# A Review of Bacterial Meningitis in Paediatric Patients admitted to the Emergency Department of Charlotte Maxeke Johannesburg Academic Hospital.


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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Paediatrics and Child Health.

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# DECLARATION

I, Kim Y Harris declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in the branch of Paediatrics, in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

.....

.....day of ....., 2016

# DEDICATION

To Bradley, Trent, Phillipa, Kay, Nuala, Lesang, Matthew and Emma for your endless patience and vigorous encouragement which I will always remember and cherish.

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For guidance in statistical methods

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# ABSTRACT

The morbidity and mortality of paediatric patients with bacterial meningitis are significantly higher in developing countries than in developed countries. We do not know the outcome of bacterial meningitis in our setting of a developing country where HIV and poor socioeconomic factors may be significant confounding factors.

Purpose of Study

To assess the neurological sequelae and mortality rates of paediatric patients with bacterial meningitis and to evaluate the risk factors for morbidity and mortality within this population.

Method

This is a retrospective observational analysis of medical records of paediatric patients aged 1 month – 14 years, with bacterial meningitis admitted to the Emergency Department at Charlotte Maxeke Johannesburg Academic Hospital over a 3-year period (2011 - 2013).

Results

One hundred and seventy one patients were enrolled with only 48 (28%) patients having confirmed meningitis. Thirty seven (77%) were male, 11 (23%) were female and 30 (62.5%) were under 12 months of age. Thirty three (68.7%) were HIV negative and 7 (14.6%) were HIV positive. No deaths were recorded.

In terms of Herson Todd Score (Appendix 1) where scores were >4.5, only 1 (2%) patient had a GCS <8/15, 18 (37.5%) had duration of illness longer than 3 days at the time of admission and 3 patients had body temperatures recorded below 36.6 degrees Celsius. Two (4.2%) presented in status epilepticus.

Within the meningitis group, neurological sequelae and hearing loss had high scores on the HTS. However, the HTS did not demonstrate a high predictor of morbidity in terms of visual disturbances or empyemas.

Two (5.7%) patients had spastic quadriplegia, 9 (18.75%) had a hemiplegia and 1 (2.08%) had ataxia. Three (6.25%) children had cranial nerve palsies.

Hydrocephalus was found in 2 (4.7%) patients, empyema / abscess in 3 (6.25%) and 3 (6.25%) had visual disturbances; one had diplopia. Hearing loss occurred in 3 (6.25%) children.

The commonest organism cultured on blood and cerebrospinal fluid was Neisseria meningitidis, followed closely by Streptococcus pneumoniae.

Conclusion

There were no deaths recorded in patients diagnosed with meningitis. HIV status was positive in less than 15% of patients. Most patients were under one year of age. The main pathogen for meningitis was N. Meningitidis followed by S. Pneumoniae. A third of patients developed neurological sequelae. HTS showed a high predictor of morbidity in neurological sequelae, and hearing loss but not for visual disturbances nor empyema/ abscess.

The acute complication rate was low compared to developing countries.

## Table of Contents


**DECLARATION** ..... 2

**DEDICATION** ..... 3

**ACKNOWLEDGEMENTS** ..... 4

**ABSTRACT** ..... 6

**ABBREVIATIONS** ..... 9

**1.0 BACKGROUND** ..... 10

**2.0 STUDY OBJECTIVES** ..... 12

**3.0 METHODS** ..... 12

**4.0 RESULTS** ..... 15

**5.0 DISCUSSION** ..... 29

**6.0 LIMITATIONS** ..... 36

**7.0 SUGGESTIONS** ..... 37

**8.0 CONCLUSION** ..... 38

**9.0 REFERENCES** ..... 39

**APPENDIX** ..... 42

# ABBREVIATIONS

| | |
|---|---|
| AVPU scale | Alert, Verbal, Pain, Unresponsive |
| CSF | Cerebrospinal Fluid |
| CMJAH | Charlotte Maxeke Johannesburg Academic Hospital |
| GBS | Group B Streptococcus |
| GCS | Glasgow Coma Scale |
| GTC | Generalised Tonic Clonic Seizures |
| HTS | Herson Todd Scale |
| HiB | Haemophilus influenza Type B |
| HIV | Human Immunodeficiency Virus |
| LP | Lumbar Puncture |
| M&M | Mortality and Morbidity Meetings |
| N. Meningitidis | Neisseria meningitidis |
| PCR | Polymerase Chain Reaction |
| PCV | Pneumococcal Conjugate Vaccine |
| Salmonella Gr D | Samonella Group D |
| S. Pneumoniae | Streptococcal pneumoniae |
| VP shunt | Ventriculoperitoneal shunt |
| WHO | World Health Organization |

# 1.0 BACKGROUND

This study was designed to evaluate the morbidity and mortality of bacterial meningitis in the paediatric population presenting to the Emergency Department of Charlotte Maxeke Johannesburg Academic Hospital. Although many studies are available evaluating bacterial meningitis in South Africa (3) (8) (15), we do not have information regarding morbidity and mortality rates at this specific hospital and furthermore we have little data of the factors driving morbidity and mortality here. We wanted to determine how our setting compares with national and international figures of mortality and morbidity in bacterial meningitis in children.

Bacterial meningitis is a major cause of death and severe disability in children in resource limited settings. WHO estimates there are 170 000 deaths annually worldwide from acute bacterial meningitis (1). Furthermore, studies have found that two thirds of deaths due to meningitis are in children less than 15 years of age in third world countries (2). In South Africa, the approximate incidence of bacterial meningitis in the general population is 4/100 000 with the highest incidence of 40/100 000 occurring in children under one year of age and 7/100 000 in the 1-4 year age group (3). This is an underestimate as these figures exclude culture negative cerebrospinal fluid.

The main pathogens responsible for acute bacterial meningitis in children outside the neonatal period include Haemophilus Influenza Type B (HiB), Streptococcus pneumoniae and Neisseria meningitidis. The mortality rate without treatment is as high as 90% for Pneumococcal and HiB meningitis (4). Since the introduction of Hib and pneumococcal vaccines in South Africa, the incidence of HiB and pneumococcal meningitis has declined. Previous estimates of global incidence of pneumococcal meningitis in children stood at 17/100 000 (5). The highest incidences of HiB meningitis and pneumococcal meningitis occur in Africa with rates of 48/100 000 and 38/100 000 respectively, particularly in areas where spurious or no vaccination programmes exist (5). According to WHO, the introduction

of HiB vaccine has led to N. meningitidis and S. pneumoniae being the most common bacterial pathogens and N. meningitidis will probably surpass the incidence of pneumococcal meningitis with increasing uptake of pneumococcal vaccine in Africa (1).

With regards to concomitant factors in bacterial meningitis, a study in Malawi found that pneumococcal meningitis occurred in two thirds of the group of children who were HIV positive (4). In addition, the authors demonstrated that HIV seropositivity was a strong predictor of mortality (36.9% vs 25.4% in HIV seronegative children ($p<0.001$) (4). The same study showed that severe malnutrition and wasting are more prevalent in HIV positive children but information is limited on prognostication of malnutrition on death and severe outcome in bacterial meningitis (4).

Poor prognostic indicators have been evaluated in various studies. A Malawian study using the Blantyre Coma Scale has shown that a decreased level of consciousness is a strong predictor of death and severe neurological outcome (4).

In a retrospective study in Greece, the occurrence of acute complications i.e. subdural effusions and arthritis was found to occur in 6.8% (152 of 2251 patients, 95% CI 5.8-7.9%) whilst sequelae i.e. severe hearing loss, ventriculitis, hydrocephalus and seizure disorders occurred in 3.3% (73 of 2207 patients, 95%CI 2.6-4.2%) (6).

# 2.0 STUDY OBJECTIVES

1.) To determine the neurological outcome of bacterial meningitis in paediatric age group 1 month to 14 years at discharge from hospital

2.) To describe the bacterial pathogens in meningitis

# 3.0 METHODS

This is a retrospective observational study done at Charlotte Maxeke Johannesburg Academic Hospital with a review of patient records and laboratory database results of all eligible participants in a three-year period from 2011 to 2013.

Screening of the ward admission book in Ward 285 (the ward where all meningitis patients are admitted) was undertaken to identify children within the defined age group who had a confirmed or provisional diagnosis of meningitis. The study population included the paediatric population at Charlotte Maxeke Johannesburg Academic Hospital admitted from the Paediatric Emergency Department between 1 January 2011 and 31 December 2013 to a general paediatric ward (Ward 285). The study sample included children diagnosed as having meningitis with an age distribution of between one month and 14 years at time of hospital admission.

Inclusion criteria

1.) Children aged between 1 month and 14 years, admitted to paediatric ward 285 with:
    a. Confirmed bacterial meningitis on CSF culture, bacterial latex agglutination or PCR positive result, OR
    b. Probable meningitis with CSF white cell count >100 cells/mm3 and CSF protein >1.0 g/L or glucose <2.2mmol/L (9,10) OR

c. Positive blood culture and signs and symptoms of meningitis

Exclusion criteria

1.) Recurrent meningitis due to structural defects in central nervous system, i.e. VP shunts
2.) CSF analysis not meeting the case definition
3.) Tuberculous Meningitis

Data collected included age, gender, HIV status, clinical signs and symptoms at presentation, during admission and on discharge. Blood and CSF culture, serological markers of infection as well as CSF chemistry was obtained from the NHLS database.

Data was entered onto a Microsoft Excel spreadsheet recording age, gender, HIV status, weight and height, clinical parameters on admission i.e. seizures, level of consciousness, status of peripheral circulation, body temperature on admission and duration of symptoms. Clinical and laboratory parameters are based on Herson - Todd Scoring System for Prediction of Morbidity shown in Appendix 1 (13).

A study code was generated and entered into the data collection sheet in order to track correct patient details without using patient identifying details.

Laboratory data included CSF culture/ bacterial latex agglutination, CSF chemistry, white cell count, c reactive protein and blood culture. This was entered onto a Microsoft Excel spreadsheet.

Clinical outcomes were recorded under the following headings: death, seizures, hydrocephalus, subdural empyema or effusions, neurological signs including level of consciousness, motor deficit, hearing loss and visual loss. For the purposes of this study, we have categorised neurological sequelae separate from other outcomes and includes patients who developed ataxia, quadriplegia, hemiplegia, monoplegia or diplegia.

Data was analysed using Stata SE version 13. Codes were generated for categorical variables. Where clinical information was recorded as signs and symptoms not present, these boxes were marked “Nil” and boxes were left empty where information was not recorded. Means and Graphs were also generated and edited using Stata.

Ethics approval was obtained – certificate number M131101.

Permission was obtained from NHLS for use of their laboratory database.

Informed consent from patients was not needed as this is a retrospective study using hospital and laboratory based records.

Permission for the study was approved by the Hospital CEO and the Head of Department of Paediatrics.

# 4.0 RESULTS

## 4.1 Patient Data

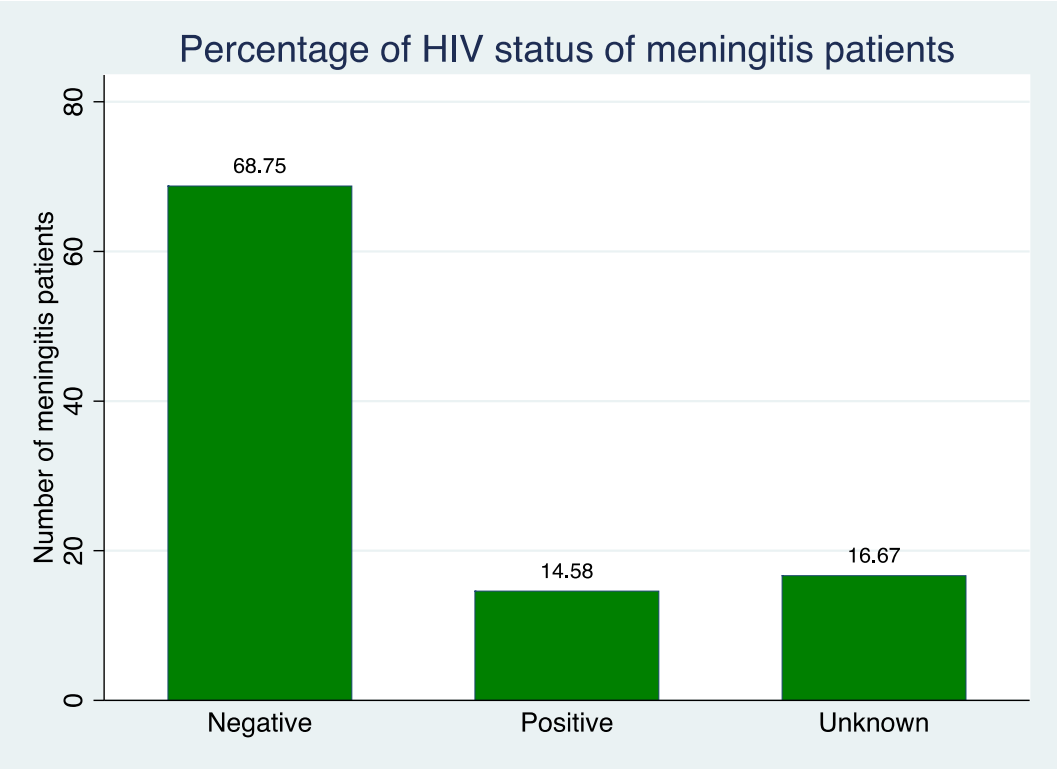
a.) Number enrolled: A total of 226 patients were enrolled into the study. 17 patients had missing notes. 37 patients did not have CSF analysis done due to various reasons i.e. not indicated from clinical picture or too unstable to have lumbar puncture done. One confirmed meningitis was excluded on the basis of age i.e. less than one month old. A total of 171 patients were analysed in the study. Forty eight (28%) patients had confirmed meningitis as per inclusion criteria.

b.) Gender: Seventy four (32.7%) were female and 145 (64.2%) were male with 7 (3.1%) of patients having no gender recorded. Of those with meningitis, 11 (23%) were female and 37 (77%) were male.

c.) Age: In the children diagnosed with meningitis, 30 (62.5%) were under 12 months of age and 18 (37.5%) patients were over 12 months old.

d.) Eighteen (37.5%) had duration of illness longer than 3 days at the time of admission

e.) HIV Status: 59.7% of all patients enrolled were HIV negative and 22.6% were HIV positive. In the meningitis group, 33 (68.7%) were HIV negative and 7 (14.6%) were HIV positive and 8 (16.7%) had an unknown HIV status. No HIV testing was done in the patients with unknown HIV status and this was confirmed on perusal of NHLS database.



4.2 Morbidity and Mortality

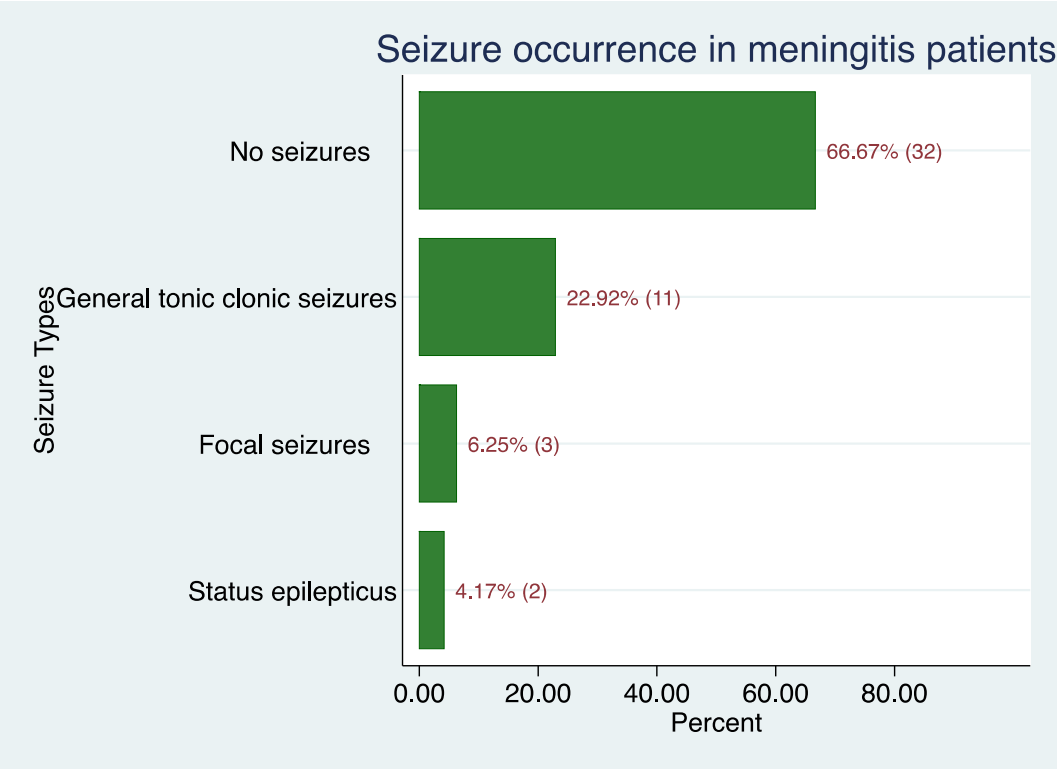
a.) There were no documented deaths in those with confirmed meningitis based on the inclusion criteria.

b.) Glasgow Coma Score (21) on admission: one (2%) patient with meningitis had GCS <8, 2 (4.1%) had a GCS 9-13 and 20 (41.7%) had a normal level of consciousness. Nineteen (39.6%) were described as irritable and 4 (8.3%) as lethargic.

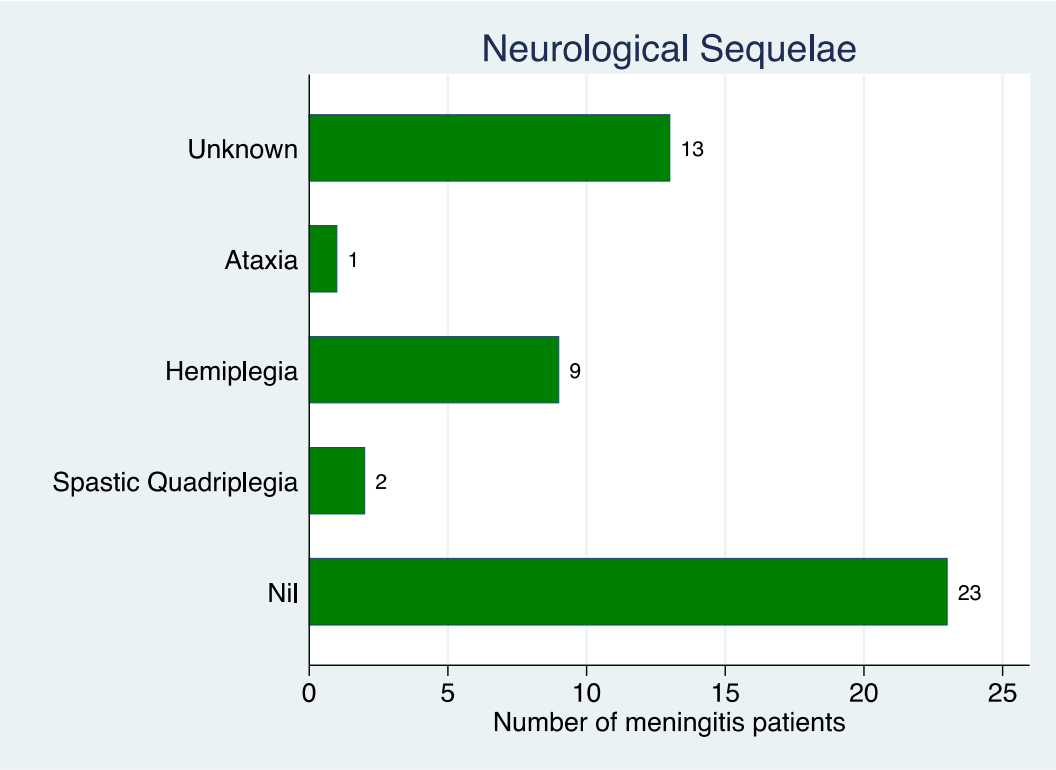
| **Level of Consciousness** | **N** | **%** |
|---|---|---|
| | | |
| **Normal** | 20 | 41.67 |
| **Irritable** | 19 | 39.58 |
| **Lethargic** | 4 | 8.33 |
| **GCS 9-13** | 2 | 4.17 |
| **GCS 4-8** | 1 | 2.08 |
| **Unknown** | 2 | 4.17 |
| | | |
| **Total** | 48 | 100 |

*Table 1: Level of Consciousness of meningitis patients*

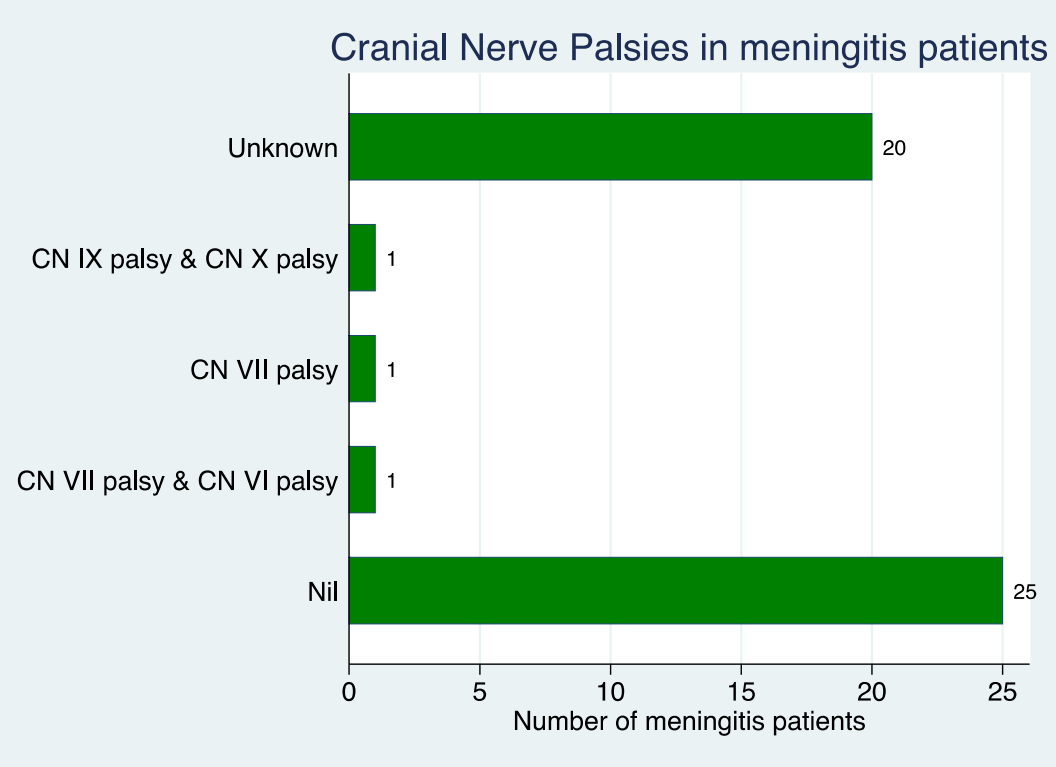
c.) Seizures: thirty two (66.7%) children had no documented seizures. Sixteen (33.3%) of the meningitis patients had seizures. Of these, 11 (22.9%) had generalised tonic clonic seizures, 3 (6.2%) had focal seizures and 2 (4.2%) presented in status epilepticus.



d.) Neurological outcome: two (5.7%) patients had spastic quadriplegia, 9 (18.75%) had a hemiplegia and 1 (2.08%) had ataxia. Twenty three (47.9%) children had a normal neurological outcome and 13 (27%) were unknown.



e.) Three (6.25%) children had cranial nerve palsies and 25 (52%) children had no cranial nerve palsies. In 20 (41.7%) children it was unknown.




f.) Two (4.17%) children had hydrocephalus and 3 (6.25%) children had empyema/abscess.

g.) Three (6.25%) patients had visual disturbances.

| Visual loss | N | % |
|---|---|---|
| | | |
| **Unknown** | 19 | 39.58 |
| **Cortical blindness** | 2 | 4.17 |
| **Diplopia** | 1 | 2.08 |
| **Nil** | 26 | 54.17 |
| | | |
| **Total** | 48 | 100.00 |

*Table 2: Visual disturbances*

The patient with diplopia did not have documented cranial nerve palsy.

The two children with cortical blindness both had other neurological morbidities. One developed hemiplegia and hydrocephalus and the other presented with a decreased level of consciousness and generalised tonic clonic seizures and was noted to have a spastic quadriplegia and hearing loss.

h.) Hearing: three (6.25%) children had hearing loss which was not specified but as it was a complication of the meningitis and not present previously, this hearing loss was presumed to be sensori-neural.

i.) Three patients had body temperatures recorded below 36.6 Degree Celsius which is of importance when calculating the HTS.

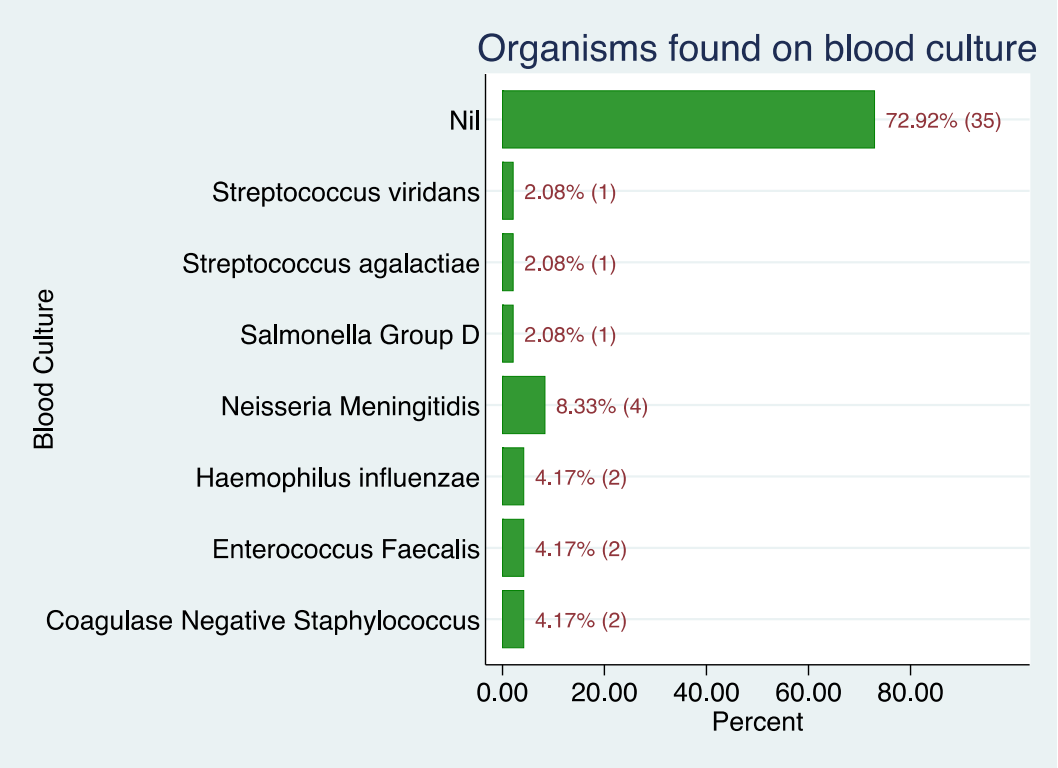
j.) Table of total neurological outcomes

| Seizures | Neurological Sequelae | Cranial nerve palsy | Empyema/ Abscess | Hearing Loss | Visual Loss | Hydrocephalus |
|---|---|---|---|---|---|---|
| 16 (33.3%) | 12 (26.5%) | 3 (6.25%) | 3 (6.25%) | 3 (6.25%) | 3 (6.25%) | 2 (4.17%) |

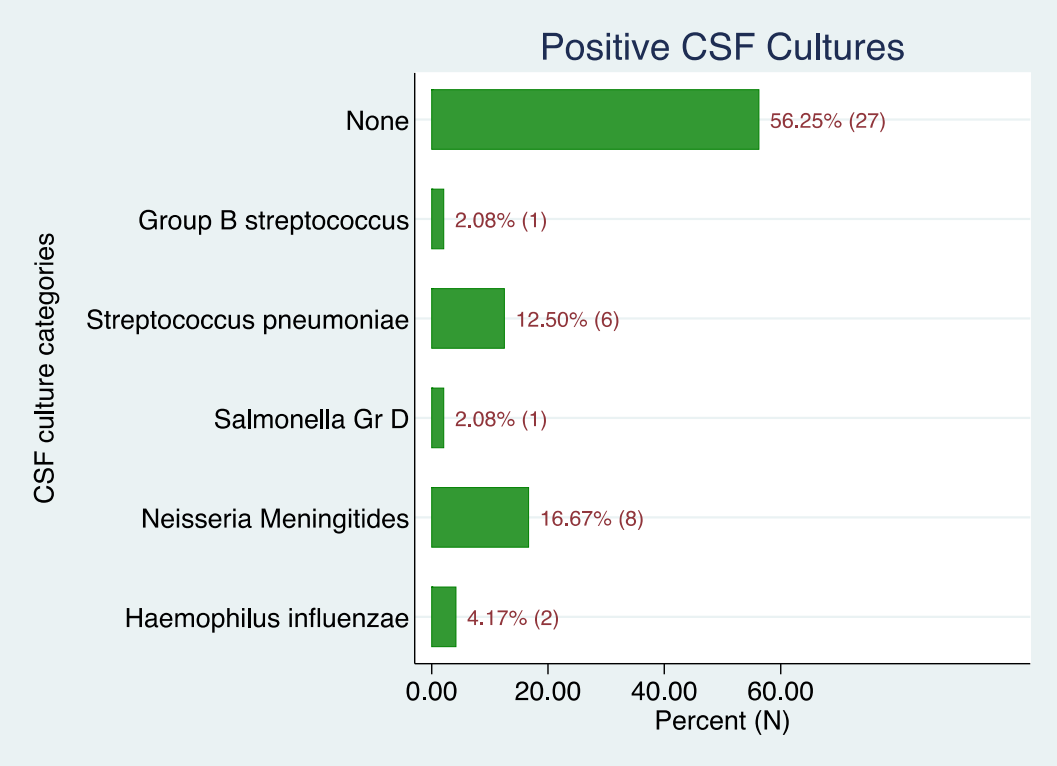
*Table 3*

4.3 Laboratory data

a.) Blood cultures: As shown in the graphs below, the blood cultures were negative in 35 (72.9%) and positive in 13 (27.1%). The positive blood cultures revealed Neisseria Meningitidis 4 (8.3%), Coagulase negative Staphylococcus 2 (4.2%), Enterococcus Faecalis 2 (4.2%), H. Influenzae 2 (4.2%), Salmonella Group D 1 (2%), Streptococcus Agalactiae 1 (2%) and Streptococcus Viridans 1(2%)



b.) CSF culture: twenty seven (56.2%) had no growth on CSF cultures. CSF cultures were positive for Neisseria Meningitidis in 8 (16.7%), Streptococcus pneumoniae in 6 (12.5%), H. Influenzae 2 (4.17%) and Salmonella Gr D in 1 (2%). Three (6.25%) were unknown



c.) Correlation of blood culture with CSF cultures

| CSF culture categories | | | | | | | |
|---|---|---|---|---|---|---|---|
| Blood culture categories | Haemophilus influenzae | Neisseria Meningitides | Salmonella Gr D | Streptococcus pneumoniae | Group B streptococcus | Nil | Total |
| Coagulase Negative Staph | 0 | 0 | 0 | 2 | 0 | 0 | 2 |
| Enterococcus Faecalis | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| Haemophilus Influenza | 2 | 0 | 0 | 0 | 0 | 0 | 2 |
| Neisseria Meningitidis | 0 | 4 | 0 | 0 | 0 | 0 | 4 |
| Salmonella Group D | 0 | 0 | 1 | 0 | 0 | 0 | 1 |
| Streptococcus Viridans | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| Nil | 0 | 4 | 0 | 4 | 0 | 25 | 33 |
| Total | 2 | 8 | 1 | 6 | 0 | 27 | 44 |

*Table 4*

In table 4 above, HiB flagged positive on both blood and csf cultures for 2/2 patients with positive csf cultures. Half of patients with a positive csf culture for N. meningitidis had positive blood cultures for the same. Also of note was that the one patient with positive Salmonella Gr D csf culture also had a positive blood culture for the same organism. However, a positive csf culture for S. pneumoniae on csf in six patients did not yield growth of the same organism on blood.

d.) Morbidity associated with CSF Positive and CSF Negative Cultures:

| | Morbidity associated with Positive CSF cultures | | | | |
|---|---|---|---|---|---|
| Morbidity | H. influenzae (N=2) | N. Meningitidis (N=8) | S. pneumoniae (N=6) | Salmonella Gr D (N=1) | GBS (N=1) |
| Neurological Sequelae | | 3 (37.5%) | 3 (50%) | 1 (100%) | |
| Cranial Nerve Palsies | | 1 (12.5%) | 1 (16.67%) | | |
| Empyema/Abscess | 1 (50%) | | | | |
| Seizures | 1 (50%) | 3 (37.5%) | 3 (50%) | 1 (100%) | |
| Severe Coma | 2 (100%) | 3 (37.5%) | 3 (50%) | 1 (100%) | 1 (100%) |
| Cortical Blindness | | | | 1 (100%) | |
| Hearing Loss | | 2 (25%) | | 1 (100%) | |

*Table 5*

e.) Morbidity associated with HIV positive patients in the meningitis group

| | Neurological Sequelae (N=12) | Cranial Nerve Palsies (N=3) | Empyema/Abscess (N=3) | Seizures (N=16) | Severe Coma (N=24) | Hearing Loss (N=3) | Visual Loss (N=2) |
|---|---|---|---|---|---|---|---|
| HIV Positive (N =7) | 2(16.7%) | 1(33.3%) | 1(25%) | 3(18.7%) | 3(12.5%) | 1(33.3%) | 0(0%) |

*Table 6*

A total of 7 patients were HIV positive in the meningitis group. Table 6 shows that 12 patients who developed neurological sequelae in the meningitis group, 2 (16.7%) were HIV positive and of 3 patients who had cranial nerve palsy 1 (33.3%) was HIV positive. Also, of the 16 patients who developed seizures 3 (18.7%) was HIV positive. For severe coma 3 (12.5%) patients were HIV positive.

f.) Correlation with the Herson Todd Scale:

All three patients in the Meningitis group who developed cranial nerve palsies had a score of 6.5 on the HTS. A score more than or equal to 4.5 predicts a greater risk of morbidity (13). 15 of 28 (53.6%) patients had a HTS >/= 4.5.

**Scoring System for Prediction of Morbidity in H. influenza Meningitis (13)**

| *Factor at Admission* | *Points* |
|---|---|
| Severe coma | 3 |
| Hypothermia (< 36.6 C) | 2 |
| Seizures | 2 |
| Shock (blood pressure < 60 mm Hg systolic) | 1 |
| Age < 12 mo | 1 |
| CSF WBC < 1000/cu mm | 1 |
| Hemoglobin < 11 gm / 100 ml | 1 |
| CSF glucose < 20 mg / 100 ml | 0.5 |
| Symptoms for more than 3 days | 0.5 |

*Appendix 1*

Nine patients with neurological sequelae in the meningitis group had a HTS > 4.5 compared to 3 patients with a score of less than 4.5.

One of 3 patients with abscess/ empyema had a score of 6.5 which was more than the predictor score of 4.5.

Only one of three patients with visual disturbance scored more than 4.5 on HTS and that patients scored 7.

Three patients with meningitis suffered hearing loss and scored >/= 4.5 on HTS.

HTS distribution for patients with meningitis who also had one of the following morbidities: neurological sequelae, hearing / visual loss, abscess/ empyema or cranial nerve palsies showed that 28 patients in total had morbidities. Five of 28 patients had more than one

morbidity with HTS between 6.5-8. First patient had hemiplegia, cranial nerve palsy, hearing loss, seizure and coma. The second, presented with hemiplegia, cranial nerve palsy, empyema, seizure and severe coma. A third patient had hemiplegia, hearing loss, seizure and severe coma. A fourth had hemiplegia, cranial nerve palsy, hydrocephalus, seizures and severe coma. The last patient presented with spastic quadriplegia and seizures as well as severe coma.

The HTS parameters where most patients scored points were severe coma and CSF WCC < 1000 cu mm.

Systolic Blood pressures were not captured in the data as these were not recorded in the notes.

# 5.0 DISCUSSION

No deaths were recorded in the study patients. The reason for this could be that lumbar punctures are not performed in unstable patients who may have demised before an LP could be undertaken. In addition, many of the files for children who died were incomplete or missing and therefore excluded from the study.

Twenty eight percent of all paediatric patients admitted to 285 at CMJAH had a proven diagnosis of meningitis. CMJAH is a tertiary hospital where complicated meningitis cases are referred. The population base for this hospital is large with very few secondary facilities close by and acutely ill children are more likely to be admitted to the closest hospital namely, CMJAH. Also ward 285 is the designated ward for infectious diseases and therefore the proportion of infectious diseases admissions would be a larger portion of the total ward admissions.

There is a male predominance of 37 (77%) vs 11 (23%) females. This is reflected in the study population which was also predominantly male 64% vs 34%. We have not explored the reasons for this gender difference. But one would need to explore the population gender distribution in this referral area and evaluate the factors which may make males more prone to meningitis compared to females. A retrospective study in Karachi conducted over a two year period also demonstrated a male predominance of 134 (69.8%) and female 58 (30.2%). The reasons for this distribution were not explored (17). In contrast McCormick et al found that 53.5% of their study population were male (4). But a systematic review of bacterial meningitis demonstrated increased risk of meningitis in males (18). One would need to conduct further analysis of factors driving this difference in our population.

Only 14.6% were HIV positive, although 16.7% had no HIV serology performed according to NHLS database. A Malawian study found that HIV seropositivity was a strong predictor of mortality 37% HIV positive vs 25% HIV negative children who died of meningitis (4). However, our study did not show any mortality figures for meningitis and therefore we cannot conclude whether or not HIV is a predictor of mortality in our study population.

It was difficult to establish from the notes whether or not patients were on HIV treatment prior to admission and unfortunately we did not collate data on immunological status of HIV positive group. So therefore, the immunological status would need further investigation in a future study.

The majority of children were HIV negative (68.7%) and this demonstrates that HIV negative children in our study are not less likely to contract meningitis. Perhaps there are other factors to account for a higher susceptibility to meningitis in this HIV negative group which we have not explored in our study. Examples of these would be poor socioeconomic background, poor nutritional status, vaccination status, overcrowding and poor sanitation and other comorbidities.

In terms of morbidity, the frequency of HIV seropositivity in severe coma and seizures were 12.5% and 18.7% respectively with neurological sequelae at 16.7%. Our study numbers were too small to evaluate the meaning of these figures and one would need a follow up prospective study to evaluate this further.

Thirty (62.5%) patients were under 12 months of age which concurs with the high incidence of infectious diseases in this age group in developing countries. In addition, 8 of these patients had neurological sequelae and 6 of the 8 had HTS >4.5. This further demonstrates that this age group are at higher risk of morbidity.

With reference to Herson Todd Scores, 37.5% of patients had symptoms beyond 72 hours. According to studies from developing countries, higher percentages of patients who presented with symptoms beyond 72 hours were recorded, i.e. 56% and 63% in Malawi and Angola respectively (14). Our figures appear to be lower. This could potentially be explained by easier access to medical facilities in an urban setting. However, this would need further evaluation as data was not always available or accurately recorded to fully explore symptoms occurrence beyond 72hours.

Twelve of 28 patients had symptoms beyond 72 hours and 7 patients had HTS >/= 4.5. Thereby, concurring with HTS those symptoms beyond 72 hours is a predictor of morbidity.

Three patients had a body temperature recorded below 36.6 degrees Celsius. Therefore only 6% of children presented with hypothermia according to the HTS of poor prognostic criteria. In this group only 2 patients had morbidity and one scored < 4.5 and the other > 4.5 on the HTS. In our study, hypothermia is a parameter of the HTS which did not show a high prediction of morbidity. Possible explanation for these findings may include that our sample size was too small, that clinical data recording of admission temperatures was not adequately recorded or were missing.

One (2%) patient had a recorded GCS (21) <8 which is a poor prognostic indicator on the HTS. A study from Greece showed a higher incidence of coma i.e. 11.7%. (6). One would expect to find higher rates of coma in our setting of a developing nation. However, the difference could be explained by missing or incomplete medical records in our study.

Also, the description of reduced level of consciousness in the medical notes was vast and included the terms encephalopathy, irritability, lethargy or reduced level of consciousness. Given that GCS (21) is a difficult scale to use particularly in very young children, we decided to incorporate the above descriptions of level of consciousness and make it synonymous with GCS<8. The Modified GCS for infants and children (22) (Table 6 in Appendix) is probably more appropriate as it incorporates non-specific terminology such as irritability and crying in assessment of level of consciousness.

Using the Modified GCS, severe coma has been shown to be a predictor of morbidity with 13 of 19 patients having a high score of 4.5 or more. Severe coma is a significant predictor of morbidity and generates the highest score on the HTS of 3. Our study concurs that severe coma is a predictor of morbidity as per HTS.

Sixteen patients (33.3%) had seizures, but in the absence of any deaths in the study this could not be correlated with mortality rates. As CMJAH is a tertiary centre, one would expect to find a high occurrence of seizures in this population as seizures and in particular, status epilepticus may be a reason for tertiary level care.

Eleven patients with seizures had neurological sequelae with 9 of 11 patients scoring >4.5 on the HTS. Our findings are consistent with studies which have demonstrated that early seizures at hospital admission are associated with worse clinical outcomes.

Neurological sequelae: Neurological sequelae occurred in 26.5% which ranks higher than a study from Greece which found neurological outcomes of 3.3%. (6).

In contrast a study in Malawi found 26.2% of children suffered neurological sequelae. This corresponds with our study findings which are consistent with figures in the developing countries.

When evaluating the HTS as a predictor of morbidity in our study, it was found all three patients in the meningitis group who developed cranial nerve palsies had a score of 6.5 on the HTS, indicating the HTS as a predictor of morbidity.

Of note more than 18 patients in the meningitis group, who did not have a documented cranial nerve palsy scored more than or equal to 4.5 on HTS. Cranial nerve palsies correlated better as predictor of poor outcome using HTS than other neurological outcomes.

There were few complications in our patients namely 2 (4.17%) children with hydrocephalus, 3 (6.25%) children with empyema/abscess. Three (6.25%) children had visual disturbances and one had diplopia. It is unlikely that diplopia occurred in the absence of a CN palsy, but this was not documented. In addition, only 3 (6.25%) children suffered hearing loss. The figures relating to visual disturbance or hearing loss may be underestimates as these are findings at discharge and not at follow up after hospital discharge. Furthermore, it is not documented that all children had visual or hearing assessments whilst in hospital which may have led to underdiagnosis particularly in hearing loss as auditory screening at this hospital is generally done at follow up appointments after discharge as opposed to screening during hospital stay. Speech therapy department is responsible for conducting hearing tests by way of automated auditory brainstem response (AABR) and/or otoacoustic emissions screening (OAE).

Blood cultures were negative in 35 (72.9%) of those with meningitis. The commonest organism on blood cultures were Neisseria Meningitidis 4 (8.3%) followed by Coagulase Negative Staphylococcus 2 (4.2%), Enterococcus Faecalis 2 (4.2%) and H. Influenzae 2 (4.2%). Salmonella Group D 1 (2%), Streptococcus Agalactiae 1 (2%) and Streptococcus Viridans 1 (2%) were also cultured. One would have to assess the clinical picture and circumstances around each case to determine how many of these organisms on blood culture were contaminants. Of note, S. pneumoniae was never cultured on blood in the meningitis group. Although N. meningitidis and HiB was cultured in 50% and 100% respectively for on both blood and csf cultures. It is difficult to speculate why this is the case. One would need to explore the factors around blood sampling like whether or not children received antibiotics prior to blood cultures. However, in South Africa deaths from S. pneumoniae have declined overall following the introduction of vaccination (15).

A vast majority, 27 (56.2%) had no growth on CSF cultures. The most common positive CSF cultures was for Neisseria Meningitis in 8 (16.7%), which is in accordance with the trend in developed countries since the introduction of S. pneumoniae vaccination (20). Streptococcus pneumoniae was cultured in CSF of 6 (12.5%) with H. Influenzae 2 (4.17%) which is also expected in terms of trend in developed countries where H. influenza vaccine is the norm (19) (20).

Looking at morbidity associated with CSF cultures, N. meningitidis is cultured more frequently than any other organism. However, Hib, S. pneumoniae, Salmonella Gr D and GBS are associated with higher occurrence of Severe Coma. N. meningitidis also appears to be associated less frequently with other morbidities when compared with other organisms in our study. However, our study numbers were too small to draw meaningful conclusions about the organisms and their impact on morbidity.

N. meningitides was seen in a number of patients without morbidity. Of course one would need to evaluate in a different study what the strains are in Johannesburg region in order to draw conclusions. Suffice to say that N. meningitides has become the most common organism since PCV and Hib vaccinations were included in the vaccination schedule. The trend towards higher morbidity in meningitis due to pneumococcus and HiB is an indication of the necessity of those immunisations.

Furthermore, N. meningitides in our study is responsible for hearing loss as opposed to HiB. This may be the consequence of vaccination programme in our country.

# 6.0 LIMITATIONS

6.1 Hospital Medical Records were used and were found to be lacking certain information like systolic blood pressures and evaluation of clinical symptoms of meningitis.

6.2 In evaluating the level of consciousness of patients, objective parameters were not always used i.e. GCS or AVPU score. Level of consciousness was described as irritable, reduced or lethargic. These descriptions were ultimately taken by researcher to mean GCS <8 in order to evaluate Herson Todd Criteria. GCS< 8 is the parameter accumulating the highest HTS and therefore important in predicting morbidity.

6.3 Formal hearing tests were not undertaken for the majority of patients in hospital. Therefore, it is possible a few patients with hearing loss were not diagnosed at hospital discharge. However, formal auditory testing is generally performed post discharge. This information which was not available in medical records.

6.4 Our study did not record any deaths in the meningitis group. Many deaths recorded were patients who died within 6 hours of admission which may indicate that patients were too unstable to have LP performed. However, the clinical information for these patients was inadequately documented and so the researcher was unable to draw conclusions about the possible cause of death.

6.5 For Laboratory results, CSF bacterial latex and CSF PCR were not requested in many patients nor done on CSF specimen. If performed, it may have generated a larger yield of confirmed meningitis cases.

# 7.0 SUGGESTIONS

7.1 A follow up prospective observational study is suggested in order to address the problem of paucity of medical information recorded and missing data.

7.2 Existing medical data for every patient admission could be recorded in a national database like redcap in order to obtain more clinical information and record parameters in an objective fashion.

7.3 Details of M&M meetings need to be fully recorded in the medical records in order to capture details of patients in a more central and relevant place.

7.4 A prospective study is likely to yield more information and provide insight about mortality rates in meningitis in our setting.

7.5 A prospective study may elucidate factors influencing morbidity and mortality which were not explored in our study. Specific parameters which may make the study more meaningful are socioeconomic status, immunological status of HIV positive children, nutritional status, vaccination status, overcrowding and poor sanitation.

# 8.0 CONCLUSION

Our study reflects a medley of characteristics similar to developed and developing countries. Of note, the low rate of HIV in our population and rate of acute complications correlates with those of developed countries. On the other hand, neurological sequelae appear to be similar to those of developing country. Overall, our figures with regard to incidence of meningitis in under one year of age are on par with international figures and reflect that this is indeed a vulnerable age group for infectious diseases. Furthermore, the N. Meningitis has now become the most common infection in meningitis and this is similar to the international trend in countries where vaccination of S. pneumoniae and H. influenza has become the norm. However, both S. pneumoniae and H. influenza are associated with a higher morbidity than N. meningitidis in our study and one would need further evaluation as to why this is the case. In terms of the HTS, coma and early onset seizures were found to be high predictors of mortality and this is in keeping with international figures.

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# APPENDIX

**Herson Todd Scoring System for Prediction of Morbidity in H. influenzae Meningitis (13)**

| *Factor at Admission* | *Points* |
|---|---|
| Severe coma | 3 |
| Hypothermia (< 36.6 C) | 2 |
| Seizures | 2 |
| Shock (blood pressure < 60 mm Hg systolic) | 1 |
| Age < 12 mo | 1 |
| CSF WBC < 1000/cu mm | 1 |
| Hemoglobin < 11 gm / 100 ml | 1 |
| CSF glucose < 20 mg / 100 ml | 0.5 |
| Symptoms for more than 3 days | 0.5 |

*Appendix 1*

## Glasgow Coma Scale (21)

| | | |
|---|---|---|
| Best eye response (E) | Spontaneous - open with blinking at baseline | 4 |
| | Opens to verbal command, speech, or shout | 3 |
| | Opens to pain, not applied to face | 2 |
| | None | 1 |
| Best verbal response (V) | Oriented | 5 |
| | Confused conversation, but able to answer questions | 4 |
| | Inappropriate responses, words discernible | 3 |
| | Incomprehensible speech | 2 |
| | None | 1 |
| Best motor response (M) | Obeys commands for movement | 6 |
| | Purposeful movement to painful stimulus | 5 |
| | Withdraws from pain | 4 |
| | Abnormal (spastic) flexion, decorticate posture | 3 |
| | Extensor (rigid) response, decerebrate posture | 2 |
| | None | 1 |

*Appendix2*

# Modified Glasgow Coma Scale for Infants and Children (22)

| | Child | Infant | Score |
|---|---|---|---|
| Eye opening | Spontaneous | Spontaneous | 4 |
| | To speech | To speech | 3 |
| | To pain only | To pain only | 2 |
| | No response | No response | 1 |
| Best verbal response | Oriented, appropriate | Coos and babbles | 5 |
| | Confused | Irritable cries | 4 |
| | Inappropriate words | Cries to pain | 3 |
| | Incomprehensible sounds | Moans to pain | 2 |
| | No response | No response | 1 |
| Best motor response | Obeys commands | Moves spontaneously and purposefully | 6 |
| | Localises painful stimulus | Withdraws to touch | 5 |
| | Withdraws in response to pain | Withdraws to response in pain | 4 |
| | Flexion in response to pain | Abnormal flexion posture to pain | 3 |
| | Extension in response to pain | Abnormal extension posture to pain | 2 |
| | No response | No response | 1 |

*Appendix 3*

R14/49 Dr Kim Harris

## HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

## CLEARANCE CERTIFICATE NO. M131101

| | |
|---|---|
| **NAME: (Principal Investigator)** | Dr Kim Harris |
| **DEPARTMENT:** | Paediatrics<br>Charlotte Maxeke Johannesburg Academic Hospital |
| **PROJECT TITLE:** | An Audit of Bacterial Meningitis in Paediatrics Patients Admitted to the Charlotte Maxeke Johannesburg Academic Hospital |
| **DATE CONSIDERED:** | 29/11/2013 |
| **DECISION:** | Approved unconditonally |
| **CONDITIONS:** | |
| **SUPERVISOR:** | Prof Gail Scher |
| **APPROVED BY:** | Professor PE Cleaton-Jones, Chairperson, HREC (Medical) |
| **DATE OF APPROVAL:** | 24/02/2014 |

**This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.**

**DECLARATION OF INVESTIGATORS**

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**

Principal Investigator Signature _____ Date _____

**PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES**