A RETROSPECTIVE STUDY ON VARIOUS CLINICO-RADIOLOGICAL AND PATHOLOGICAL DIAGNOSIS FOR TUBERCULOUS MENINGITIS AMONG AFGHANI IMMIGRANTS

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ABSTRACT

Objective: The manifolds of mycobacterium is very enigmatic and can only be ruled out through clinical experience. To understand these variables, an extensive study of clinico-radiology, pathological aspects, and comorbidity is critical. The purpose of the present study is to encompass various clinical, imaging, microbiological, and radiological parameters for rapid differential diagnosis for tuberculous meningitis.

Material and Methods: This retrospective case series study was carried out in Lady Reading Hospital from 2014-2016, and a total of 90 Afghani patients were studied for their clinical presentation, radiological records, and pathology lab results along with underlying co-morbid conditions

Results: Our results showed that, among these 90 patients, Female patients (24, 26.7%) were outnumbered by male patients 66 (73.3%), and Convulsion (3, 3.33%) was least presenting symptom as compared to Fever (78, 86 %.). A majority had complications in their cranial nerves (60, 66.7%), whereas few had in hypoglossal nerves (1, 1.1%). Imaging studies revealed intense hydrocephalus that was more common in males (27, 30%) than female patients (10, 11.11%).

Conclusions: Clinical parameters (Fever, Headache, and Meningeal stiffness), Imaging considerations (Cranial and Abducens nerve palsy, Hydrocephalus, and cerebral infarction) and Pathological factors (↑CSF Glucose and ↓ CSF Protein, elevated WBC count in blood and CSF) are potential diagnostic indicators for tuberculous meningitis infection among these Afghani immigrants.

Key Words: Tuberculous Meningitis, Clinico-radiological, Comorbidity, Afghani immigrants.

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INTRODUCTION

Tuberculous meningitis, a pernicious central nervous system infection that is responsible for the substantial number of mortality and morbidity in Asian and African countries. Among these countries, Pakistan has been ranked as the eighth country with highest incidence cases of tuberculous meningitis [1] . Tuberculous meningitis is a severe infectious manifestation of tuberculosis that is characterized by progressive proliferation of granulomatous inflammation in the basal meninges of the central nervous system [2]. This devastating event gives rise to other serious complications that include cerebral vascular infarction, hydrocephalus, and cranial nerve palsy leading to the death of the affected individual if left untreated. A major obstacle in diagnosing this condition is the unusual representation of disease symptoms that recapitulate typical meningitis, which is either caused by other common infectious agents or cerebrovascular anomaly [3].

Curative therapy and management of this disease are a serious challenge among physicians worldwide [4]. Diagnostic procedures and duration and dosage of anti-tubercular medicines are provocative and still not well established. Most of these TBM cases are hardly diagnosed, giving enough time to tuberculosis to compromise the entire central nervous system. There are three types of focal lesions formed by mycobacterium tuberculosis on the central nervous system, such as intracranial tuberculomas, meningitis, and cerebral abscess [5]. Biochemical analysis of cerebrospinal fluid revealed that elevated lymphocytes and protein concentration and low glucose levels are promising diagnostic markers for diagnosing TBM infection. Moreover, magnetic resonance imaging can promptly identify neuro-physiognomies to prevent cerebral vicissitudes and infra-tentorial lesions, and histopathological and microbiological inspection through tuberculin test, rapid culturing and PCR based detection are also promising diagnostic tools to confirm TBM presence

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and to begin empirical treatment promptly [6,7] . These neurological manifestations of TBM infection are conspicuous in HIV affected individuals and present with extrapulmonary development [8]. So, the fate and course of treatment for TBM accurately rely upon the clinical stage of TBM. Other Co-morbid conditions and cranial neuropathy act as a fuel for disease aggravation [9]. Another risk factor associated with TBM patients is the generation of infectious vasculitis that poses an imminent threat for stroke. Therefore, the present study determined the TBM prevalence in Afghani immigrants residing in Khyber Pakhtunkhwa (KPK) and also identified pathological and clinical and radiological variables for efficient diagnosis and treatment outcome of anti-tubercular therapy.

MATERIAL AND METHODS

The research design of this study is a retrospective case series study, which was carried out in Lady Reading Hospital, Peshawar Pakistan. The study duration of this research was two years (2014-2016), and a total of 90 patients suffering from TBM were recruited based on the availability of their medical and imaging records (CT, MRI) along with chest radiological data and pathological reports. These patients were critically assessed and categorized on ICD (International Statistical Classification of Diseases and Related Health Problems) [10] and Modified British Medical Research Council (BMRC) [11]. Disease severity in TBM sufferers was assessed through Glasgow Coma Grade Scale and the overall examination of these sufferers was based on imaging studies, clinical presentation, medical history, and pathological investigation. The obtained data were scrutinized with a statistical intervention (Pearson correlation coefficient and mean/standard deviation) with the assistance of Statistical Package for the Social Sciences 17 software.

RESULTS

Initially, there were 94 patients recruited for the study, but only 90 patients qualified the inclusion criteria while the rest of the 4 patients were excluded because of their displaced medical and laboratory records. A total of 90 TBM patients were scrutinized, and their average mean age was in between 19-61 years (Mean 49±1) (Table-1). The most common clinical manifestation among these patients was fever (n=79), and convulsions (n=3) were observed to be the least presenting feature (Table-1). Comorbid conditions such as Stroke were seen in 5 patients, and only four were HIV co-infected TBM patients, respectively. Cranial nerve (n=60) and hypoglossal nerve (n=22) were the sites where complications arose among these patients. Most of the patients (n=33) had completed the course of the treatment regimen, but relapse was observed among 13 patients. Pathological analysis of Blood and CSF showed an aberrant level of CSF Glucose concentration, atypical culturing results, and normal Hemoglobin, as summarized in Table-2**.**

The average concentration of hemoglobin and platelets were 262 ± 177x10^9/dL, and the level of RBC was recorded to be approximately 2589 ± 3422/mm^2. Some interesting findings were observed concerning CSF Glucose and Protein Levels. In twenty-seven patients, CSF glucose level was approximately 48 ± 13 mg/dL whereas in 14 patients, the level exceeded up to 67.11 ± 12.43mg/dL, greater than 50mg/dL. Few patients (n=04) had glucose concentration >45mg/dL. Low CSF protein levels observed among most of these patients (n=18) had, whereas few patients (n=05) had a high protein level as compared to the standard value (250 mg/dL). The recorded value of TBM patient's white blood cells in Blood and CSF was 11.6 ± 4.5x10^9/L and 211 ± 197.59, respectively. However, a different set of values was obtained in the case of 22 patients who had WBC level strikingly high (16.7 ± 6.12x10^9/L) than the standard value (10 x 10^9/L). CSF culturing was performed using liquid medium BACTEC 960 MGIT, and it was observed that 21 (23.34%) patients cultured positive for mycobacterium tuberculosis, double confirmed with bacterial Analytical profile index (APIs) whereas contrary for the rest of the (76.66%) patients [Table-2]. Another aspect of this study was imaging studies (CT, MRI, and Chest radiographs). These studies showed intense hydrocephalus and cerebral infraction that was predominant in males (27, 30%) than females (10, 11.11%) [Table-3]. Another fascinating observation was seen that few males patients (3, 3.33%) had basal meningeal enhancement, and that could be attributed to their immunocompromised state [12]. Chest radio-graphical studies showed that 29 patients had pulmonary infiltrated, milary tuberculomas observed in 6 male patients, while the 8 patients had pulmonary cavities. (Table-3) Labor consolidation was absent in males except for 3 female patients. No other abnormalities were observed in the majority of the patients. Modified BMRC assessment showed that a maximum number of TBM patients (55, 61.1%) were categorized in

Clinical Grade I followed by (26, 28.8%) in Grade II and a handful of patients (09, 10.09%) were in Grade III respectively.

Table-1: Patient's demographics and clinical manifestation.

Variants	Mean (%)
Age (Range)	49 (19-61)
Males	66 (73.3)
Female	24 (26.7)
Comorbidity and Symptoms Duration	
Stroke	5 (4.6)
HIV infected	4 (4.6)
Symptoms duration	95 (5-180)
Therapy Outcome	
Full recovery	33 (36.7)
Relapse	13 (13.7)

Variants	Mean (%)
Fever	78 (86.7)
Headache	76 (84.4)
Meningeal stiffness	54 (60)
Visual disturbances	32 (35.56)
Weight loss	29 (32.22)
Confusion	14 (16.09)
Convulsions	3 (3.33)
Nerve Involvement	**Mean (%)**
Cranial	60 (66.7)
Abducens	22 (24.44)
Olfactory	5 (5.56)
Accessory	2 (2.2)
Hypoglosial	1 (1.1)

Table-2: Pathological investigation of blood and cerebrospinal fluid.

Lab findings (n=90)	Mean ± SD	Range
Blood WBCs (x10^9/L)	11.56 ± 4.56	24.14
Platelets (x10^9/L)	261.5 ± 177.06	391.54
Hemoglobin (g/dL)	13.24 ± 1.72	4.88
CSF RBCs (/mm^3)	2588.75 ± 3422.11	15377.00
CSF WBCs (/mm^3)	211 ± 197.59	897.77
CSF Lymphocytes (%)	72.16 ± 29.12	93.50
CSF Glucose (mg/dL)	48.44 ± 13.45	98.85
CSF Protein (mg/dL)	255.17 ± 150.76	989.57
Liquid Culture Results (BACTEC MGIT 960)	**Mean (%)**	
Positive	21 (23.34)	
Negative	69 (76.66%)	
*SD= 33.941 ±104.53		

Table-3: Imaging and radiographic results of tuberculous meningitis patients.

X-ray Findings	Males (N/%)	Females (N/%)
Pulmonary Infiltrate	22 (24.4)	7 (7.78)
Millary Tuberculosis	6 (6.67)	-
Pulmonary Cavities	3 (3.33)	5 (5.56)
Labor Consolidation	-	3 (3.33)
Hilar Nymph Node Enlargement	3 (3.33)	2 (2.22)
No abnormality	23 (25.5)	16 (17.78)

Imaging findings	Males (N/%)	Females (N/%)
Hydrocephalus	27 (30)	10 (11.11)
Cerebral infarction	23 (25.5)	6 (6.67)
Tuberculomas	6 (6.67)	5 (5.56)
Basal enhancement	3 (3.33)	-
No pathology	8 (8.89)	2 (2.22)

DISCUSSION

To improve the diagnosis of tuberculous meningitis, countless attempts are made by utilizing various pathological tests and clinical assessment [13,14]. The comprehensive investigation for TBM diagnosis is comprised of the history of exposure, illness duration, and the presence of focal signs, and total WBC count and CSF WBC and Glucose concentration [7,13]. However, diagnostic specificity and sensitivity somehow anomalous and falls between 50-90%, [15] and that is due to diverse TBM clinical presentation, a pitfall in diagnostic experience, and a high index of suspicion might lead to life threating concerns other than late diagnosis [4,14]. The extra-meningeal disease was predominant as compared to basal enhancement in radiological findings [16] . HIV co-morbidity further exacerbates the TBM condition [12]. Studies conducted in the Asian population show that more than 30% of the total sample had HIV, whereas, in our study, it was 4.6% [17]. Laboratory findings showed aberrant CSF glucose and protein levels, high lymphocyte concentration, and acellular CSF.

A large number of studies showed that CSF lymphocytes preponderance is the strongest predictor of TBM, but only 2 patients had WBC value above 10x10^9/ml [18,19]. Around 60% of TBM sufferers had meningeal stiffness, which is a typical aspect of this condition [5]. Recurrent history of Fever [14] and Headaches [7] are already notable hallmarks of TBM, which was positive for more than 80% TBM affected individuals. The culturing results of CSF were positive for 23.34% of TBM sufferers, which comparatively low as compared to other studies conducted in Pakistan [5,18,20]. However, culture studies are still useful for resistant isolates identification. Imaging studies showed that hydrocephalus and cerebral infarction were more prevalent in males than females, which is more than the data reported in previous studies [16,19]. Many clinical studies conducted in Pakistan reported that about 1-2% of their patients had basal meningeal enhancement [5,18] whereas, in our study, 3.4% of male patients had this condition.

On the other hand, Tuberculomas was found in 6.9% of male patients and 4.5% in female patients. Approximately 46% of Pulmonary TB in a similar study, [20] whereas 33% of our patients had this condition. Hence, it suggests that Chest X-ray is a still promising diagnostic tool for diagnosing respiratory concerns. The limitation of our study was the lack of patients' follow-ups that hindered their assessment for therapy's probable outcome. That is one of the potential causes of TB relapse and poor treatment outcomes. Our study revealed a high prevalence rate of TBM among Afghani immigrants, accentuated TB relapse, and co-morbidities (Stroke and

HIV) that aggravate disease progression. This research may help physicians for empirical and ethical TBM management in Hospitals, and private health care clinics.

CONCLUSION

Tuberculous meningitis is an eviscerating neurological anomaly with extra pulmonary presentation posing an imminent threat to the Pakistani populace, and Afghani immigrants play a vital role due to their poor socioeconomic and health status. This debilitating condition is hard to diagnose due to the scarcity of essential resources and ambiguous diagnostic test sensitivities. Disease recurrence is another financial strain that jeopardizes the patient's survival. Visual disruption, altered mental status, and high CSF RBC are frequent with TBM. Imperative predictors for TBM diagnosis are Throbbing headache, Cranial nerve palsy, and disease duration. To avert socio-economic burden and disease dissemination, rapid and robust anti-tubercular therapy must be put into action to ameliorate patient's quality of life and rule out TBM suspicion.

AUTHORS CONTRIBUTION

Fahad Hassan Shah: Investigation and writing-original draft preparation
Abid Ali Khan: Supervision
Saeed Ahmad: Data curation
Syed Turab Ali Shah: Literature review
Jamshaid Ahmad: Methodology
Sadia: Manuscript preparation and proof reading
Saad Salman: Statistical Analysis and supervision

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