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Main Pathogens in Infection of Different CSF Diversion Techniques in Abo El-Resh Population

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Abstract

Background: CSF diversion devices' infection is one of the crucial complications faced in paediatric patients with hydrocephalus, whether communicating or non-communicating. Yet, it can be prevented mostly by precautious preoperative preparations, intraoperative meticulous sterilization, and intensive sterile post-operative wound care. In this study, we are evaluating postoperative CSF devices' infection according to the clinical presentation, CSF analysis and culture results to apply different management strategies for various situations and the efficacy of these plans to control shunt infection in paediatric age group.

Aim of Study: Detection of the main pathogens in CSF infection in different CSF diversion techniques. together with detection of sensitivity patterns among Pathogens. And to set the Most preferable empirical drug used in patients with CSF diversion devices infection in Abo El Reesh Hospital.

Patients and Methods: 147 paediatric patients with age group up to 13 years old were studied at Abo El Reesh Hospital, Cairo University Kasr Al-Ainy who had a history of applied different CSF diversion techniques presenting with symptoms and signs suggestive of CSF infection over the duration period of 12 months between April 2019 and April 2020. 68 patients had initial VP shunts applied in Abo El Reesh and 5 EVDs post tumour resection, the rest of the patients had initial VP shunts applied in other hospitals and were referred for further management of CSF infection. We reviewed the clinical presentation and diagnostic criteria and management strategies used to treat the patients.

Results: In 147 paediatric patients with previously inserted CSF diversion device, with a median age of 1.5 years. 81 patients had no culture growth, while 66 patients resulted in 70 culture growth with the most common pathogen was klebsiella followed by CoNs. 83% of the patients improved, 12.24% improved with neurological deficit, and 4.76% died. Patients who were treated by conservative management had the highest improvement rate.

Conclusion: Proper management strategy includes preoperative preparation, intraoperative precautions and early diagnostic evaluation considering CSF analysis, clinical presentation, and general condition to achieve reduction of CSF diversion devices' infection.

Key Words: *CSF diversion devices – CSF infection – CSF analysis.*

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Introduction

THE complications of shunts are divided into: Mechanical complications and infective complications.

1- Mechanical complications: It includes under-shunting (obstruction, disconnection, or migration of any components of a shunt system either at the ventricular or peritoneal end.), over shunting (ventricular collapse and slit ventricles, subdural collection, spinal headache), bleeding from subcutaneous vessels or leak from the puncture site **[1].**

2- Infective complications: It includes shunt tract abscess that is diagnosed by CT brain scan with contrast or MRI brain with contrast that can also spread locally of disseminate systemically. The patients may be presented clinically by nonspecific symptoms like as fever, irritability, headache, skin necrosis. Other complications include inflammation overlying the shunt device and most importantly ventriculitis which is the inflammation of the ventricular system of presented with headache, vomiting, fever, decreased conscious level. It is diagnosed by (CT or MRI brain with contrast) accompanied with CSF analysis and CSF C&S. These patients can develop loculated hydrocephalus that can be treated by endoscopic fenestration after resolution of infection **[2].**

3- Other complications: They are seizures, craniosynostosis, microcephaly or skull deformi-

ties, inguinal hernia and hydrocele, ascites, pseudocyst formation, malposition of catheter tip either at time of surgery as in preperitoneal fat or may pull out of peritoneal cavity with growth [3], perforation of a viscus or Its infection either due to bacteraemia all through the blood stream to central nervous system (CNS) or direct invasion of the CNS through dural defects or local infection spread [4]. The choroid plexus may be a site of invasion of bacteria but it's still with a few evidence. Other bacteria were found in the meninges or infiltrating the leptomeningeal blood vessels in meningitis. These data suggest that several highly vascularized sites are potential entry locations. To cross the blood brain barrier pathogens must carry effective molecular tools [4]. Some pathogenic proteins conjugate with receptors on the eukaryotic cells and promote endocytosis to crossing the blood brain barrier while others adhesive proteins allowing them to invade the CNS. The certain pathways for each pathogen to activate and invade the cells are specific for each and needs to be studied to allow blockage of their interaction and disease progression [4]. Inflammatory response: Inflammatory activation of endothelial cells by pathogenic invasion regulates the adhesion of certain molecules as ICAM-1 which promote the leukocyte invasion, especially granulocytes in the CSF, are the diagnostic hallmark of meningitis [4]. Early inflammatory response and bacterial invasion seem to progress in parallel and products of activated leukocytes which contribute to early damage of the blood brain barrier. Once bacteria have entered the subarachnoid space, they replicate, undergo autolysis, and cause further inflammation [4]. Heat killed bacteria and pathogen-associated molecular patterns (PAMP) of pathogens as lipoprotein (LP) and lipopolysaccharide (LPS) cause meningitis indistinguishable from living bacteria leading to multiple inflammatory signal cascades and rapid inflammatory response causing meningitis [4]. Neuronal damage: Up to 50% of survivors of bacterial meningitis suffer from neurological deficits. The hippocampus seems to be the most targeted area of the brain with an unclear predisposition. CSF diffusion from the extracellular fluid to the ventricular delivers soluble bacterial and inflammatory toxic mediators causing ventriculitis [4]. Neuronal damage in meningitis is clearly multi-factorial, involving bacterial toxins that may cause cytolysis neurons and microglia by inducing rapid mitochondrial damage, cytotoxic products of immune competent cells, and indirect pathology secondary to intracranial complications. In insufficiently treated patients or resistant bacteria toxic activity may be significantly prolonged and harm neuronal functions [4].

Material and Methods

This descriptive, cross-sectional study was conducted on 147 paediatric patients with age group up to 13 years old were studied at Abo El Reesh Hospital, Cairo University Kasr Al Ainy who had a history of applied different CSF diversion techniques presenting with symptoms and signs suggestive of CSF infection over the duration period of 12 months between April 2019 and April 2020. 68 patients had initial VP shunts applied in Abo El Reesh and 5 EVDs post tumour resection, the rest of the patients had initial VP shunts applied in other hospitals and were referred for further management of CSF infection. All data were collected from the patients' files at the outpatient clinic or after admission to wards, after the permission and explanation of the procedure of obtaining CSF samples and its outcome prior the investigation and data collection. This study was carried out in accordance with the guidelines approved from the ethical committee prior to this study conduction.

Inclusion criteria:

Paediatric patients under the age of 13 years old, who initially underwent VP shunt application in Abo El Reesh Hospital or patients with initial VP shunt application in other hospitals referred to our department for further management of infection 2. Patients presented to us either at outpatient clinic or admitted in ward. 3. Patients with all types of CSF diversion techniques including all types of shunts and applied de novo EVDs post tumour resection. 4. Clinical presentation, CSF analysis related to CSF infection. Patients and Methods 59

Exclusion criteria:

Patients above the age of 13 years old. 2. Similar clinical presentations with no prior CSF diversion technique application.

All Patients included in this study were subjected to the following:

Clinical assessment:

1. History taking: (age, complaints, surgical history including the type of CSF diversion and its site and course, history of fever, convulsions, vomiting, abdominal pain, and any associated medical history). 2. General assessment: Including Temperature, vital signs, routine labs, abdominal examination. 3. Neurosurgical assessment: (conscious level stretch signs of meningism, shunt reservoir function, CSF tapping and CSF analysis, local device tract examination and other further investigations).

Investigations:

Specific CSF microbiology and analysis (e.g. Total leukocytic count, protein in CSF, glucose in CSF and culture/sensitivity).

Management plan:

It had been classified into 2 plans either: Conservative management or surgical management with antibiotic administration according to the following criteria: The CSF diversion device applied. Clinical examination for the patient as in conscious level

state, vomiting, fever, or shunt tract complication. CSF microbiology analysis especially TLC and Protein count along with the growth/no growth results of cultures taken. According to those criteria along with the patient's guardian's will and consent to perform any surgical procedure or even for any medical treatment introduction.

The diagnosis of different CSF diversion devices infection will be based on clinical presentation and CSF microbiology analysis. CSF samples obtained will be analysed accordingly by CSF Total Leukocytic Cell count (TLC), PMNLs that are normally not present in CSF samples, their presence indicates inflammation and bacterial infections. Lymphocytes have a normal range less than 20 cells; a higher percentage may reflect the presence of viral infection as viral meningitis or autoimmune diseases, CSF protein level that has a normal range of 15 mg/dl till age of 2 years old and up to 25 mg/dl till age of 15 years old, CSF glucose level, and culture and sensitivity by gram stain and microscopic examination. • All CSF samples obtained with TLC more than 20 will be cultured to obtain antibiotic sensitivity accordingly. • Empirical antibiotics can be given after tapping CSF sample until results are available. • After culture and sensitivity results are handled out, specific antibiotics will be prescribed according to the sensitivity. Antibiotics can be administrated either parenterally or intraventricular through an EVD. • All procedures are to be held in the Neurosurgery departments, Emergency department and outpatient clinic in Abo El Reesh Hospital, Cairo University Kasr Al Ainy.

Study outcomes:

1- Primary outcomes: Detection of the main pathogens in CSF infection in different CSF diversion techniques.

2- Secondary outcomes: 1. Detection of sensitivity patterns among Pathogens. 2. Most preferable empirical drug used in patients with CSF diversion devices infection. 3. Building CSF registry in Abo El Reesh.

Management plan for the studies 147 patients: A. Conservative management: Patients who underwent conservative management. Patients who had either mild symptoms, no hydrocephalic changes or DCL, with TLC less than 150, received parenteral medical treatment, either according to culture and sensitivity results or empirically in negative cultures according to the rest of CSF analysis and CT inflammation findings. Medical treatment is continued for 2 weeks, followed by a new CSF sample analysis with improvement of symptoms and TLC is less than 25. Surgical management: Patients who underwent surgical intervention combined with medical treatment. Patients who had moderate to severe clinical symptoms including high TLC >150, high CSF protein level, DCL and hydrocephalic changes, with or without any other signs of shunt tract inflammation or signs of meningism. Patients with VP shunts underwent shunt removal, application of EVD, and patients with tumour removal initially applied EVDs, both received administration of either parenteral medical treatment or Intraventricular injection through the applied EVD, either empirically or culture based, in patients with closed head or shunt removal and parenteral medical treatment in patients with opened head. Medical treatment is continued for 10 to 14 days, and a new sample is drawn to analyse the improvement of infection, or if treatment modification is needed. After improvement of all clinical conditions, with resolving symptoms, 3 successful CSF samples are drawn each with 2 days apart for all CSF parameters follow up, where CSF sample is found clear, and CSF TLC is less than 30. EVD is removed and a new shunt is applied in a new site. This management plan also includes Patients with failed conservative management who developed further clinical deterioration, increased CSF TLC count more than 150, or had persistent CSF culture growth in successive culture samples.

Results

The study was conducted on 147 paediatric patients less than 13 years old with different CSF diversion techniques over the duration period of 12 months between April 2019 and April 2020 with clinical presentation, signs, and investigation results of CSF infection. 68 patients had initial VP shunts applied in Abo El Reesh and 5 EVDs post tumour resection, the rest of the patients had initial VP shunts applied in other hospitals and were referred for further management of CSF infection.

Demographic data:

A- *Sex distribution of CSF diversion techniques infection:*

Out of 147 patients, 84 male patients were presented with infection and that's a total percentage of 57.1% more than female patients who represented 63 from the total number of patients with a total percentage of 42.9% (Fig. 1).

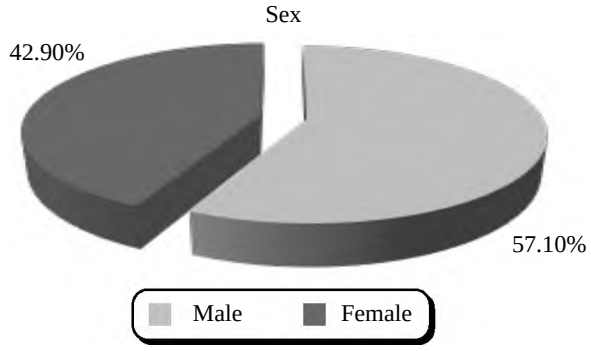

Fig. (1): Percentage of patients regarding sex distribution.

B- *Age distribution of patients presented with shunt infection:*

The age distribution of patients with CSF diversion techniques infection was between a minimum of 1 month and maximum of 13 years old with a mean (±) SD is 2.55 (±) 3.03 and median value of 1.50. Maximum number of patients studied were in the age group under the age of 1 year (66 patients), followed by patients aged from 1 year of age till 6 years (64 patients), and finally patients aged more than 6 years old till 13 years old (17 patients). Table (1) showing the statistical values representing age distribution.

Table (1): Statistical values representing age distribution.

	Mean	Standard Deviation	Median	Minimum	Maximum
Age in years	2.55	3.03	1.50	0.08	13.00

Indications for initial CSF diversion device insertion:

The most common indication for initial CSF diversion technique insertion was congenital hydrocephalus followed by tumour excision (Table 2).

Table (2): Percentage for each indication for initial CSF diversion device insertion.

Congenital Malformations	137	93.2%
Post traumatic	1	0.7%
Tumours	9	6.1%

CSF diversion techniques used:

The most initially applied devices were VP shunts with a total number of 142 patients (96.6%) and EVDs post tumour resection with total number of 5 patients (3.4%) in this study as shown in Table (3).

Table (3): Percentage and number of CSF diversion devices used.

	Count	%
Device:		
VP shunt	142	96.6
EVD	5	3.4

Clinical presentation:

Regarding the 147 cases, the most presenting symptom in patient with CSF shunt infection was fever and vomiting the highest 2 symptoms where 129 patients of 147 (87.7%) each, while disturbed conscious level (DCL) was 57 patients (38.8%), abdominal pain in 37 patients (25.5%), convulsions in 29 patients (19.7%) and other shunt tract complications as rigid tracts and inflammations in 19 patients (12.9%) as shown in Fig. (2).

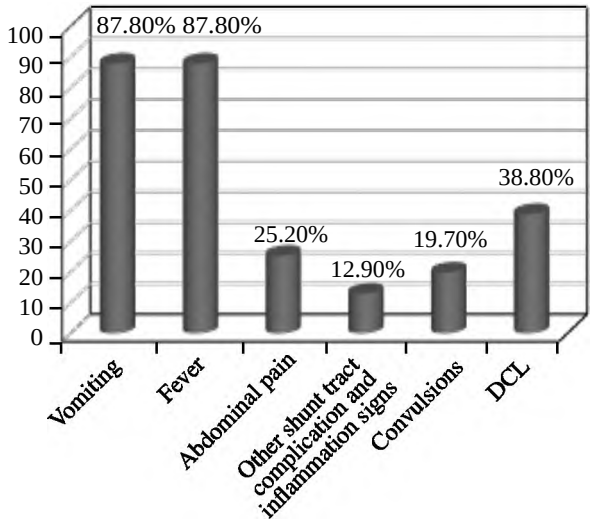

Fig. (2): Percentage for each clinical presentation.

Laboratory findings in CSF analysis:

This includes CSF TLC, including PMNLs percentage and Lymphocytes percentage, CSF protein, CSF glucose.

1- *CSF Total Leucocytic count (TLC):* Regarding the rest of CSF samples analysis shown in table 9, we studied patients with TLC more than 20 cells/ mm^3 CSF TLC mean (±) SD for the total number of cases studied is 800.91 (±) 1774.55, with minimum value of 20 and maximum value of 10000.

2- *CSF Polymorphonuclear leukocytes (PMNLs) and Lymphocytes percentages:* In our study, a total percentage of PMNLs % and lymphocytes % have a mean (±) SD value of 50.63 (±) 37.49 and 19.82 (±) 21.79 respectively, with minimum value of 0 for both and maximum value of 98 and 90 respectively.

3- *CSF protein and glucose:* In our study, CSF protein median was 150 with minimum range of 6.3 and maximum range of 4279. Glucose median was 36 with minimum of 0 and maximum of 119 as shown in Table (4).

Table (4): Total CSF analysis components count's statistical values.

	Mean	Standard Deviation	Median	Minimum	Maximum
TLC	800.91	1774.55	140.00	20.00	10000.00
PMNLs %	50.63	37.49	70.00	0.00	98.00
Lymph %	19.82	21.79	20.00	0.00	90.00
CSF Glucose	41.10	21.73	36.00	0.00	119.00
CSF Protein	379.07	632.00	150.00	6.30	4279.00

CSF culture and sensitivity results in 147 patients with clinicalsuspicion of CSF diversion techniques infection:

CSF Culture growth and sensitivity results were positive in 66 patients with 70 pathogens documented in culture and sensitivity (44.9%) and negative in 81 patients (55.1%) (Fig. 3).

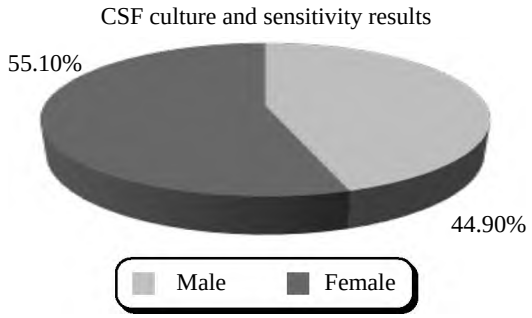

Fig. (3): CSF Culture growth and sensitivity results.

Table (5): Pathogens growth in CSF samples obtained from 147 patients' CSF devices.

Culture results	Count	%
CoNs	13	8.8
Klebsiella	16	10.9
Acinetobacter	2	1.4
Enterobacter	2	1.4
Pseudomonas Aeruginosa	8	5.4
MRSA	11	7.5
E. coli	1	0.7
Other bacteria	3	2.0
Other bacteria details:		
Sternotrophomonas	1	0.7
Gram negative bacilli	1	0.7
Alpha haemolytic streptococci	1	0.7
Fungal (CSF Culture):		
Candida tropicalis	1	0.7
Candida non albicans	2	1.4
Candida albicans	3	2.0
Combined cultures:		
Klebsiella and Acinetobacter	1	0.7
Klebsiella and E. coli	1	0.7
CoNs and E. coli	1	0.7
MRSA and Pseudomonas	1	0.7

Table (6): Total number of growth vs no growth of pathogens in both CSF diversion devices.

	Device				*p*-value
	VP shunt		EVD		
	Count	%	Count	%	
CSF Culture:					
Growth	63	39.7	3	69.2	0.006
No growth	79	60.3	2	30.8	

The most common organisms of CSF devices infection:

All 66 patients' positive culture results included only one pathogen growth, except for 4 patients, that were positive to 2 strains of pathogens.

The highest prevalence of CSF infection pathogens was Klebsiella grown in 16 patients (10.9%) (15 VP shunts and 1 EVD), the second most common pathogen growth was Coagulase negative staphylococci (CoNs) in 13 patients and (8.8%), the third most common pathogen growth was Methicillin-resistant Staphylococcus aureus (MRSA) in 11 patients (7.5%) (10 VP shunts and 1 EVD) and the fourth most common pathogen growth was Pseudomonas aeruginosa in 8 patients (5.4%). The fifth most common pathogen growth was Candida fungal species with a total of 6 patients (4.1%), 3 Candida albicans, 2 Candida nonalbicans and 1 Candida Tropicalis. The sixth and seventh pathogen growth were 2 patients (1.4%) had Enterobacter growth and 2 patients had Acinetobacter growth (1.4%) (1 VP shunt and 1 EVD). The eighth and ninth pathogen growth were in E. coli in 1 patient (0.68%) and other pathogens growth in 3 samples with a total 2% (all were cultured from VP shunts), specified as Strenotrophomonous, Gram negative bacilli and alpha haemolytic streptococci [1 sample each (0.7%)]. 4 patients had combined culture results of Klebsiella and Acinetobacter, Klebsiella and E. coli, CoNs and E. coli, and MRSA and Pseudomonas aeruginosa. The negative cultures resulted in 81 patients, while positive cultures resulted in 66 patients which is statistically significant with *p*-value = 0.006 (Tables 5,6).

Antibiotics sensitivity against most common pathogens:

Regarding the studied pathogens' growth, antibiotics were used according to the culture and sensitivity results.

1- Klebsiella: The most sensitive antibiotics were Imipenem in 12 cultures, Meropenem in 10 cultures, followed by Amikacin in 9 cultures, Ciprofloxacin, and Levofloxacin in 7 cultures each, Polymyxin B in 7 cultures and Colistin in 5 cultures. Amikacin had the best outcomes followed by Polymyxin B.

2- Coagulase negative staph. (CoNS): The most sensitive antibiotics were Vancomycin in 12 cultures, followed by Ciprofloxacin in 11 cultures, Amikacin in 10 cultures, Levofloxacin in 10 cultures, Linezolid in 9 cultures and Doxycycline in 8 cultures. Vancomycin had the best outcomes followed by Levofloxacin.

3- Methicillin-resistant Staphylococcus aureus (MRSA): The most sensitive antibiotics were Vancomycin in 12 cultures, ciprofloxacin in 9 cultures, Amikacin, and levofloxacin in 7 cultures each, Erythromycin in 6 cultures and Linezolid in 5 cultures.

4- Pseudomonas aeruginosa: The most sensitive antibiotics were Amikacin in 6 cultures, followed by Ciprofloxacin in 5 cultures, Levofloxacin in 4 cultures and Imipenem and Meropenem in 3 cultures each.

5- Fungal Infections: The most sensitive antibiotics were Amphotericin B in 3 cultures, followed by Polymyxin B in 2 cultures and Nystatin and ketoconazole in 1 culture each.

6- Acinetobacter: The most sensitive antibiotics were Polymyxin B, Imipenem and Meropenem in 2 cultures each and Tigecycline in 1 culture.

7- E. coli: The most sensitive antibiotics were Amikacin in 3 cultures, followed by. Ciprofloxacin, Imipenem and meropenem in 2 cultures each. The following Table (7) showing the most sensitive Antibiotics regarding all samples with E. coli and their *p*-values with their statistical significance in comparison to their sensitivity to other pathogens studied.

8- Enterobacter: The most sensitive antibiotics were Polymyxin B, Imipenem, Meropenem, colistin and Ofloxacin each found in 1 culture.

9- Other Pathogens detected: In cases of VP shunted patients, 3 other types of pathogens were detected Gram negative bacilli, Stenotrophomonas, Alpha haemolytic streptococci. The most sensitive antibiotics were amikacin in all 3 cultures, sulbactam in 2 cultures and cefuroxime, cefotaxime, ceftazidime, and gentamycin in 1 culture with statistical significance in comparison to their sensitivity to other pathogens studied.

10- No growth: They represent a total number of 81 patients from the 147 patients studied (55.10%), 79 VP shunted patients (97.5%) and 2 patients with EVD applied (2.5%).

Empirical parenteral antibiotics were used, alone or combined, as a part of treatment of no growth cultures according to the rest of the CSF analysis with TLC less than 150 and CSF protein that exceeded 25mg/dl (normal range) with signs of inflammation, mild clinical symptoms or rejection of surgical intervention by the guardians.

Management plan of the studies 147 patients:

This planwas set according to the Device applied, patient's clinical condition, culture and sensitivity based or imperially according to the rest on CSF analysis results.

A- *Conservative management:*

75 patients were treated by conservative management by parenteral antibiotics only. 53 patients improved with no neurological deficits (70.7%) while 22 patients (29.3%) clinical and laboratory examinations were not improving and needed further management by surgical intervention combined with antibiotic administration.

B- *Surgical intervention combined with antibiotics:*

94 patients were treated by surgical management combined with antibiotics. 72 patients were initially treated by this management, 67 patients were treated by shunt removal and application of EVD (71.3%), 5 patients initially applied EVDs post tumour resection (7.8%) and 22 patients (23.4%) had failed conservative treatment and needed further surgical intervention and antibiotic administration.

Table (7): The plans of management and their percentage regarding the studied group.

Plan of management	Number of patients	Percentage
Surgical	94	63.95
Conservative	75	51.02

Outcome: Most of the patients who underwent CSF culture and sensitivity with negative culture results with associated mild clinical condition underwent conservative management (81.3%), while patients with positive culture results had a higher incidence to surgical management combined with medical treatment (70.8%) with *p*-value <0.001 as shown in Table (8). 9 patients from whose who underwent conservative management didn't improve with persistent infection and needed further surgical management.

Table (8): The relation between culture results and plan of treatment.

	Surgical with medical treatment		Conservative		*p*-value
	N	%	N	%	
Sternotrophomonas	1	100	0	0.0	<0.001
Pseudomonas aeruginosa	7	87.5	2	25	
MRSA	11	100	2	18.1	
Acinetobacter	2	100	1	50	
Klebsiella	15	93.75	4	25	
E. coli	1	100	0	0.0	
Gram negative bacilli	1	100	1	100	
Enterobacter	2	100	0	0.0	
CoNs	10	76.92	3	23.08	
Candida tropicalis	1	100	0	0.0	
Candida non albicans	2	100	0	0.0	
Candida albicans	3	100	0	0.0	
Alpha haemolytic streptococci	1	100	0	0.0	
No growth	31	38.27	63	77.8	
Combined culture	4	100	0	0.0	

Outcome of CSF devices infection according to each management plan:

The outcome is classified into 3 groups:

1- Patients who improved after parental treatment, intraventricular injection, surgical intervention, or combined forms with no neurological deficit.
2- Patients who improved but with neurological deficit, such as brain atrophy, convulsions, motor, sensory or cranial nerve affection.
3- Dead.

The relation between management plan and outcome groups:

a- Conservative management: 71 patients improved with no neurological deficits (94.7%) and 4 patients improved with neurological deficits (5.3%). The incidence of improvement with no neurological deficit is statistically significant with *p*-value <0.001.
b- Surgical intervention combined with antibiotics: 69 patients improved with no neurological deficits (73.4%), 18 patients improved with neurological deficits (19.15%) and 7 patients died (7.45%). The incidence of death and improvement with neurological deficit is statistically significant with *p*-value 0.018 and <0.001 respectively. (Table 9).

Table (9): Relation between outcome and management plans.

Outcome	Management plans		*p*-value
	Conservative	Surgical intervention + antibiotics	
Improved	94.7%	73.4%	<0.001
Improved with neurological deficit	5.3%	19.15%	
Dead	0.0%	7.45%	0.018

The relation between Morbidity/Mortality rate and Culture results:

Regarding the studied cultures in 147 patients, 7 patients (4.76%) died. with CSF devices' infection, Klebsiella had total number of 3 deaths, followed by MRSA with 2 deaths, 1 patient with combined culture result of MRSA and pseudomonas aeruginosa and 1 patient with fungal infection (candida albicans). No deaths were recorded in the rest of studied pathogens or patients with no culture growth. Regarding Morbidity rate, 18 patients recovered with neurological deficits, 7 patients had negative culture results with high CSF TLC and protein levels. 9 patients had positive culture results, 3 had Fungal infections, 3 patients were infected with klebsiella, 2 were infected with CoNs, and 3 patients were infected with MRSA, Pseudomonas aeruginosa, and Enterobacter respectively.

The relation between Mortality rate and Managementplan:

All dead patients and 18 patients (including 4 patients who failed conservative management) who improved with neurological deficit were managed by surgical intervention combined with antibiotics administration.

Discussion

VP shunt placement is one of the most performed neurosurgical procedures and is necessary to treat most forms of hydrocephalus. Unfortunately, complications related to their application are common, and multiple shunt revisions are almost expected throughout a patient's lifetime. Infection considered one of the most common causes of shunt malfunction, with a considerable variation worldwide resulting in increased morbidity and mortality levels with the majority acquired intra-operative or in the postoperative period **[5].**

This descriptive, cross-sectional study was conducted on 147 paediatric patients with age group up to 13 years old, at Abo El Reesh Hospital, Kasr Al Ainy, Cairo University (outpatient clinic or after admission) who had a history of applied different CSF diversion techniques presenting with symptoms and signs suggestive of CSF infection over the duration period of 12 months between April 2019 and April 2020. 68 patients had initial VP shunts applied in Abo El Reesh and 5 EVDs post tumour resection, the rest of the patients had initial VP shunts applied in other hospitals and were referred for further management of CSF infection. Specific CSF analysis including microbiology to detect the main pathogen causing the infection.

Although the risk factors for shunt infection is unclear, it's believed that age and sex may have a prevalence regarding the rate of infection. Regarding the sex distribution in our conducted study, males were the dominant gender with a total percentage of 57.1% compared to females with a total percentage of 42.9%. Ebrahim et al. **[5],** Gündeşlioğlu et al. **[6]**, and Yakut et al. **[7]** were in favour with male predominance with percentages higher than 55%. In the study conducted by Gulsen et al. **[8],** females were predominant with 52%.

In our study, the incidence of shunt infections is significantly higher in patients aged under the age of 1 year old (44.9%) followed by the age group less than 1 year old (43.5%) and the age group from 6 to 13 years old (11.6%) with median age of 1.5 years. Ebrahim et al. **[5]**, and Gündeşlioğlu et al. **[6],** were in favour with our results with the most infection incidence between the age of 1 to 6 months.

Many studies have shown that certain aetiological factors of hydrocephalus may be associated with the increased rates of CSF diversion devices' infections. Regarding our study, the most common indi-

cation for initial CSF diversion technique insertion was congenital malformations (including congenital hydrocephalus and meningoceles) with 93.2%, followed by tumors (mostly post posterior fossa tumour excision) with 6.1%, and post traumatic with 0.7%. The most initially applied devices were VP shunts (96.6%) and EVD (applied initially in cases with post tumour excision) (3.4%).

Ebrahim et al. *[5]*, Gündeşlioğlu et al. *[6]*, Yakut et al. *[7]*, and Gulsen et al. *[8]*, findings regarding the most initial cause for shunt application were in favour with our study where congenital malformations (including congenital hydrocephalus and meningoceles) represented the majority. Regarding Ebrahim et al. *[5]*, congenital malformations representing 83.4%, followed by post traumatic hydrocephalus with 13.3%, and post meningitic hydrocephalus in 3.3%. Regarding Gündeşlioğlu et al. *[7]*, congenital malformations represented 60.6%, followed by intracranial haemorrhage of prematurity with 33.3%, 3% with tumours and 3% of an unknown cause. Regarding Yakut et al. *[7]*, congenital malformations represented 65.5%, followed by tumours with 12.4%, post infection hydrocephalus with 12.2%, intracranial haemorrhage with 7.9% and post traumatic hydrocephalus with 2.1%. Regarding Gulsen et al. *[8]*. All patients presented with communicating hydrocephalus. All the previously mentioned studies were conducted upon patients with initially applied VP shunts.

As for the clinical manifestations in our study, most patients with shunt infections present with nonspecific clinical picture as vomiting and fever with 87.7% each. Presentation with more specific symptoms, as disturbance in conscious level, signs of meningism, convulsions, or device tract related complications and inflammations were found with lower percentages: 38.8%, 19.7%, and 12.9% respectively. Gündeşlioğlu et al. *[6]*, and Yakut et al. *[7]* showed the same highest prevalence for fever and vomiting as the main clinical presentation as our study. Ebrahim et al. *[5]*, the most common clinical presentations were fever and vomiting with 46.7% and 43.3% respectively, followed by signs of inflammation (including wound infection, exposed reservoirs) with 33.3%. Regarding Gündeşlioğlu et al. *[6]*, the most common presentation was vomiting with 66.7%, anorexia with 57.6%, fever with 51.5% and head circumference growth in 39.4%. Regarding Yakut et al. *[7]*, fever was the most common presentation in 37.2%, followed by its combination with vomiting in 30% of the cases and its combination with signs of meningism in 10.6% of the cases. The laboratory CSF analysis is crucial regarding the decision making for diagnosis, treatment and follow-up from CSF chemistry analysis up to CSF culture and sensitivity. In our study, CSF chemistry analysis included Total Leukocytic Count (TLC), CSF protein and CSF glucose.

Beginning with Total Leukocytic Count (TLC) with median value of 140/mm^3 (range, 20 to 10000). CSF protein in our study had a median of 150 mg/dl (range, 6.30 to 4279), and CSF analysis for glucose had a median of 36 mg/dl (range, 0 to 119) with mean (±) SD is 796.92 (±) 1776.33. According to Gündeşlioğlu et al. *[6]*, Gulsen et al. *[8]*, TLC median was lower by 3 folds (50/mm^3), Glucose median was lower in Gulsen et al. *[8]*, (25 mg/dl) while CSF protein values were relatively the same or slightly higher. Regarding Yakut et al. *[7]*, TLC median was lower by 2 folds (100/mm^3), while CSF protein and glucose were relatively the same as our study. This difference in TLC level may indicate the presence of higher severity if infection in our study and that maybe due to operating repeatedly most of the shunt application cases in the emergency ORs, repeated generalized infections in childhood period that can lower the patients' immunity leading to susceptibility of shunt infection or low socioeconomic level of most patients with inadequate post-operative home care. None of the compared studies included the clarity of CSF sample in their research points which would claim it would have a qualitative rather than a quantitative significance for CSF infection.

CSF culture and sensitivity plays the main role in this study, which management plan and treatment are based on. The percentage of infection with pathogenic growth (may include more than 1 pathogen per sample) was lower than those with no pathogenic growth with (44.9%) verses (55.1%). Regarding our entire studied group, the most common pathogen cultured was Klebsiella in 16 patients (10.9%) which may indicate patient's low immunity with hematogenous spread from another organs, spread from intraperitoneal cavity infection, patients with meningocele, bowel infection and perforation, presence of severe inflammatory process in the brain up to pyogenic loculations, or wound contamination. CoNs were isolated in 13 patients' samples (8.8%) as the second most common pathogen may be due to contamination with bacteria during application of shunt intraoperatively or inoculation by skin flora through wound, followed by MRSA in 11 samples (7.5%), Pseudomonas aeruginosa in 8 samples (5.4%), fungal infections in 6 samples (4.1%), and other pathogens detected in the rest 8 samples as Acinetobacter, E. coli, Enterobacter and other bacteria (Stenotrophomonas, alpha haemolytic streptococci and Gram negative bacilli) (5.44%).4 patients had 2 pathogens isolated from 1 sample (Klebsiella and Acinetobacter, Klebsiella and E. coli, CoNs and E. coli, MRSA and Pseudomonas aeruginosa) with a total of 2.72%. Ebrahim et al. *[5]*, was the only study in favour with our results with 76.7% of the patients with no pathogenic growth, while Gündeşlioğlu et al. *[6]*, Yakut et al. *[7]*, and Gulsen et al. *[8]*, had a higher percentage of studied samples with pathogenic growth 51%, 69.6% and 100% respectively.

Regarding the positive growth culture results in other studies, at least one pathogen was isolated

per culture but none of them was in favour with our study. In Ebrahim et al. [5], most isolated organism was Coagulase positive.Staphylococcus aureus and Coagulase negative Staphylococcus epidermidis with 28.6% each, followed by Klebsiella, E. coli and Pseudomonas aeruginosa with 14.3% each. In Gündeşlioğlu et al. [6], most isolated organism was Coagulase negative Staphylococcus epidermidis (82.6%) followed by Enterococcus (8.6%), E. coli and Pseudomonas aeruginosa with 4.3% each. In Yakut et al. [7], most isolated organism were Coagulase negative staphylococci (42.5%), followed by Pseudomonas aeruginosa (14.9%), Klebsiella and Coagulase positive Staphylococcus aureus with 10.1% each. In Gulsen et al. [8], most isolated organism was Coagulase negative Staphylococcus epidermidis (44%) followed by Klebsiella, Streptococcus pneumoniae and Enterococcus faecalis with 12% each.

According to the sensitivity results, patient start the management plan with the most sensitive and suitable antibiotic to avoid any hypersensitivity and allergic reactions under the observation and recommendation of paediatric infection and clinical pharmacology department. According to our study the most sensitive and used antibiotics for Gram positive organisms (MRSA and Alpha haemolytic streptococci) were Vancomycin, Fluoroquinolone (Levofloxacin and ciprofloxacin) and Amikacin, While for Gram negative organisms (Klebsiella, Pseudomonas, E. coli, Enterobacter, Acinetobacter, Stenotrophomonas and Gram negative bacilli) Carbapenems (Meropenem and Imipenem), followed by Amikacin, Levofloxacin/Ciprofloxacin and Polymyxin B and as For CONs Vancomycin was the most sensitive. In Fungal infections the most sensitive and used treatments were Amphotericin B and Polymyxin B. In favour with our study Gulsen et al. [8], Most used antibiotic for Gram positive organisms was Vancomycin and for Gram negative organisms was Meropenem.

In our study, the management plan was set according to the Device applied, patient's clinical condition, culture and sensitivity based or empirically according to the rest on CSF analysis results. We classified it into 2 plans:

Conservative management plan for patients who had either mild symptoms, no hydrocephalic changes or DCL, with TLC less than 150, received parental medical treatment, either culture based or empirically. Medical treatment is continued for 2 weeks, followed by a new CSF sample analysis with improvement of symptoms and TLC is less than 25. 75 patients were treated according to this plan (51.02%), where 22 patients didn't improve and needed further combined surgical and medical treatment (29.3%). 53 patients improved with no neurological deficit after conservative management with no further need for surgical intervention.

Surgical management by either shunt removal in open head patients, or application of EVD after shunt removal in closed head patients and post tumour excision. This management plan is combined with parental or intraventricular antibiotic administration for patients who had moderate to severe clinical symptoms including high TLC >150, high CSF protein level, DCL, hydrocephalic changes, signs of shunt tract inflammation or meningism. Antibiotics are either empirically or culture based. Medical treatment is continued for 10 to 14 days, and a new sample is drawn for further analysis. After improvement of all clinical conditions and 3 successful CSF samples with no culture growth and CSF TLC is less than 25. EVD is removed and a new VP shunt is applied in a new site. This management plan also includes Patients with failed conservative management. 94 patients were treated according to this plan (63.95%) including 22 patients who underwent conservative management and didn't improve. Ebrahim et al. [5], also classified management plan for infected cases into 2 Plans:

Patients less than 18 months with open head representing 70% of studied cases. For those who has TLC less than 300, with abnormal CSF chemistry with or without CSF culture growth, medical parenteral antibiotics were administrated, either empirically or culture based, for 10 to 14 days then re-evaluation of clinical and CSF sample. If TLC was 300-1000 then VP shunts are removed, and repeated tapping is done, CSF analysis is done every 3 days, if TLC is less than 5, a new shunt is applied. If infection is persistent and no apparent improvement occurred, EVD is applied.

Patients more than 18 months with closed head representing 30% of studied cases. For those who has TLC more than 300, with abnormal CSF chemistry with or without CSF culture growth, medical parenteral antibiotics were administrated, either empirically or culture based, for 10 to 14 days then re-evaluation of clinical and 3 successful CSF sample with TLC less than 5. If TLC was more than 300, shunt removal was considered with EVD application or shunt externalization. Parenteral antibiotics or intraventricular antibiotic administration according to culture and sensitivity then a serial of CSF samples is obtained with improvement of clinical condition, once TLC is less than 5, a new shunt is inserted.

Regarding Yakut et al. [7], also classified the management plan for infected cases into 2 Plans: Administration of parenteral antibiotics only with no shunt removal, which was not effective in most of the cases or showed minimal efficacy in patients with infections discovered in its first stage. This plan was applied in 23.5% of the studied patients.

Removal of infected shunt and application of EVD under the umbrella of appropriate antibiotic

administration until infection clearance. This plan was applied to 76.4% of the studied patients.

Gulsen et al. **[8]**, used only 1 management plan which is removal of infected shunt, application of EVD and giving antibiotic regiment according to culture and sensitivity results.

Regarding the outcome according to the plan of treatment for each culture results in our study, it was found that most of the patients with negative culture results associated with mild clinical condition underwent conservative management (81.3%), while patients with positive culture results had a higher incidence for surgical management combined with medical treatment (70.8%).

Regarding the relation between the management plans and outcome in our study, 94 patients were treated by Surgical intervention combined with antibiotics, 73.4% improved with new applied shunts and discharged, 19.1% improved with neurological deficit, and 7.45% died. The incidence of death and improvement with neurological deficit is statistically significant with *p*-value 0.018 and <0.001 respectively. 75 patients were treated by Conservative medical treatment, 73.4% of them improved with no neurological deficit and 5.3% improved with neurological deficit. The incidence of improvement with no neurological deficit is statistically significant with *p*-value <0.001.

This may reflect those patients with negative culture results but high CSF chemistry results and TLC less than 150, and patients with mild symptoms may have better improvement and can be treated by conservative medical treatment with no surgical intervention as a first line management.

Regarding the 30 patients in Ebrahim et al. **[5]** study, 96.7% of the patients improved and 3.3% died, without studying the prevalence of a certain management plan.

Regarding the mortality rate in relation to culture results and management plans in our study, 7 patients died (4.76%) out of 147 patients where 1 patient had a combined culture with 2 resulted pathogen. MRSA and Klebsiella had total number of 3 deaths and 2 deaths respectively. All mortality cases underwent surgical intervention with antibiotic administration. No deaths were recorded in patients with negative cultures under conservative medical treatment.

Regarding Morbidity rate in relation to culture results and management plans in our study, 18 patients improved with neurological deficits, 18 of them underwent surgical intervention with antibiotic administration and 4 underwent conservative management. 7 patients had negative culture results and high CSF chemistry results, 3 patients had fungal infections, 3 were infected by klebsiella, 2 were infected by CoNs and 3 patients were infected by MRSA, Pseudomonas aeruginosa and Enterobacter respectively.

Conclusion:

CSF diversion devices' infection is one of the serious complications that should be handled carefully to decrease its morbidity and mortality rates and ensure the best quality of life for paediatric patients with the least number of neurosurgical interventions through their life span. Nosocomial gram-negative bacilli should be avoided by preoperative antibiotic intake by one hour, treatment of any serious conditions that can prolong hospital stay with good nutrition in a shunt applied patient. Once acquired, they should be treated rapidly with suitable culture-based antibiotics.

A trial of parenteral antibiotics in low virulence and negative growth cultures with mild clinical presentations should be considered before invasive surgical procedures. In our conducted study upon 147 paediatric patients with previously inserted CSF diversion devices, 68 patients had initial VP shunts applied in Abo El Reesh and 5 EVDs post tumour resection. The median age was 1.5 years. 81 patients had no culture growth, while 66 patients resulted in 70 culture growth with the most common pathogen was klebsiella (10.9%) followed by CoNs (8.8%). 83% of the patients improved, 12.24% improved with neurological deficit, and 4.76% died. Patients who were treated by conservative management had the highest improvement rate.

Recommendations: According to our study results, our recommendations to decrease shunt infection are good preoperative preparation with under full coverage of antibiotics and well-prepared operative theatres. Trial of parental antibiotic treatment should be put into consideration for patients with mild symptoms and low TLC count with close follow-up as they seem to be sufficient. Decreasing hospital stay or ICU admission days as possible to decrease the number of high virulent nosocomial infections and guardians' education regarding the postoperative wound care and generalized regular check up with paediatricians to minimize the any immune deficiency disorder and super imposed infections that may haematologically spread. Also, studying the initial time of shunt application is recommended related with the patients' age. It's also recommended to use Amikacin as a prophylactic antibiotic after shunt operations as it was the most sensitive antibiotic to most pathogens in our study.

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مسببات العدوى الرئيسية فى مختلف جراحات تحويل مسار السائل المخى فى أطفال مستشفى ابو الريش

فى هذا البحث قمنا بدراسة ١٤٧ حالة من حالات الأطفال بمستشفى أبو الريش يتراوح عمرهم من سن يوم الى سن ١٣ عام. جميع هولاء الأطفال لديهم تاريخ مرضى باجراء جراحة لتحويل مسار السائل النخاعى وهم الان يعانون من علامات تشير لوجود عدوى بالسائل النخاعى وذلك فى الفترة مابين ابريل ٢٠١٩ حتى ابريل ٢٠٢٠.

من هولاء المرضى ٦٨ تم تركيب الصمام لهم بمستشفى أبو الريش و٥ منهم تم تركيب درنقة خارجية لهم بعد جراحة استئصال ورم بالمخ وبقية المرضى تم تركيب الصمام لهم بمستشفى أخرى وحضروا الينا لمعالجة علامات التهاب السائل النخاعى.

من هولاء الـ١٤٧ حالة وجدنا ان المزارع البكتيرية سلبية فى ٨١ حالة بينما فى الـ٦٦ حالة الأخرى حصلنا على ٧٠ مزرعة إيجابية وكان اكثر أنواع البكتيريا شيوعاً هو الكليبسيلا.

حدث تحسن للمرضى فى ٨٣٪ من الحالات و١٢,٢٤٪ تحسنوا مع وجود خلل بالجهاز العصبى و٤,٧٦٪ توفوا.

من بين هولاء المرضى وجدنا ان المرضى الذين تم علاجهم تحفظيا هم المرضى أصحاب اعلى معدلات التحسن .