Approach to the diagnosis of Tuberculosis meningitis in children admitted to Port Moresby General Hospital

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07th October 2020

Introduction

- Globally, TB causes more deaths (infectious diseases)
- Top 10 cause of death worldwide
- In 2017, approx. 1.6 million TB deaths
- CNS TB is most severe form of TB
- Approx. 5 to 10 % of all EPTB cases

(WHO, Global TB Report, 2018)

- TB Meningitis most lethal form of CNS TB
- Diagnosis of TBM in low resource setting is very challenging
- In PNG, childhood TB is a huge burden
- Contributes substantially to
  - child mortality
  - malnutrition and
  - impaired neurological and
  - cognitive development
- Early diagnosis and treatment is essential in improving outcome,

(PNG Child Health Policy and Plan, 2015)

Aims/Objectives

1. Assess the current practice of diagnosing TBM in children admitted to PMGH

2. Determine how these current practices of diagnosing TBM can be improved

   (clinical, pathological and radiological investigations)

Research question

- Does the current practice of diagnosing TBM reliable and based on the best available evidence?

Method

Study design and study population

- **Study design:** Prospective observational study
- **Study Site**: Port Moresby General Hospital, Paediatric ward
- **Study duration**: April 2019 to May 2020
- **Study population:**
  - Paediatric patients who have clinical signs and symptoms of TB and
  - suspected of CNS TB or TBM
- **Sample size**. 50 participants

Recruitment criteria

- **Inclusion criteria:** children > 1 month old to 12 years
- **Exclusion criteria:**

    1) neonates and children > 12 years old ,

    2) children with prior underlying cerebral lesions such as stroke or cerebral palsy, or diagnosed with Epilepsy

Variables measured

- Symptoms and signs at onset of illness

- Csf results

- Gene x-pert findings

- CT scan findings

- CXR findings

- Treatment and responses at one month

- Patient outcome and final outcome

Data collection, entry and analysis; and Ethics

- Data collection and entry- prepared questionnaire/ excel spread sheet
- Data analysis was performed using SPSS
  - Median and IQR for numerical variables
  - Frequency and percentages for categorical variable
- Ethical approval was obtained from the SMHS Ethics Committee

Results

Table 1. Demography Characteristics

Total participants	50
Male	26 (52%)
Age in months	Median=45, IQR= (20.75-85.25)
Weight in Kg	Median=15, IQR= (8.75-20.50)
Height in cm	
Weight for length (malnutrition)	25 (50%)

Table 2. Clinical history at onset of illness of TBM

Symptoms	Frequency (%)
Severe headache	23 (46%)
Lethargy/weakness	26 (52%)
Fever	43 (86%)
Confusion	4 (8%)
Unconsciousness	6 (12%)
Seizures	35 (70%)
Coughing	29 (58%)
Falling down	5 (10%)
Others	9 (18%)
Contact with Tb	25 (50%)
Previous TB treatment	5/48 (10%)
Completed previous Rx	2/4 (50%)

Table 3. Signs at onset of illness TBM

Signs	Frequency (%)
Temperature (> 37.2)	26 (52%)
Conscious and alert	25 (50%)
Seizure	36 (72%)
GCS (9-12)	22 (44%)
Neck stiffness	37 (74%)
Focal motor deficit	11 (22%)
Oculomotor palsy	3 (6%)
Facial Palsy	5 (10.5)

Table 3. CSf results and TBM

	Frequency (%)
Lumbar puncture performed	37 (74%)
Lymphocytes (> 80%)	32 (64%)
Neutrophil (>5/ul)	28 (%)
Red cells (>1)	2 (4%)
Glucose – normal (40-80mg/dl)	36/37 (97%)
- abnormally low (<40%)	1/37 (3%)
Protein - Abnormally high (> 45mg/dl)	21 (42%)

Table 4. GeneX-pert and TBM

	Frequency (%)
MTB on Csf	13/39 (33%)
MTB on Gastric Aspirate	9/49 (18%)
MTB on Fine Needle Aspiration	2/49 (4%)
1st line DRTB detected	3/49 (6%)
Gene X-pert on Csf change Management	17/46 (37%)

Table 5. CT scan, CXR and TBM

	Frequency (%)
CT performed	39 (78%)
Contrast	39/39 (100%)
Normal CT	3/39 (8%)
Ring enhancing lesion	13/39 (33%)
Meningeal enhancement	35/39 (90%
Enlarged ventricle	29/39 (74%)
cerebral edema	16/39 (41%)
Infarct/stroke	10/39(26%)
CT change Management	36/40 (90%)
CXR performed	**46 (92%)**
CXR changes	34 (68%)
CXR suggestive of TB	26 (52%)

Table 6. Treatment and responses at one month

	Frequency (%)
First line DS TBM	46 (92%)
2nd line MDR TB	4 (8%)
Response to treatment at one month	
Much improved neurologically	39 (78%)
No significant improvement neurologically	9 (18%)
Deteriorated	3 (6%)
Complication at one month after commencing treatment	
Seizure	3/49 (6%)
hydrocephalus	30/49 (61%)
Spasticity	16/49 (33%)
Limb contracture	2/49 (4%)
Progressive malnutrition	5/49(10%)
GCS (9-12)	22/49 (45%)

Table 7. Patients outcome and final outcome

	Frequency (%)
Normal conscious state	31/49 (63%)
No gain of consciousness	17/49 (35%)
Cerebral palsy	29/49 (59%)
Other severe neurological sequelae	24/49 (49
Survived and discharge	49 (100%)

Discussion

- TB meningitis is real burden in PNG
- Has increase mortality and morbidity
- Very challenging diagnosing TB meningitis, though algorithm being developed but never been tested in PNG
- Our study showed at least 50% or more of the population studied has fever, cough, seizure, confusion, household contact with TB and lethargy/ weakness.

- The study also showed
  - CSF- more lymphocytes, abnormally high protein and normal glucose
  - CT- majority has meningeal enhancement and enlarge ventricle
  - CXR- changes which suggestive of TB in more than 50% of population studied
  - Gene x-pert detected MTB in CSF more compared to other sample collected for testing

- The investigative findings somewhat consistent with what we already know.
- And other studies on diagnosing TBM listed below support our findings

- Most of the patients were on first line treatment and recovering after 1 month of treatment, though they experienced complications- hydrocephalus and spasticity

- Most patients are still in the ward- around 3/5 of these patients are fully conscious and has cerebral palsy.

- (Miltode, G, etal, Plos One, 2015)(Bang,D, BMC infectious Disease, 2016)(WHO, Global TB report, 2018)

- We do acknowledge that there are limitation of the study. The limitations were:
  - Missing data
  - Small sample size
  - Data maybe inaccurate entered

Conclusion

- We are doing well in diagnosing and managing TB meningitis patients in our setting

- The current practice is reliable and has been well documented in some literatures

- Based on these results, we can design a standardized algorithm for PNG in diagnosing TB meningitis

- This will further improve detection, management and prevent comorbidities and deaths relating to TB meningitis

Acknowledgement

I would like to acknowledge the following people

- Prof Trevor Duke-RCH, Melbourne University
- Prof John Vince-Deputy Dean, SMHS
- Dr. Francis Pulsan- Pediatrician and lecturer, SMHS
- Pediatricians in PMGH and colleague registrars
- Dr. M. Clement and radiology team–Radiologist, PMGH
- Ward 1BA and 1CD staff
- Patients and guardians-PMGH