MENINGITIS RAPID DIAGNOSTIC TEST FOR CASE MANAGEMENT IN A FEVER HOSPITAL

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Abstract: Background and aim: Acute bacterial meningitis (ABM) is a severe infectious disease that is endemic in Egypt. Great efforts are spent to provide continuous updates about its epidemiology and outcomes. The current study aimed to evaluate role of rapid reagent tests in the diagnosis of ABM. **Methods:** This was a prospective cross-sectional observational study. The study included 350 cases admitted with suspected meningitis. Lumbar puncture (LP): for collection of cerebrospinal fluid (CSF) samples. CSF examinations (physical, chemical, cytological and microbiological examinations) and rapid reagent test were done. Blood culture was done. MRI was performed before L.P for indicated cases. Detailed analysis of demographic characteristics, clinical symptoms & signs. Interpretation of the results of laboratory investigations. The causative microorganisms and prognosis of all ABM cases were studied. **Results:** Preexisting illnesses presented in 74.5% of patients with ABM. 40% of the patients didn't receive antibiotics before admission. 56.4% of the organisms were classified Streptococcus pneumonia (S. pneumonia), staphylococcus aureus (S.aureus), Staphylococcus epidermis (S. epidermidis), group B streptococcus (GBS),and Enterococci Listeria monocytogenes (L. monocytogenes). 43.6% of bacteria causing ABM were Neisseria meningitides (N. meningitides), Escherichia coli (E coli), Hemophilus influenza type b (Hib). ABM carried a high mortality rate (22.7%). ABM resulted in long term hazards in 21.8%**.** There was a highly significant positive correlation (P<0.001) between the rapid reagent strip test and laboratory leukocytes count, protein, and glucose concentration in cases of ABM.
Conclusion: ABM affects a wide range of patients' age. Rapid reagent test provides quick and reliable diagnostic tool for ABM.

Keywords: Acute bacterial meningitis; pneumonia; etiology; prognosis

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INTRODUCTION

Meningitis is a life-threatening disease with variable causative organisms. Infection routes may be from the ears, nasopharynx, head trauma, congenital central nervous system (CNS) defects, or bloodborne (WHO, 2017). ABM results in grave morbidity and mortality because of severe meningeal inflammation (WHO, 2017). Many causative organisms might cause ABM (Viallon et al., 2011). Viral meningitis is another form of the disease and is called aseptic meningitis. It is a self-limited disease with an indolent course (Martinot et al., 2018). Other causes not related to infections are malignant cells, drugs, and blood following subarachnoid hemorrhage (McGill et al., 2016). The incidence of ABM is 40 per 100,000 in developing countries (Brouwer & van de Beek, 2018). It is one of the endemic diseases in Egypt (Afifi et al., 2007). It leads to long-term severe sequelae such as hydrocephalus, cognitive defects, and hearing loss (van de Beek et al., 2006). Previous studies reported on the grave of the disease (Afifi et al., 2007; Pavan et al., 2021), focusing on the need for updated data about meningitis. This study evaluated using the rapid reagent tests in the diagnosis of ABM and discussed the etiological organisms encountered in ABM in Egypt.

MATERIALS AND METHODS

This was a cross-sectional study conducted in Mansoura fever hospital. It was conducted after approval of the research ethics committee, and informed written consent was obtained from all patients. We recruited patients (350) who presented to Mansoura fever hospital with pictures suspicious of meningitis. Patients were recruited according to the following inclusion and exclusion criteria. **Inclusion criteria:** a) patients presenting with acute fever and an additional symptom; severe headache, stiffness of the neck, mental status changes, vomiting or purpura fulminans, b) infants presenting with acute fever and stiffness of neck, bulging fontanel, lethargy, poor feeding or vomiting. **Exclusion criteria:** a) patients presenting with suspected meningitis following head injury or neurological operations. b) participants refusing to participate in the study.
All patients underwent history taking and clinical examination. The following procedures were performed:
L.P: CSF was obtained from the subarachnoid space using a sterile spinal needle (27 G) inserted between the 4th and 5th

lumbar vertebrae. Two ml of CSF were collected in three sterile tubes. The first tube (a) was for direct Gram stain, bacteriological cultures and antibiotics sensitivity testing. The second tube was for physical (color, aspect), chemical (glucose, protein, lactate concentration), and cytological examination (b). the third tube was used to test the CSF using reagent strips (c)

CSF analysis: Specimen centrifugation was done. The supernatant was aspirated, leaving approximately 0.5ml of fluid in the specimen tube. Examination included physical characters as color and aspect, cytological examination for evidence of leukocytosis, chemical examination of protein, glucose and lactate concentrations microbiological examination using Gram stain smears, and culture on nutrient agar plates, aerobically and anaerobically.

Using rapid reagent strips at L.P. room

Roche -10 reagent strips are strips containing 10-patches for complete urine examination. In the current study these strips were used to evaluate leukocytic count, and the concentration of protein, glucose in patients CSF. At L.P room the attending physician inserted the strip into the tube (c) one second and the test areas must be wet. The test strip was then withdrawn, wiping its edge against the tube's rim removing extra fluid. After 60 seconds, change in color was monitored against the standards.

Blood examinations and blood culture

The cases were monitored for evidence of improvement or deterioration. Follow-up included the following variables: Glasgow coma scale (GCS), convulsions, headache, and nuchal rigidity.

The occurrence of long- term sequelae was noted including a) visual problems, b) hearing deficit, c) neurological weakness, and d) altered mental state.

Ethical approval: This study was conducted after approval of the research ethics committee of faculty of medicine, Zagazig university on 22nd April 2019 with a number of 5369-22-4-2019.

RESULTS

We recruited 350 patients. One hundred and ten patients had confirmed ABM diagnoses. ABM occurred at all age groups. 34.5% of patients had clinical symptoms 1 – 3 days , 47.3% of patients had clinical symptoms 4-7 days and 18.2% had clinical symptoms 8 – 14 days before coming to the hospital. Preexisting illnesses presented in 74.5% of patients with ABM. Pneumonia, sinusitis and otitis media were the most common antecedent infections. 40% of the patients didn't receive antibiotics before admission (Table 1).

The ABM patients presented by fever (90.9%), severe headache (88%), nuchal rigidity (90.9%), irritability (31.8%) Kernig sign (72.7), and Brudziniski sign (69%). Altered consciousness level of any degree (16.3%), seizures (14.5%). In infants, a bulging anterior fontanel (60%), abnormal crying (40%) and poor suckling (75%) were highly significant in ABM (Table 2).

CSF of all patients with ABM was turbid / purulent.

From 110 ABM patients 87 (79.1%) of ABM patients had a CSF leukocyte count in the range of >100 - 1,000 cell/mm^3. 23 cases (20.9%) had a leukocyte count >1,000 cell/mm^3. From 110 ABM patients 90 (80%) had CSF neutrophil percentage >50%. 94 of 110 ABM patients (85.5%) had elevated CSF protein (>80mg/dl). 90 of 110 ABM patients (81.8%) had decreased CSF glucose (< 50mg/dl). 97 of 110 ABM patients (88.2%) had decreased CSF/serum glucose (<0.6).

99 of 110 ABM patients (90%) had elevated CSF lactate (>26mg/dl) (Figure 1).

56.4% of the organisms were classified (S. pneumonia, S. aureus, S. epidermidis, GBS, and L. monocytogenes). 43.6% of bacteria causing ABM were N. meningitides, E coli, Hib.

In children (6 months -6 years), E. coli was first common bacteria causing ABM and GBS was second common bacteria. (Table 3)

S. aureus was the common bacteria causing ABM in age >6 – 18 years old.

S. pneumoniae was the common bacteria causing ABM in age group >18 - >60 years old.

N. meningitidis the second common cause in the same age group (Table 3).

There is highly significant Positive correlation between the reagent strip results and the laboratory results (P<0.001) (Figure 2, 3). 95 of 110 ABM patients had correlated results (sensitivity 86.4%) for CSF leukocytic count, 90 of 110 ABM patients had correlated results (sensitivity 81.8%) for CSF protein concentration. 86 of 110 ABM patients had correlated results (sensitivity 78.2%) for CSF glucose concentration.

ABM had mortality 22.7% (single infant complicated by hydrocephalus, two female patients (40,16 years old) complicated by septicemia, the other cases were above 55 years old). 12 from 25 died patients were admitted to the hospital after 8 days of the appearance clinical symptoms without taking any antibiotics.

Long- term sequelae occurred in 21.8 % of infected patients as hearing deficit, paralysis, impaired cognitive function, and memory problems (Table 4)**.**

DISCUSSION

ABM affected 31.43% of the studied population. The incidence of bacterial meningitis differs between different studies (Abdelkader et al., 2017; Martinot et al., 2018). In developing countries, bacterial meningitis still acts as the primary contributor to meningitis cases, while in developed countries, bacterial meningitis has become less prominent with proper anti-capsular vaccines (Martinot et al., 2018).

As supported by previous results, ABM affects all age groups (Ibrahim et al., 2020; Martinot et al., 2018). Meningitis was evident among infants and children (Okike et al., 2014). This would be influenced by environmental factors and the availability of vaccinations against pathogens causing meningitis, such as the Hib vaccine (Aneja, 2015).

Preexisting predisposing disease presented in 74.5% of the current study ABM patients. Pneumonia, sinusitis and otitis media were the most common antecedent infections. A previous study reported that lung disease preceded pneumococcal meningitis in 40% of patients (Dery & Hasbun, 2007).

In this study ABM was associated with grave morbidity and mortality. In other studies, without any treatment, the mortality rate reached 70%, and one-fifth of the survivors suffered permanent disabilities such as hearing loss, neurologic disability, or limb loss (Okike et al., 2014; Tokimura et al., 2019).

In the current study, 56.4% of the organisms were classified (S. pneumonia, S. aureus, S. epidermidis, GBS, and L. monocytogenes). This agreed with the results of other previous studies (Abdelkader et al., 2017; Afifi et al., 2007). This explores the change in disease epidemiology as N. meningitides was the leading cause of bacterial meningitis (CDC, 2015). Several other studies declared increased prevalence of S. pneumonia world (CDC, 2017; Gudina et al., 2018; Nasiri et al., 2019).

In current study, E. coli and GBS are the most common causes of ABM in children (6 months – 6 years). S. aureus was the most common cause of ABM in age (6 – 18 years). In agreement with Aneja study (Aneja, 2015), the most common etiological agent of ABM in children was found to be S. aureus. In several previous studies, urine reagent strips were used in CSF evaluation. The current study shows that regent strips corelate with the laboratory results as regard WBCs count (95/110 with a sensitivity of 86.4 %), CSF protein concentration (90/110 with a sensitivity of 81.8% %), and CSF glucose concentration (86/110 with sensitivity 78.2%) respectively. A higher rate of agreement between reagent strips and laboratory results was also reported by earlier studies (Kumar et al., 2014; Mazumder et al., 2018).

Strength and limitations: We recruited a large number of patients. The diagnosis was made according to strict diagnostic criteria. We used a rapid reagent test and correlated it with the diagnosis to confirm its role in the rapid diagnosis of cases of ABM.

CONCLUSION

ABM affects a wide range of patients' age. Rapid reagent strip test provides quick and reliable diagnostic tool for ABM. There is a highly significant positive correlation ($P<0.001$) between the rapid reagent strip test of CSF and laboratory CSF leukocytes count, protein concentration, and glucose concentration in cases of ABM.

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Sameh M. Abdel Moneum: Main idea, follow up of the cases, reviewer of draft, final approval.
Aya M.Al Amely: choose the patients, follow up the patients, collects the results, master sheets, draft writing. **Naglaa A. Khalifa:** The laboratory investigations, reviewer of results, final approval. **Ahmed L. Sharaf:** follow up the cases, reviewer of results, reviewer of draft.

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Table 1. Demographic data of 110 ABM patients admitted to MFH

Age N (%)	**6 -12 month**	**5 (4.5%)**
	>1year -6 year	10 (9.1%)
	>6 -18 year	12 (10.9%)
	>18 -40 year	25 (22.7%)
	>40 year-60 year	30 (27.3%)
	> 60 year	28 (25.5%)
Sex N (%)	**Male**	68(61.8%)
	Female	42 (38.2%)
Residence N (%)	**Rural**	77 (70.0%)
	Urban	33 (30.0%)
Recent illness N (%)	**Otitis media**	16 (14.5%)
	Sinusitis	21 (19.1%)
	Pneumonia	37 (33.6%)
	Tonsillitis	8 (7.3%)
	None	28 (25.5%)
Spinal anesthesia N (%)		1 (0.9%)
Travel abroad N (%)		6 (5.5%)
Antibiotic intake N (%)		66 (60.0%)

Table 2. Clinical symptoms and signs of the study patients

Clinical picture	**Frequency**	**Percentage**
Fever	100	90.9%
Severe headache	97	88.2
Vomiting	30	27.3%
Photophobia	18	16.4%
Neck rigidity	100	90.9%
Irritability	35	31.8%
Skin rash	10	9.1%

Altered consciences	18	16.4%
Seizures	16	14.5%
Kernig sign	80	72.7%
Brudzinski sign	76	69.1%
Local nerve signs	8	7.3%
AF bulge (N= 5)	3	60%
Abnormal cry (N= 10)	4	40%
Weak suckling (N= 8)	6	75%
Data is expressed as percentage and frequency. AF (anterior fontanel)		

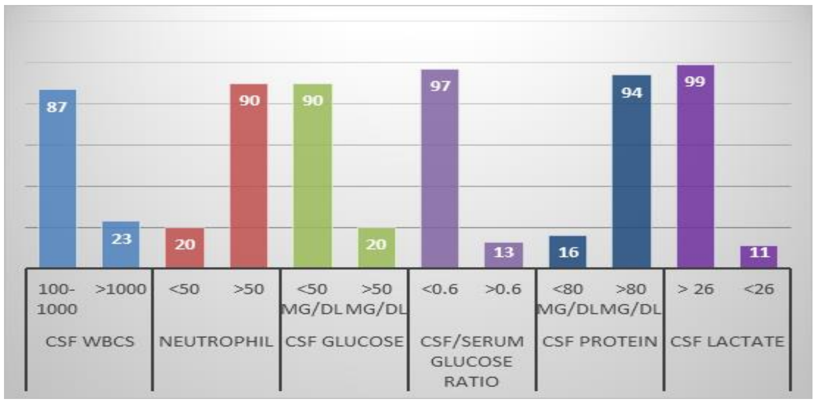
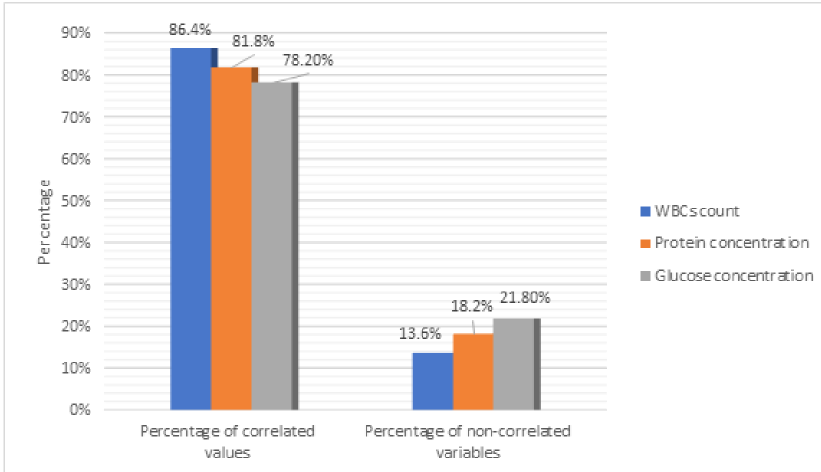


Figure 1. CSF markers that could indicate ABM

Table 3. Frequency of bacteria causing ABM according to age group by cultures

Age group	Causing bacteria	Frequency	Percentage
6-month -1 year	E. coli	3	60.0%
	GBS	2	40.0%
1 - 6 year	E. coli	4	40.0%
	S. aureus	3	30.0%
	GBS	3	30.0%
>6 – 18year	S. aureus	5	41.7%
	S. epidermidis	2	16.7%
	N. meningitidis	3	25.0%
	S. pneumonia	1	8.3%
	E. coli	1	8.3%
>18- 40 year	N. meningitis	4	16.0%
	S. pneumonia	7	28.0%
	S. aureus	2	8.0%
	Hib	8	32.0%
	L. monocytogenes	3	12.0%
	S. epidermidis	1	4.0%
40- 60 year	N. meningitidis	7	23.3%
	S. pneumonia	8	26.7%
	Hib	7	23.3%
	S. aureus	2	6.7%
	S. epidermidis	6	20.0%
>60 year	S. pneumonia	8	28.6%
	S. aureus	7	25.0%
	L. monocytogenes	2	7.1%
	N. meningitidis	6	21.4%
	E. coli	5	17.9%
Data is expressed as percentage and frequency.			



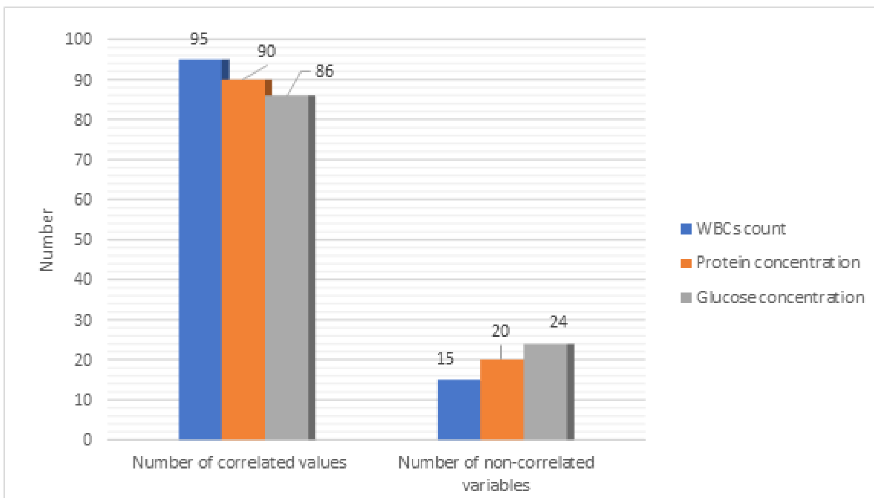


Figure (2,3): Correlation between reagent strip test and laboratory CSF WBCs count, CSF protein and glucose concentrations.

Table 4. Prognosis of the cases of ABM

Outcome	No.	%
Cured	61	55.5
Died	25	22.7
Sequalae	24	21.8
Data is expressed as percentage and frequency.		