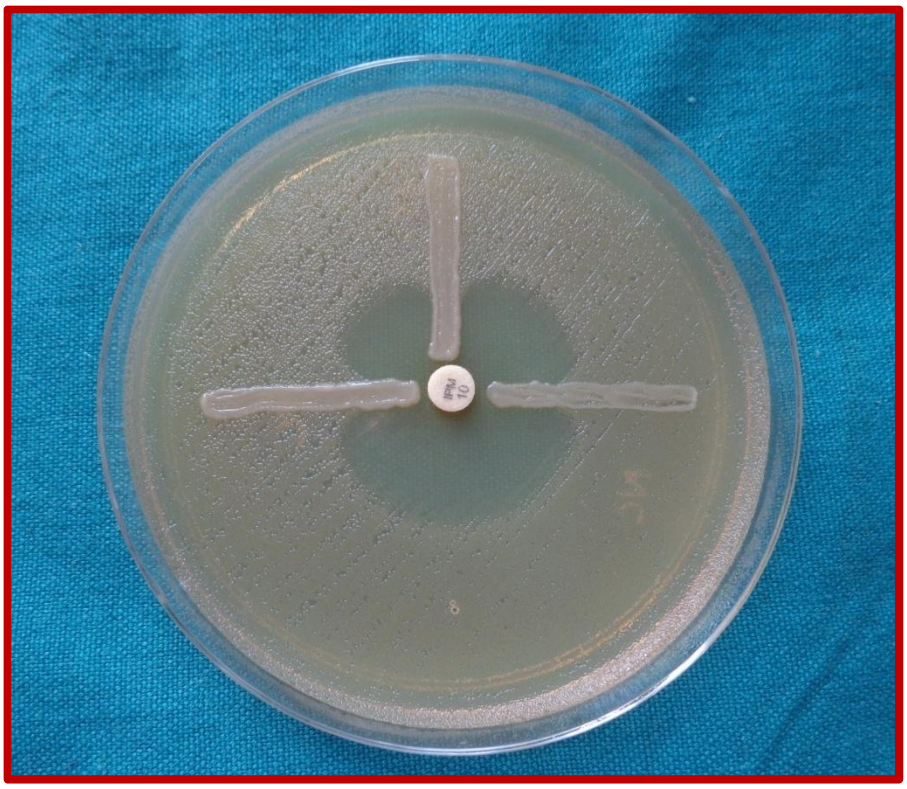


Fig. 24: Combined disc test for MBL detection using Imipenam and Imipenam + EDTA

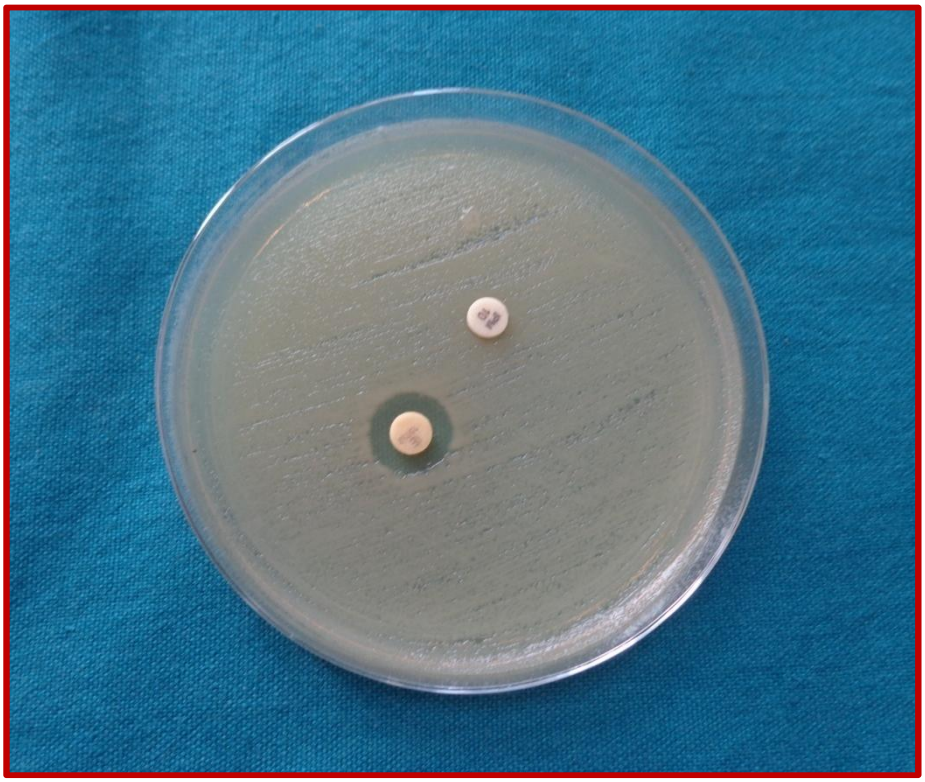


Fig. 25: E-test for triple ESBL detection using Ezy MIC strips
With test strain and ATCC *E.coli* 25922

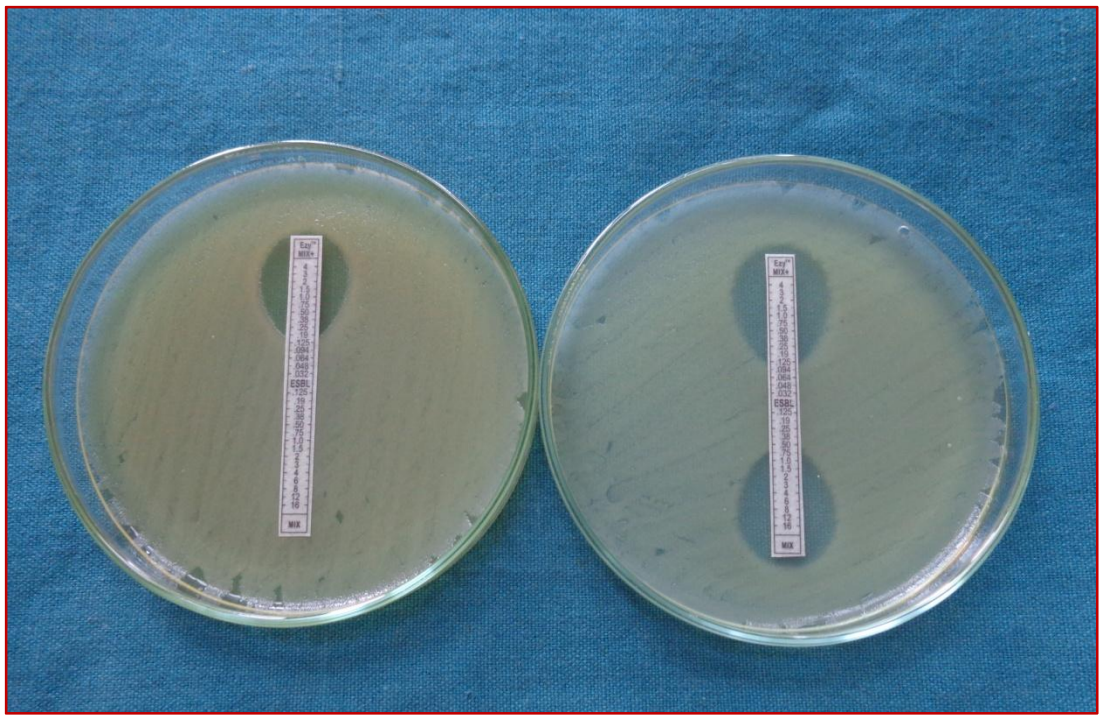
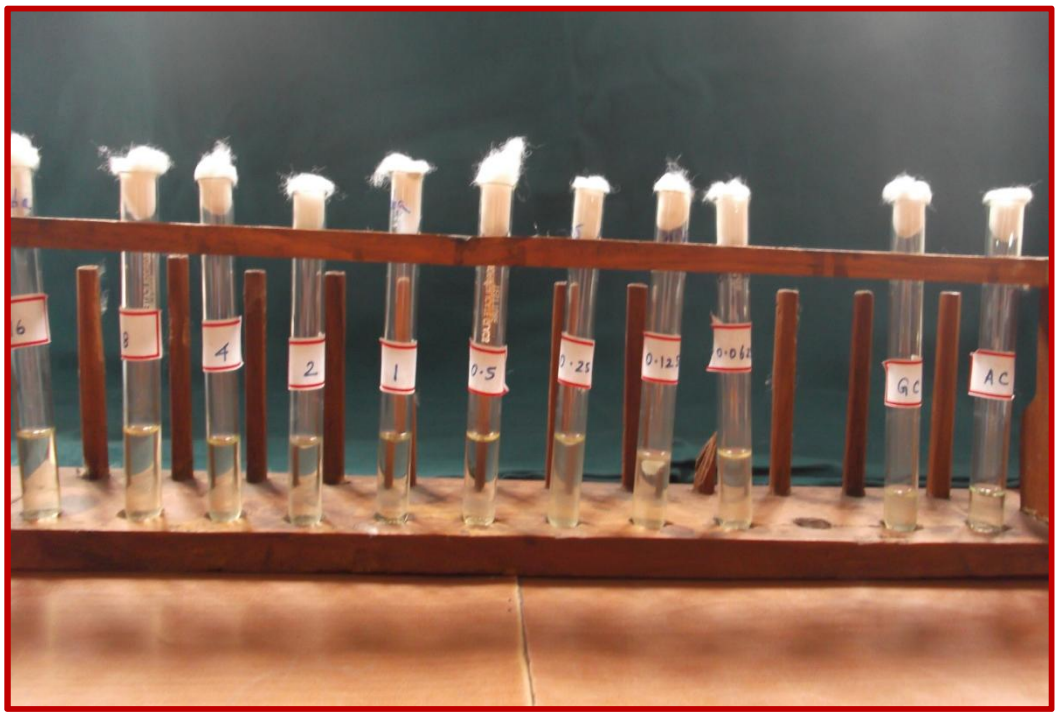


Fig. 26: MIC of Vancomycin for S.aureus (MIC 0.5µg/ml)



DISCUSSION

Insertion of ventriculoperitoneal shunt is the mainstay in the management of hydrocephalus in children and adults enabling the drainage of excess cerebrospinal fluid (CSF) from the cerebral ventricles into the peritoneal cavity. Infection of CSF shunts is one of the serious complications in the post operative period and also in the long run, resulting in increased morbidity and mortality. Seizures and neurological disturbances occur as a sequelae of infection, thus disabling the patient.

This study was performed with the intention of evaluating the incidence of infection, to identify the predisposing risk factors and the causative pathogens involved, to determine their antibiotic sensitivity and resistance pattern and to suggest an empirical antibiotic therapy for the patients.

During the study period altogether 2120 surgeries were performed by the neurosurgeons including 426 CSF shunt related procedures (20.1%) performed in 397 patients. Of these, 275 surgeries were primary VP shunt insertions (64.55%) and 151 were shunt revisions (35.45%). Nearly 1/3rd of the shunt procedures performed were shunt revisions (Table - 1). Estimation of the data from the National Hospital Discharge Survey in the US from 1988 to 1991 reveals that 33,000 patients underwent shunt placement procedures annually, with nearly half of these for revision of an existing shunt.[3,45]

In this study, 60.2% of shunt related procedures were performed in males and 39.8% in females. In the study group who met the eligibility criteria and underwent shunt revisions, 59.84% were males and 40.16% were females. In a study conducted by McGirt et al 52% of the shunts were placed in male patients.[40](Table - 2)

In this study, 108 children (39.27%) and 167 adults (60.73%) underwent primary VP shunt insertions. Considering those who developed malfunction and subsequently underwent revisions the pediatric population was significantly higher (80.33%) than the adult population (19.67%) (Table - 4). In a study conducted by Sarguna P et al 77.78% of shunt infections was reported in patients below 15 years of age.

The aetiology of hydrocephalus in children who required shunt revisions in this study were congenital malformations like meningomyelocele (7.38%), aqueductal stenosis (4.92%) and Dandy Walker malformations (4.92%). The other common causes of hydrocephalus in children were preceding meningitis (22.95%) and intracranial mass lesions (6.56%). In adults the conditions frequently causing hydrocephalus were intracranial hemorrhage (6.56%) and meningitis (4.92%) (Table - 5). In a study conducted by A.V.Kulkarni et al in 2001, the following causes were documented for hydrocephalus: myelomeningocele (21.7%) intraventricular hemorrhage

(19.1%), tumors (14%), aqueductal stenosis (8%), meningitis (4%),trauma (2.3%) and hemorrhage (1.3%).[35]

The common clinical manifestations of patients with shunt malfunctions in the study group were fever (31.15%), vomiting (34.43%), headache (17.21%), wound infection (17.21%) progressive increase in head size (14.75%), altered sensorium (13.11%), seizures (11.48%) and CSF leak (7.38%). Fever, vomiting and altered sensorium were the common symptoms in both children and adults. Seizures were more common in children and headache was more common in adults (Table - 8). In a study conducted by Drake JM et al, the common symptoms and signs of presentation in patients with infected CSF shunts were fever (69.2%), vomiting (31%), increased head circumference (19.2%), wound erythema (27%), CSF leak (15.4%) and seizures (3.8%).[19]

Among the 397 patients who underwent CSF shunt procedures, 122 symptomatic patients underwent revision surgeries. Of these, 101 patients (82.79%) underwent one revision surgery and 26 of these were culture positive. (21.31%) (Table- 6). 21 patients underwent multiple revisions and 16 of them were culture positive (13.11%). These 21 patients underwent a total of 50 revision procedures. Of them 15 underwent 2 revisions (30), 5 patients underwent 3 revisions (15) and 1 patient underwent 5 revisions. The overall infection rate in the study was 10.58%.

The incidence of shunt infection in various studies is in the range of 4 to 15%. In a study of VP shunt infection conducted by M.F Cotton et al 39 infections were identified from 372 shunt procedures giving an incidence of 10.5%.This finding was similar to the present study.[42]

Majority of shunt infections occur in the early post operative period. In this study 27.87% of VP shunt infections occurred within 1 month of shunt infection, 58.2 % of infections within 3 months and 74.59% occurred within a period of 6 months post operatively (Table 7). Study conducted by Choux et al reported that 66% of infections were diagnosed within 1 month of surgery and nearly 80% within 6 months.[13]

The most common risk factor associated with shunt related infection is the age of the patient. This study also highlights age as a risk factor for shunt infection. About 68.12% of infections occurred in infants under 1 year of age. A high incidence of infection was noted in children between 7 and 12 months (35.71%) followed by infants less than 6 months of age (21.43%).The incidence of infection was relatively less in patients aged 5 years and above (Table - 9). Casey et al had observed in a cohorts study that the infection rate in children less than 6 months of age was 19% compared to 7% in children above that age.[11]

Young age is one of the main risk factors for acquiring shunt infection, the reason suggested being an immature immune system and a higher

concentration of microbial flora on the skin with more adherent strains.[2] Other significant risk factors for CSF shunt infections include premature birth,etiology of hydrocephalus, previous shunt infection and shunt revisions.

In this study, shunt infections were more common in children with hydrocephalus due to congenital malformations (42.86%), meningitis (21.43%) and intracranial mass (11.91%). In adults, infection was common in patients with hydrocephalus due to intracranial hemorrhage (7.14%) and meningitis (4.76%) (Table - 10). This was similar to a study conducted by Suzan Sacar et al which reported that shunt infections were common in congenital hydrocephalus (32%), meningitis (23%) and intracranial mass (23%) and less common in patients with intracranial hemorrhage (9%).[58]

In this study, it was also observed that there was a marked association of shunt infection with previous shunt revisions. 21 patients had undergone more than one revision surgery and 16 of them were culture positive (76.19%).Whereas in those who underwent one revision surgery (101) only 26 were culture positive (25.74%). McGirt et al in their study had observed a 4 fold increase in the risk of shunt infection in patients with previous shunt infection.[40]

Measurement of CSF glucose and protein levels and cell counts can prove to be very valuable in identifying shunt infection. In this study, CSF protein levels were raised in 66.67% of infected patients and glucose levels

were reduced in 64.29% of infections. Most of the CSF specimens with positive culture were acellular.CSF pleocytosis was observed only in 7.14%. (Table - 12)

Macroscopic examination of the CSF specimens was also not indicative of underlying infection. Of the 81 CSF specimens received, 31 were culture positive but only 4 specimens were turbid.

Gram staining of CSF specimens has been shown to be very useful for preliminary diagnosis of infection and identification of the nature of pathogen involved.

In this study, gram staining was done for all the CSF specimens. Of the 30 specimens which showed pus cells and presence of organisms, 26 were culture positive (32.1%), and 4 were culture negative (4.94%). Gram staining was positive more in infections with gram positive cocci (16) than Gram negative bacilli (10). Of the 51 CSF specimens which revealed no pus cells or organisms, 5 were culture positive (6.17%). (Table-11)

Analysis of these results shows that Gram staining was positive in 83.87% of culture positive specimens and negative in 16.13%. A study done by Nelson et al showed gram staining positivity in 82% of gram positive cocci and 91% of gram negative bacilli.[44]

Blood counts analyzed in the study showed leukocytosis in 71.43% of shunt infections and anaemia in 33.33% was seen only in pediatric patients.(Table - 13)

In this study, 81 CSF specimens, 67 shunt tubes, 9 pus specimens and 3 peritubal collections were collected from 122 patients with shunt malfunction.Of the 81 CSF specimens, 25 initial specimens were culture positive (30.86%). 6 repeat CSF specimens obtained from previously infected patients were also culture positive (7.41%). Of the repeat specimens, same pathogen was isolated from 5 cases and a different organism from one.

Among the 67 shunt tubes processed, 29 specimens obtained for the first time from patients were culture positive (43.28%). 10 specimens obtained from the same patients were also culture positive, 8 of them with the previous pathogen isolated and 2 with a different organism.Of the other specimens, 66.67% each of pus and peritubal collections were culture positive.(Table -14)

In this study, 44 bacterial organisms were isolated from 42 patients with shunt infections. The causative pathogens included 21 isolates of gram positive cocci (47.73%) and 23 isolates of gram negative bacilli (52.27%). Of these, monomicrobial infection occurred in 40 patients and polymicrobial infection in 2 patients (2 isolates each).(Table -15)

The commonest organism isolated in this study was *Staphylococcus epidermidis* (22.73%) [Table 16]. Other common pathogens isolated were S*taphylococcus aureus* (20.45%) and *Pseudomonas aeruginosa* (15.91%). Other organisms less commonly isolated were gram negative bacilli like *Escherichia coli* (6.82%),*Klebsiella oxytoca(*6.82%),*Proteus vulgaris* (6.82%) *Acinetobacter baumanii* (6.82%),*Klebsiella pneumoniae* (4.55%),*Proteus mirabilis* (4.55%) and gram positive cocci like *Enterococcus faecalis* (2.27%) and *Staphylococcus lugdunensis* (2.27%). A study performed by Sharpio S et al reported isolation of *Staphylococcus epidermidis* (45%), *Staphylococcus aureus* (20%), *Micrococcus* (5%) and gram negative bacilli (15%).

Mixed infection occurred in 2 patients with following isolates- *Staphylococcus epidermidis +Proteus mirabilis* and *Staphylococcus aureus +Acinetobacter baumanii*. Both the patients with mixed infection had previously undergone external drainage procedures of the peritoneal end of VP shunt tube. (Table-17)

Bacteraemia was observed in 3 patients with VP Shunt malfunction *Staphylococcus epidermidis* was isolated from blood, shunt tip and CSF of 1 patient with VP Shunt infection. *Klebsiella oxytoca* and *Enterococcus faecalis* were the pathogens isolated from blood culture of two other patients, in whom the CSF culture was negative.(Table-18)

All the isolates of gram positive cocci were sensitive to Vancomycin (100%).Most of the isolates of *Staphylococcus epidermidis* were moderately sensitive to amoxycillin-clavulanic acid (80%), amikacin(60%) and chloramphenicol (60%). Isolates of *Staphylococcus aureus* were found to be more sensitive to amoxycillin-clavulanic acid (77.78%) and amikacin (77.78%). 7 strains were methicillin resistant (77.78%). *Staphylococcus lugdunensis* was sensitive to ampicillin, ciprofloxacin, cefotaxime, and amoxycillin-clavulanic acid. *Enterococcus faecalis* was sensitive to amikacin, amoxycillin-clavulanic acid and high level gentamicin.(Table-19)

In a study conducted by Poonam Sharma et al, 88% of the CONS isolated were methicillin resistant. All the isolates were sensitive to vancomycin(100%) and 75% of isolates were sensitive to chlramphenicol and 70% to clindamycin. Most of the strains were resistant to other drugs.[49]

Most of the gram negative bacilli were sensitive to cefoperazone-sulbactum. *Pseudomonas aeruginosa* showed high sensitivity to amikacin,cefaperazone-sulbactum and imipenam (85.71% each). *E.coli* was 100% sensitive to amikacin and cefaperazone-sulbactum, but mostly resistant to other drugs. *Klebsiella oxytoca* was moderately sensitive to amikacin and ofloxacin (66.67%). Isolates of *Klebsiella pneumoniae* were 100% sensitive to, ofloxacin and cefaperazone-sulbactum. *Proteus vulgaris* was highly sensitive to amikacin and cefaperazone- sulbactum (100%) and moderately

sensitive to ofloxacin (66.67%). *Proteus mirabilis* was highly sensitive to cefaperazone-sulbactum (100%), but moderately sensitive to other drugs. *Acinetobacter baumanii* was highly sensitive to imipenam (100%) and moderately sensitive to amikacin and cefaperezone-sulbactum (66.67%).

Most of the strains isolated in this study were detected to be ESBL producers. ESBL production was observed in 66.67% of isolates of *Escherichia coli* and *Klebsiella oxytoca,* 50% of isolates of *Klebsiella pneumoniae* and 100% of *Proteus mirabilis*. One strain of *Pseudomonas aeruginosa* (14.29%) isolated in this study was detected to be an metallo β lactamase producer.(Table-21 &22)

Minimum inhibitory concentration of imipenam was tested for isolates of *Pseudomonas aeruginosa*. 6 isolates were interpreted to be sensitive to imipenam with MIC break points ranging from 1 μg/ml to 4 μg/ml. One isolate was resistant with MIC break point of 32 μg/ml.(Table-25)

Minimum inhibitory concentration of vancomycin tested for gram positive cocci showed all srains of *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Enterococccus faecalis* and *Staphylococcus lugdunensis* to be sensitive to vancomycin with MIC break points ranging from 0.25 μg/ml to 2 μg/ml for *Staphylococcus aureus* and 0.5 to 4 μg/ml for *CONS* and *Enterococcus faecalis*. (Table -24)

In this study, *Staphylococcus epidermidis* was the commonest organism isolated (22.73%), which showed only moderate sensitivity to drugs except vancomycin and most of these strains were isolated from pediatric patients with CSF leak or wound infection suggesting the possibility of virulent disease causing isolates than colonizing isolates. This reflects the higher skin carriage rate of resistant strains of *Staphylococcus epidermidis* from the hospital environment.

In this study, Gram negative bacilli were isolated in significant numbers. Most of them occurred in patients with bowel perforation ,peritubal collection and in those who had undergone prior revisions with external drainage procedure .

The treatment protocol of VP shunt infection in the neurosurgery department consists of removal of the infected shunt, appropriate antimicrobial therapy and reinsertion of a new shunt after a period of antibiotic therapy with some form of external drainage procedure.For those undergoing first time insertions, perioperative prophylactic antibiotics were given intravenously with ceftriaxone and amikacin.

During the study period, 2 patients with shunt infection died giving a mortality rate of 4.76 % , 1 patient was a case of post-TBM hydrocephalus and developed shunt infection following bowel perforation with many relapses and underwent 5 revision surgeries. The initial isolate was

Escherichia coli and the subsequent isolates were *Pseudomonas aeruginosa* which was a MBL producer. The other patient was a case of post traumatic hydrocephalus with sub arachnoid hemorrhage who developed shunt infection and died.

SUMMARY

- This study was done for a period of 1 year involving 397 patients of all age groups and both sexes, who underwent a total of 426 shunt related procedures. 275 patients underwent primary ventriculoperitoneal shunt insertions and 122 patients underwent shunt revisions.

- 122 patients who developed symptoms and signs of shunt malfunctions were included in the study population. Of them 101 patients underwent single revision and 21 patients underwent multiple revisions during the study period.

- 42 patients were infected giving an infection rate of 10.58%.16 patients had relapses and underwent multiple revisions.

- The study group included 59.84 % of males and 40.16% of females.

- Children accounted for 80.33% of the study population and adults accounted for 19.67 %.

- The common aetiological conditions for hydrocephalus necessitating shunt were congenital malformations(40.98%), meningitis (32.79%), intracranial mass (9.02%)and hemorrhage(7.38%.)

- The clinical features of patients with shunt malfunction included fever, vomiting, headache, seizures, altered sensorium, wound discharge and CSF leak.

- Majority of the shunt infections occurred within a period of 1 month of shunt insertion (27.87%) and most of the infection had occurred within 6 months(74.59%).

- Most of the infections occurred in children less than 1 year of age (57.14%), thus proving young age as a significant risk factor.

- The incidence of shunt infection was remarkably higher in patients with hydrocephalus due to congenital malformations (45.24%) and meningitis (26.19%).

- Abnormal biochemical parameters were observed in most of the cases with shunt infection with reduced CSF glucose levels (64.29%) and raised CSF protein levels (66.67%).

- Polymorphonuclear leukocytosis and anaemia were seen in a significant proportion of infected cases.

- Gram staining was positive in 37.04% of CSF specimens. 86% of these were culture positive.

- Altogether 44 pathogens were isolated, gram negative bacilli (52.27%) predominating over gram positive cocci (47.73%) unlike several studies.

- The commonest pathogen isolated was *Staphylococcus epidermidis* (23.73%) and the other common pathogens isolated were *Staphylococcus aureus*(20.45%) and *Pseudomonas aeruginosa* (15.91%). The less commonly isolated organism were *Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae , Proteus vulgaris, Proteus mirabilis, Acinetobacter baumanii, Enterococcus faecalis and Staphlyococcus lugdunensis* .

- Mixed infection was seen in 2 patients.

- Bacteraemia was observed in 3 cases of shunt malfunction in whom only one shunt tip/CSF was culture positive.

- Gram positive cocci were highly sensitive to vancomycin and amoxycillin-clavulanic acid and moderately sensitive to amikacin.

- Most of the gram negative bacilli were sensitive to cefaperazone-sulbactum and imipenam.

- Most of the strains of *Staphylococcus aureus* (77.78%) isolated from shunt infection were methicillin resistant.

- ESBL production was also seen in more numbers in isolates of *Escherichia coli* and *Klebsiella oxytoca* and *Proteus mirabilis.*

- MBL production was observed in one isolate of *Pseudomonas aeruginosa.*

- MIC of vancomycin for gram positive cocci was in the sensitive range for all isolates.

- MIC of imipenem for *Pseudomonas aeruginosa* for 6 isolates was in the sensitive range. 1 isolate was resistant.

- Treatment protocol followed was shunt removal, intravenous antibiotic therapy and shunt reinsertion which was done immediately in certain patients or after 1 to 2 weeks of antibiotic therapy with external ventricular drain placement as and when the conditions warranted.

CONCLUSION

- Ventriculoperitoneal shunt infection is one of the major complications associated with mortality and morbidity resulting in neurological disturbances.
- The infection rate in patients with ventriculoperitoneal shunt was 10.58%.
- A large number of infections occurred in children with congenital malformations and following meningitis.
- Most of the infections occurred within 6 months of surgery.
- CSF gram staining and biochemical parameters were very useful n identification of shunt infection enabling empirical antibiotic therapy.
- *Staphylococcus epidermidis* was the commonest pathogen isolated.
- *Pseudomonas aeruginosa* was isolated in many patients with external drainage procedures suggesting nosocomial infection.
- Promising results are obtained by early removal of the shunt hardware accompanied by appropriate antibiotic therapy until CSF culture turns negative, followed by shunt replacement.
- With the emergence of methicillin resistant strains, ESBL and MBL producers, diligent use of antibiotics will restrict the spread of drug resistant strains in the community and environment.

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ABBREVIATIONS

CLSI	-	Clinical & Laboratory Standards Institute
CONS	-	Coagulase Negative Staphylococci
DDST	-	Double disk diffusion synergy test
ESBL	-	Extended Spectrum β Lactamases
GNB	-	Gram-negative bacilli
GPC	-	Gram-positive cocci
MBL	-	Metallo β Lactamases
MIC	-	Minimum Inhibitory Concentration
MRSA	-	Methicillin Resistant *Staphylococcus aureus*
S. aureus	-	*Staphylococcus aureus*
S. epidermidis	-	*Staphylococcus epidermidis*
E.coli	-	*Escherichia coli*
P.aeruginosa	-	*Pseudomonas aeruginosa*
CSF	-	Cerebrospinal Fluid
VP Shunt	-	Ventriculoperitoneal shunts

APPENDIX

A. STAINS AND REAGENTS

Gram staining

Methyl violet (2%)	l0g
Absolute alcohol	100 ml
Distilled water (primary stain)	1 litres
Grams Iodine	10g
Potassium Iodide	20g
Acetone Decolourising agent	
Carbol fuchsin 1% Secondary stain	

B. MEDIA USED

1. Mac Conkey agar

Peptone	20g
Sodium taurocholate	5g
Distilled Water	1 ltr
Agar	20g
2% neutral red in 50% ethanol	3.5ml
10% lactose solution	l00mI

Dissolve peptone and taurocholate in water by heating. Add agar and dissolve it in steamer. Adjust pH to 7.5. Add lactose and neutral red shake well and mix. Heat in free steam (100°C) for 1 hour, then autoclave at 115°C for 15 minutes.

2. Blood agar (5% sheep blood agar)

Peptone	l0g
NaCl	5g
Distilled water	1 Ltr
Agar	10g

Dissolve ingredients in distilled water by boiling, and add 5% sheep blood(sterile) at 55°C, adjust pH to 7.4.

3. Chocolate agar

Sterile defibrinated blood	10 ml
Nutrient Agar (melted)	100 ml

When the temperature was about 75°C, sterile blood was added with constant agitation. After addition of blood, kept in water bath and heating was continued till the blood changed to chocolate colour. Cooled to about 50° C and about 15ml poured into petri dishes with sterile precaution.

4. Mueller- Hinton Agar

Beef infusion	300ml
Caesein hydrolysate	17.5g
Starch	1.5g
Agar	10g
Distilled water	1ltr
pH	7.4
Sterilise by autoclaving at 121ºC for	20 mins

5. Brain-heart infusion broth

Calf brain infusion	200 g/l
Beef heart infusion	250g/l
Proteose peptone	10g/l
Dextrose	2g
NaCl	5g/l
Disodium phosphate	2.5g/l

Suspend 37 g in 1000 ml of distilled water and boil to dissolve the medium completely. Dispense as desired and sterilize by autoclaving at 15 lbs pressure(121^{o}C) for 15 minutes.

C. MEDIA REQUIRED FOR BIOCHEMICAL IDENTIFICATION

1. Oxidase Reagent

Tetra methyl p-phenylene diamine dihyrochloride- 1% aqueous solution.

2. **Catalase**

3% hydrogen peroxide

3. Indole test

Kovac's reagent

Amyl or isoamyl alcohol	150ml
Para dimethyl amino benzaldehyde	10g
Concentrated hydrochloric acid	50ml

Dissolve the aldehyde in the alcohol and slowly add the acid. Prepare in small quantities and store in the refrigerator. Shake gently before use.

4. Christensen's Urease test medium

Peptone	1g
Sodium chloride	5g
Dipotassium hydrogen phosphate	2g
Phenol red	6ml
Agar	20g
Distilled water	1 ltr
10% sterile solution of glucose	l0ml
Sterile 20% urea solution	l00ml

Sterilize the glucose and urea solutions by filtration. Prepare the basal medium without glucose and urea, adjust to pH 6.8-6.9 and sterilize by autoclaving in a flask at 121°C for 30min. Cool to about 50°C, add the glucose & urea, and tube the medium as slopes.

5. Simmon's Citrate Medium

Koser's medium	1 ltr
Agar	20g
Bromothymol blue 0.2%	40ml

Dispense, autoclave at 121°C for 15 min and allow to set as slopes

6. Triple Sugar Iron medium

Beef extract	3g
Yeast extract	3g
Peptone	20g
Glucose	1g
Lactose	l0g
Sucrose	l0g
Ferric citrate	0.3g
Sodium chloride	5g
Sodum thiosulphate	0.3g
Agar	12g
Phenol red 0.2% solution	l2ml
Distilled water	1 ltr

Heat to dissolve the solids, add the indicator solution, mix and tube. Sterilize at 121°C for 15 min and cool to form slopes with deep butts.

7. Glucose phosphate broth

Peptone	5g
Dipotassium hydrogen phosphate	5g
Water	1 ltr
Glucose 10% solution	50ml

Dissolve the peptone and phosphate and adjust the pH to 7.6. Filter, dispense in 5ml amounts and sterilize at 121°C for 15min. Sterilize the glucose solution by filtration and add 0.25ml to each tube.

Methyl Red Reagent

Methyl Red	10mg
Ethyl alcohol	30ml
Distilled water	20ml

Voges Proskauer Reagent

Reagent A:	Alpha naphthol	5g
	Ethyl alcohol	100ml
Reagent B:	Potassium hydroxide	40g
	Distilled water	100ml

8. Peptone water fermentation test medium.

To the basal medium of peptone water, add sterilised sugars of 1% with indicator bromothymol blue with Durham's tube.

Basal medium peptone water

Sugar solutions:

Sugar	1ml
Distilled water	l00ml
pH	7.6.

9. Mannitol motility medium

Agar	5g
Peptone	1g
Potassium nitrate	1g
Mannitol	2g
Phenol red indicator	
Distilled water	l000ml
pH	7.2

10. Phenolphthalein diphosphate agar

- Sterilize a 1% aqueous solution of sodium phenolphthalein diphosphate by filtration and store at 4ºC
- Add 10ml of this solution to 1000ml melted nutrient agar cooled to 50ºC and pour plates
- Grow the staphylococcus overnight at 37ºC on the medium
- Invert the plate and pour a few drops of ammonia solution SG 0.88 into the lid
- Read as positive a culture whose colonies turn bright pink within a few minutes. The colour soon fades.

11. Potassium nitrate broth

Potassium nitrate (KN03)	0.2gm
Peptone	5.0gm
Distilled water	100ml

The above ingredients were mixed and transferred into tubes in 5 ml amount and autoclaved.

12. Phenyl alanine deaminase test

Yeast Extract	3g
Dl-Phenylalamine	2 g
Disodium hydrogen phosphate	l g
Sodium Chloride	5 g
Agar	12g
Distilled water	1 lr
pH	7.4

Distributed in tubes and sterilized by autoclaving at 121° C for 15 minutes, allowed to solidify as long slopes.

13. Sugar fermentation medium

Peptone	15g
Andrade’s indicator	10 ml
Sugar to be tested	20g
Water	1litre

Andrade’s indicator is prepared from 0.5% aqueous acid fuchsin to which sufficient 1M sodium hydroxide has been added to turn the colour of the solution yellow.

Dissolve the peptone and Andrade’s indicator in 1litre of water and add 20g of the sugar; sugars to be tested generally include glucose, sucrose, lactose and maltose. Distribute 3ml amounts in standard test tubes containing an inverted Durham tube. Sterilize by steaming at 100 degree C for 30 min on 3 consecutive days.

PROFORMA

Name: OP/IP No.

Age: Ward:

Sex: Address:

Occupation:

Presenting Complaints:

Risk Factors:

- Age of Onset of illness
- Etiology of Hydrocephalus
- Previous Shunt infection
- Previous Shunt procedures

Physical Examination:

- Temperature
- Pulse Rate

- Blood Pressure
- Respiratory Rate
- Head Circumference

Systemic examination:

- CNS- Consciousness and Orientation

    -Gait

    -Neck Stiffness

    -Fontanelles (in infants)

    -Cranial Nerves

    -Motor System

    -Sensory System

- CVS
- RS
- P/A-Shape-Distension

    -Movements of abdominal wall

    -Tenderness / Rigidity

    -Dullness / Fluid thrill

    -Bowel sounds

Laboratory Evaluation:

- Haemoglobin
- TC,DC,ESR
- Blood Urea and Sugar
- Serum Creatinine and electrolytes
- Urine routine
- Wound Swab
- CSF analysis

  -Cytology

  -Protein

  -Glucose

  -Gram stain

  -Culture

- USG Abdomen
- CT Brain